



Comparison of epidemiological and clinical characteristics of COVID-19 patients with and without Wuhan exposure history in Zhejiang Province, China*

Jiang-shan LIAN¹, Huan CAI¹, Shao-rui HAO¹, Xi JIN², Xiao-li ZHANG¹, Lin ZHENG¹,
 Hong-yu JIA¹, Jian-hua HU¹, Shan-yan ZHANG¹, Guo-dong YU¹, Jue-qing GU¹,
 Chan-yuan YE¹, Ci-liang JIN¹, Ying-feng LU¹, Ji-fang SHENG¹, Yi-da YANG^{†‡}

¹State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, National Clinical Research Center for Infectious Diseases, Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, Department of Infectious Diseases, the First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou 310003, China

²Department of Gastroenterology, the First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou 310003, China

[†]E-mail: yidayang65@zju.edu.cn

Received Mar. 11, 2020; Revision accepted Apr. 8, 2020; Crosschecked Apr. 14, 2020; Published online May 9, 2020

Abstract: Background: A novel coronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), first identified in Wuhan, China, has been rapidly spreading around the world. This study investigates the epidemiological and clinical characteristics of coronavirus disease 2019 (COVID-19) patients in Zhejiang Province who did or did not have a history of Wuhan exposure. Methods: We collected data from medical records of confirmed COVID-19 patients in Zhejiang Province from Jan. 17 to Feb. 7, 2020 and analyzed epidemiological, clinical, and treatment data of those with and without recorded recent exposure in Wuhan. Results: Patients in the control group were older than those in the exposure group ((48.19±16.13) years vs. (43.47±13.12) years, $P<0.001$), and more were over 65 years old (15.95% control vs. 5.60% exposure, $P<0.001$). The rate of clustered onset was also significantly higher in the control group than in the exposure group (31.39% vs. 18.66%, $P<0.001$). The symptom of a sore throat in patients in the exposure group was significantly higher than that in the control group (17.30% vs. 10.89%, $P=0.01$); however, headache in the exposure group was significantly lower than that in the control group (6.87% vs. 12.15%, $P=0.015$). More patients in the exposure group had a significantly lower level of lactate dehydrogenase (LDH) and aspartate aminotransferase (AST) than those in the control group. There was no significant difference in any degree of COVID-19 including mild, severe, and critical between the two groups. Conclusions: From the perspective of epidemiological and clinical characteristics, there was no significant difference between COVID-19 patients with and without Wuhan exposure history.

Key words: Coronavirus disease 2019 (COVID-19); Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); Zhejiang Province; Wuhan

<https://doi.org/10.1631/jzus.B2000112>

CLC number: R512.99

[‡] Corresponding author

* Project supported by the National Major Science and Technology Research Projects for the Control and Prevention of Major Infectious Diseases in China (No. 2017ZX10202202) and the National Natural Science Foundation of China (No. 81770574)

ORCID: Yi-da YANG, <https://orcid.org/0000-0001-6261-0953>

© Zhejiang University and Springer-Verlag GmbH Germany, part of Springer Nature 2020

1 Introduction

Recently, a novel coronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was reported from Wuhan, China and has been rapidly spreading around the world. The coronavirus

disease 2019 (COVID-19) is a newly identified infectious disease with the capacity for rapid human-to-human transmission and varied fatality due to acute respiratory distress syndrome (ARDS), multi-organ failure, and other serious complications (Huang et al., 2020; Zhu et al., 2020). By Dec. 8, 2019, several cases in Wuhan, China had been reported with most patients working at or living around the local Huanan Seafood Wholesale Market (Chen et al., 2020). After Dec. 8, the number of patients increased rapidly, although many patients had not been in or near the Huanan Seafood Wholesale Market. During the same period of time, many Wuhan residents began leaving the city to return to their hometowns to join with family to celebrate Spring Festival, the Chinese New Year. As a result of the overlap of emergence of the infection and surge of travel during the national holiday season, the COVID-19 disease began to spread quickly across China (Wu et al., 2020). Recognizing the problem, the Chinese government quickly took extreme measures to contain the spread of the virus, actions that included quarantining the entire city of Wuhan. Despite these efforts, however, the number of patients with COVID-19 rapidly increased. By Feb. 7, 2020, China had 31 161 patients diagnosed as COVID-19, with a large portion (22 112 cases) in Hubei Province with about half of those cases in the city of Wuhan (11 618 cases).

The epidemic situation in Zhejiang Province was relatively serious because many people from Wuhan returned to family homes within Zhejiang Province. The first case of COVID-19 in Zhejiang Province was diagnosed on Jan. 17, with the number of infections rapidly increasing after that date. Initially, these diagnosed patients were identified as having come from Wuhan. However, by Jan. 21, the first case of COVID-19 without Wuhan exposure was confirmed. Since then, the number of patients without Wuhan exposure gradually increased. At this time, very little was known about possible changes of epidemiological and clinical characteristics of the virus during human-to-human transmission.

SARS-CoV-2, influenza A, and other influenza viruses are single-stranded RNA viruses with a capsule envelope. These viruses cause upper respiratory tract infections and pneumonia in humans and are rapidly transmitted from person to person. For example, another influenza, pandemic type A (H1N1),

arose in early 2009 (probably in Mexico and the United States) and then reappeared in North America in September over a 7-month period. H1N1 kept mutating during human-to-human transmission, causing continuous severe disease and mortality (Deng et al., 2012; Vazquez-Perez et al., 2013). Researchers found that adaptive mutations in H1N1 influenza virus in humans during the 2009 pandemic enhanced the virulence of the virus when studied in mice (Xu et al., 2011; Otte et al., 2015). However, researchers currently do not know if the virulence and pathogenicity of the SARS-CoV-2 virus increases or decreases during human-to-human transmission.

In this study, we analyze information on differences in epidemiological and clinical characteristics of COVID-19 patients, including those with and without a history of exposure to the virus in Wuhan. In addition to striving to better understand these characteristics, our goal was to investigate whether or not the virulence and pathogenicity of the SARS-CoV-2 virus was enhanced or decreased during human-to-human transmission.

2 Methods

2.1 Data sources and ethics

We began a retrospective study focusing on the epidemiological and clinical characteristics of confirmed cases of COVID-19 from Jan. 17 to Feb. 7, 2020. All cases enrolled were quantitative real-time polymerase chain reaction (qRT-PCR)-positive for SARS-CoV-2 and were retested several times during their hospital stays. The data were collected uniformly by the Health Commission of Zhejiang Province (China), where all patients were assigned to specific hospitals for unified treatment according to Zhejiang Province's emergency rule. The diagnosis of COVID-19 infection was based on World Health Organization (WHO) interim guidance and all data were shared with WHO (WHO, 2020), with the primary analytic results reported to the authority of Zhejiang Province, China. Since the collection and analysis of all cases were determined by the Health Commission of Zhejiang Province under national authorization and considered as part of the continuing public health outbreak investigation, our study was exempt from institutional review board approval.

For further analysis, patients were divided into two groups indicating whether a patient had or did not have Wuhan exposure within one month. Patients with a history of Wuhan exposure were assigned to the “exposure group,” and patients without Wuhan exposure history were assigned to the “control group.” The subtype definition of COVID-19 patients was based on the diagnosis and treatment scheme for COVID-19 in China based on minor modification of WHO standards (Wu and McGoogan, 2020). The degree of COVID-19 was categorized as mild, severe, or critical: mild type included non-pneumonia and mild pneumonia cases; severe type was characterized by dyspnea, respiratory frequency of ≥ 30 min, blood oxygen saturation of $\leq 93\%$, $\text{PaO}_2/\text{FiO}_2$ ratio of < 300 , and/or lung infiltrates of $> 50\%$ within 24–48 h; critical cases were those that exhibited respiratory failure, septic shock, and/or multiple organ dysfunction/failure.

2.2 Procedures

We obtained epidemiological, demographic, clinical, laboratory, management, and outcome data from patients’ medical records. Data were retrieved and reviewed by two independent observers. Clinical outcomes were followed up to Feb. 12, 2020. Missing or vague dates were confirmed by direct communication with health care providers. Throat-swab specimens from upper respiratory tract and sputum from all patients were collected on admission and transported in a sputum cup with a tightly closed lid. Nasopharyngeal swab samples were transported in preservation tubes containing the virus preservation solution. Laboratory confirmation of COVID-19 was done in the First Affiliated Hospital, School of Medicine, Zhejiang University (Hangzhou, China) and other hospitals were under the authorization of the Center for Disease Control and Prevention (CDC) at the Zhejiang Province, by previously reported qRT-PCR methods. All patients were given chest X-rays or chest computed tomography (CT) scan at admission. Patients with other common respiratory viruses, including influenza A and B viruses, respiratory syncytial virus, parainfluenza virus, and adenovirus, were excluded from this study.

2.3 Outcomes

In this study, we collected and calculated epidemiological data including Wuhan exposure, by

contacting confirmed patients and people in family clusters. We calculated the incubation period as being from the specific date of a person having contact with a confirmed COVID-19 patient to the date of illness onset. Other information collected included other anthropometrics, demographics, symptoms and signs of the patient at the time of admission to hospital. Additional data collected included results from laboratory tests and chest X-ray/CT scans, comorbidity, co-infection with other respiratory pathogen treatments (including drugs, intensive care, and mechanical ventilation), and other clinical outcomes.

2.4 Statistical analysis

For continuous variables, mean \pm standard deviation (SD) and median (interquartile range, IQR) were used for normally and abnormally distributed data, respectively, followed by un-paired *t* test and non-parametric test when applicable. Categorical variables were expressed as number (percentage) and compared by χ^2 test. A two-sided α of less than 0.05 was considered statistically significant and SPSS (IBM SPSS Statistics 26.0) was used for all analyses.

3 Results

3.1 Demographic and epidemiologic characteristics

In this study, a total of 788 patients with confirmed COVID-19 were enrolled from Jan. 17, 2020 to Feb. 7, 2020 in Zhejiang Province. Clinical outcomes were followed-up through Feb. 12, 2020. As shown in Table 1, there were 393 patients with, and 395 without a history of Wuhan exposure, with corresponding ages of (43.47 ± 13.12) years and (48.19 ± 16.13) years ($P < 0.001$). Patients in the control group were on average older than those in the exposure group. The number of patients aged 15–49 years in the exposure group is significantly higher than that in the control group (68.19% vs. 52.41%, $P < 0.001$). However, the number of patients aged over 65 years in the control group is significantly higher than that in the exposure group (15.95% vs. 5.60%, $P < 0.001$). There were no significant differences in the percentage of current smokers nor in percentage of women patients between the two groups. In addition, there were no significant differences in the presence of any coexisting medical conditions between the two groups,

Table 1 Demographic and epidemiologic characteristics of 788 COVID-19-infected patients with and without Wuhan exposure history

Characteristics	Exposure group (n=393)	Control group (n=395)	P value
Age (year)	43.47±13.12	48.19±16.13	<0.001
Age group			
0–14 years	7 (1.78%)	9 (2.28%)	0.802
15–49 years	268 (68.19%)	207 (52.41%)	<0.001
50–64 years	96 (24.42%)	116 (29.36%)	0.127
≥65 years	22 (5.60%)	63 (15.95%)	<0.001
Male sex	216 (54.96%)	191 (48.35%)	0.064
Current smoker	29 (7.34%)	25 (6.33%)	0.576
Coexisting condition			
Any	108 (27.48%)	110 (27.85%)	0.937
Hypertension	66 (16.79%)	60 (15.19%)	0.561
Diabetes	23 (5.85%)	34 (8.61%)	0.169
Chronic liver disease	14 (3.56%)	17 (4.30%)	0.715
Cancer	3 (0.76%)	3 (0.76%)	1.000
Chronic renal disease	4 (0.51%)	3 (0.76%)	0.725
Heart disease	3 (0.76%)	8 (2.03%)	0.223
COPD	1 (0.25%)	2 (0.51%)	1.000
Asthma	5 (1.27%)	1 (0.25%)	0.123
Immunosuppression	0 (0.00%)	1 (0.25%)	1.000
Family cluster	71 (18.66%)	124 (31.39%)	<0.001
Onset of symptom to			
Outpatient clinic (d)	2 (1.0–3.5)	2 (1.0–5.0)	0.019
PCR confirmation (d)	4 (2.0–6.5)	5 (3.0–7.0)	0.009
Admission (d)	3 (1.0–5.0)	4 (2.0–7.0)	<0.001
Severity on admission			
Mild	354 (90.08%)	356 (90.13%)	1.000
Severe	31 (7.89%)	30 (7.59%)	0.895
Critical	8 (2.04%)	9 (2.28%)	1.000

Patients with Wuhan exposure history as “exposure group,” and patients without Wuhan exposure history as “control group.” Data are presented as mean±standard deviation (SD), number (percentage), or median (interquartile range, IQR). COPD: chronic obstructive pulmonary disease; PCR: polymerase chain reaction

including rates of hypertension, diabetes, chronic liver disease, heart diseases, cancer, asthma, immunosuppression, chronic renal disease, and chronic obstructive pulmonary disease (COPD).

The control group had a higher proportion of patients that had higher clustered onset than the exposure group (31.39% vs. 18.66%, $P<0.001$). Since early patients were not screened in Wuhan, it is difficult to determine the specific date of contact with a confirmed COVID-19 patient; therefore, the incubation period could not be calculated for these patients. A total of 188 patients in the control group had a specific date of contact with confirmed COVID-19 patients and their calculated incubation period was 5 d

(IQR: 3–9 d; range: 1–16 d). As shown in Fig. 1, from the first case of COVID-19 diagnosed in Zhejiang Province on Jan. 17, the number of patients with exposure history of Wuhan gradually increased. By Jan. 21, the first case of COVID-19 without Wuhan exposure was confirmed and the number reached a peak by Jan. 28. After that date, the number of patients without Wuhan exposure history exceeded that of patients with Wuhan exposure history. After the strong epidemic prevention and control measures initiated by the Zhejiang government by Jan. 28, the epidemic began coming under control as evidenced by the concurrently decreasing number of cases. There was no COVID-19 patient with Wuhan exposure

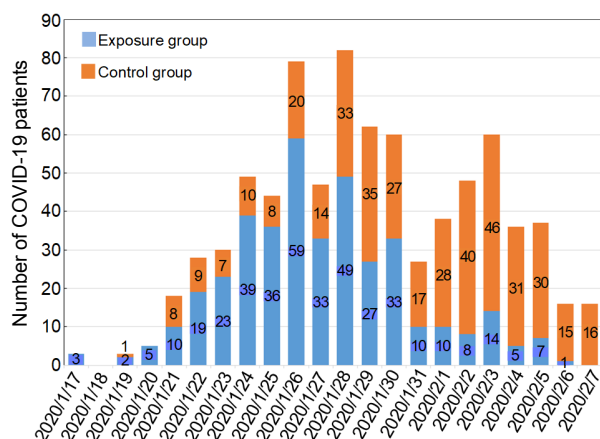


Fig. 1 Onset of illness among 788 cases of COVID-19 in Zhejiang Province, China

Patients with Wuhan exposure history as “exposure group,” and patients without Wuhan exposure history as “control group”

history after Feb. 7. Our results showed that most patients’ incubation time of COVID-19 was within two weeks.

Because the COVID-19 outbreak began in Wuhan, the epidemiological history of patients was more complete in the exposure group than in the control group. In the exposure group, the time from onset of symptom to outpatient visit, qRT-PCR positive for SARS-CoV-2, and admission was shorter than that in the control group ($P<0.05$), with no significant differences in the degree of COVID-19 symptoms recorded (mild, severe, or critical).

3.2 Clinical features and laboratory abnormalities

Table 2 shows the clinical characteristics of the patients. Fever (80.71%) and cough (64.21%) were the most common symptoms, followed by sputum production (33.63%), fatigue (17.64%), muscle ache (11.55%), gastrointestinal symptoms (11.17%), nasal obstruction (5.96%), shortness of breath (4.70%), and hemoptysis (1.90%). There were no significant differences among those symptoms between patients in the exposure and control groups. However and importantly, the presence of a sore throat in the exposure group was significantly higher than that in the control group (17.30% vs. 10.89%, $P=0.01$). The percentage of the symptom of headaches in the exposure group was significantly lower than that in the control group (6.87% vs. 12.15%, $P=0.015$).

On admission, patients in the exposure group had significantly lower levels of lactate dehydrogen-

ase (LDH; exposure group vs. control group, 204 U/L vs. 222 U/L; $P=0.001$) and aspartate aminotransferase (AST; exposure group vs. control group, 24 U/L vs. 27 U/L; $P=0.001$). There were no significant differences in the leucocytes, neutrophils, lymphocytes, platelets, hemoglobin, hematocrit, international normalized ratio, albumin, aminotransferase, bilirubin, serum sodium, serum potassium, blood urea nitrogen, serum creatinine, creatine kinase, C-reactive protein, or procalcitonin between the two groups. CT scan data are critical for disease identification and diagnosis and for all patients in the study there were no significant differences between the two groups of those with normal, unilateral pneumonia, bilateral pneumonia, or multiple mottling and ground-glass opacity.

3.3 Treatment and outcomes

All patients were isolated in designated hospitals and had supportive, needed, and currently recommended medication. Most patients (84.77%) received some forms of antiviral treatment including interferon- α sprays, arbidol hydrochloride capsules (100 mg po tid), and lopinavir and ritonavir tablets (500 mg po bid) (Table 3). More patients in the exposure group received interferon- α and lopinavir/ritonavir combined therapy than those in the control group (24.43% vs. 17.47%, $P=0.001$). More patients in the control group than in the exposure group received a combined therapy of interferon- α , lopinavir/ritonavir, and arbidol (35.70% vs. 23.92%, $P<0.001$). Patients in the exposure group received earlier antiviral treatment than those in the control group. The time from onset of illness to antiviral therapy was shorter in the exposure group than in the control group (3 d vs. 4 d, $P<0.001$). There were no significant differences in the number of patients receiving glucocorticoid therapy between the two groups.

In this study, 1.53% patients in the exposure group received mechanical ventilation while 3.04% patients in the control group were ventilated ($P=0.232$). The ventilator adopted pressure-controlled synchronized intermittent mandatory ventilation (P-SIMV) mode, with the inhaled oxygen concentration of 35%–100% and the positive end-expiratory pressure of 6–12 cmH₂O (1 cmH₂O=98.06 Pa). However, significantly fewer patients in the exposure group were admitted into intensive care unit (ICU) than

Table 2 Radiographic and laboratory findings of 788 COVID-19-infected patients with and without Wuhan exposure history

Characteristics	Exposure group (n=393)	Control group (n=395)	P value
Fever	320 (81.42%)	316 (80.00%)	0.652
Cough	261 (66.41%)	245 (62.03%)	0.207
Sputum production	134 (34.10%)	131 (33.16%)	0.821
Hemoptysis	6 (1.53%)	9 (2.28%)	0.604
Sore throat	68 (17.30%)	43 (10.89%)	0.010
Nasal obstruction	27 (6.87%)	20 (5.06%)	0.297
Muscle ache	42 (10.69%)	49 (12.41%)	0.504
Fatigue	67 (17.05%)	72 (18.23%)	0.709
Shortness of breath	17 (4.33%)	20 (5.06%)	0.737
GI symptoms	36 (9.16%)	52 (13.16%)	0.089
Headache	27 (6.87%)	48 (12.15%)	0.015
Blood routine			
Leucocyte ($\times 10^9 L^{-1}$; normal range: 4–10)	4.8 (3.8–6.0)	4.8 (3.8–6.0)	0.945
> $10 \times 10^9 L^{-1}$	11 (2.80%)	7 (1.77%)	0.353
< $4 \times 10^9 L^{-1}$	113 (28.75%)	121 (30.63%)	0.586
Neutrophil ($\times 10^9 L^{-1}$; normal range: 2–7)	2.96 (2.19–4.10)	2.95 (2.32–3.90)	0.517
Lymphocyte ($\times 10^9 L^{-1}$; normal range: 0.8–4.0)	1.2 (0.9–1.6)	1.2 (0.9–1.5)	0.676
< $0.8 \times 10^9 L^{-1}$	67 (17.05%)	67 (16.96%)	1.000
$\geq 0.8 \times 10^9 L^{-1}$	326 (82.95%)	328 (83.04%)	1.000
Platelet ($\times 10^9 L^{-1}$; normal range: 83–303)	183 (147–224)	178 (148–217)	0.487
< $100 \times 10^9 L^{-1}$	12 (3.05%)	15 (3.80%)	0.696
$\geq 100 \times 10^9 L^{-1}$	381 (96.95%)	380 (96.20%)	0.696
Hemoglobin (g/L; normal range: male 131–172, female 113–151)	139 (127–151)	137 (127–150)	0.579
Hematokrit (%; normal range: male 38.0–50.8, female 33.5–45.0)	40.6 (37.6–44.3)	40.2 (37.8–43.7)	0.651
Coagulation function			
International normalized ratio (normal range: 0.85–1.15)	1.01 (0.97–1.08)	1.03 (0.97–1.10)	0.180
Blood biochemistry			
Albumin (g/L; normal range: 40–55)	41.42 (38.60–43.80)	41.40 (38.14–43.80)	0.582
Alanine aminotransferase (U/L; normal range: 9–50)	21.0 (15.0–32.0)	22.0 (15.0–35.0)	0.080
Aspartate aminotransferase (U/L; normal range: 15–40)	24.0 (19.0–31.2)	27.0 (20.0–35.0)	0.001
Total bilirubin ($\mu\text{mol/L}$; normal range: 0–26)	9.75 (7.18–12.92)	9.40 (7.00–13.85)	0.789
Serum sodium (mmol/L; normal range: 137–147)	138.5 (136.7–140.1)	138.3 (136.0–140.1)	0.379
Serum potassium (mmol/L; normal range: 3.5–5.3)	3.82 (3.59–4.08)	3.87 (3.60–4.20)	0.222
Blood urea nitrogen (mmol/L; normal range: 3.1–8.0)	3.80 (3.05–4.59)	3.74 (3.00–4.70)	0.968
Serum creatinine ($\mu\text{mol/L}$; normal range: male 57–97, female 41–73)	66.0 (55.0–78.0)	66.0 (56.0–77.0)	0.937
Creatine kinase (U/L; normal range: 50–310)	68.0 (55.0–78.0)	69.0 (46.6–112.5)	0.860
Lactate dehydrogenase (U/L; normal range: 120–250)	204.0 (165.0–254.0)	222.0 (173.0–296.0)	0.001
Infection-related biomarker			
C-reactive protein (mg/L; normal range: 0–8)	7.8 (2.4–21.5)	8.2 (3.5–23.5)	0.325
Procalcitonin (ng/mL; normal range: 0.0–0.5)	0.05 (0.03–0.07)	0.05 (0.02–0.08)	0.132
Chest X-ray/CT finding			
Normal	47 (11.96%)	40 (10.13%)	0.428
Unilateral pneumonia	85 (21.63%)	79 (20.00%)	0.599
Bilateral pneumonia	141 (35.88%)	155 (39.24%)	0.340
Multiple mottling and ground-glass opacity	120 (30.53%)	115 (29.11%)	0.697

Data are presented as number (percentage) or median (interquartile range, IQR). GI: gastrointestinal; CT: computed tomography

Table 3 Complications, treatments, and outcomes in patients with and without Wuhan exposure history

Variable	Exposure group (n=393)	Control group (n=395)	P value
Complication			
Acute respiratory distress syndrome	31 (7.89%)	27 (6.84%)	0.588
Septic shock	1 (0.25%)	1 (0.25%)	1.000
Liver function abnormality	39 (9.92%)	43 (10.89%)	0.727
Acute kidney injury	6 (1.53%)	7 (1.77%)	1.000
Treatment			
Anti-coronavirus treatment	326 (82.95%)	342 (86.58%)	0.166
Timing from onset of illness to antiviral therapy (d)	3 (1–5)	4 (1–7)	<0.001
Antivirus regimen			
Interferon- α +lopinavir/ritonavir+arbidol	94 (23.92%)	141 (35.70%)	<0.001
Interferon- α +lopinavir/ritonavir	96 (24.43%)	69 (17.47%)	0.007
Lopinavir/ritonavir+arbidol	38 (9.67%)	35 (8.86%)	0.620
Lopinavir/ritonavir	35 (8.91%)	33 (8.35%)	0.702
Other	63 (16.03%)	64 (16.20%)	0.844
Mechanical ventilation			
Non-invasive	5 (1.27%)	2 (0.51%)	0.286
Invasive	1 (0.25%)	10 (2.53%)	0.011
CRRT	0 (0.00%)	0 (0.00%)	
ECMO	0 (0.00%)	0 (0.00%)	
Glucocorticoids	56 (14.25%)	44 (11.14%)	0.200
Maximum dosage (mg)*	40 (40–80)	40 (40–80)	0.953
IVIG	35 (8.91%)	27 (6.84%)	0.293
Admission to intensive care unit	5 (1.27%)	17 (4.30%)	0.015
Discharged from hospital	210 (53.44%)	112 (28.35%)	<0.001

* Glucocorticoid dosages were converted into an equivalent of methylprednisolone. Data are presented as number (percentage) or median (interquartile range, IQR). CRRT: continuous renal replacement therapy; ECMO: extracorporeal membrane oxygenation; IVIG: intravenous immunoglobulin

those in the control group (1.27% vs. 4.30%, $P=0.015$) by Feb. 12, 2020. At present, we are aware of no patients who have received continuous blood purification due to renal failure and extracorporeal membrane oxygenation (ECMO) in the two groups. Liver injury was the most common complication, followed by ARDS and acute kidney injury, but the differences of these complications were not statistically significant between the two groups. By the end of Feb. 12, all patients had survived and patients in the exposure group had significantly higher rate of hospital discharge than those in the control group (53.44% vs. 28.35%, $P<0.001$).

4 Discussion

As previously noted, an outbreak of a novel coronavirus (SARS-CoV-2) was first recorded in Wuhan, China in Dec. 2019, and soon spread to other

parts of the world. Because of the high transmissibility of the virus, WHO classified this situation as a public health emergency of international concern (PHEIC) (Li et al., 2020; Zhu et al., 2020). On Jan. 23, 2020, China quarantined the entire city of Wuhan to contain the spread of COVID-19. Although the Chinese government made great efforts to control the spread of the epidemic, the epidemic continued to spread nationwide.

Viral mutation can occur over successive human-to-human transmissions, increasing the probability of adaptation to human hosts during a pandemic outbreak and as a virus mutates, its virulence and pathogenicity may either increase or decrease (Wong et al., 2019). One example of this is pandemic type A (H1N1) influenza which appeared in early 2009 and, as previously noted, reappeared in North America in September. Researchers have reported that an amino acid substitution in the hemagglutinin (HA), D222G, was present in a significant proportion of patients

with a severe and fatal outcome. Mutations in HA, non-structural protein 1 (NS1), and polymerase basic protein 2 (PB2) of influenza viruses have been associated with virulence during virus passage (Goka et al., 2014).

The data from Wuhan revealed high mortality of COVID-19. Chen et al. (2020) showed that 11 (11%) of 99 patients who contracted the disease worsened in a short period of time and died of multiple organ failure. Another study from Wuhan showed that among 138 hospitalized patients with confirmed COVID-19, 26% received ICU care with a mortality rate of 4.3% (Wang et al., 2020). In a study by Yang et al. (2020) the mortality rate for critically ill patients exceeded 60%. The Chinese CDC recently published the largest case series to date of COVID-19 in mainland China (72314 cases, updated through Feb. 11, 2020), where the fatality rate was 2.3% (1023 of 44672 confirmed cases) (Wu and McGoogan, 2020). At this time, the overall national mortality rate in China has been lower than that in Wuhan City.

Our study showed that the number of patients aged over 65 years in the control (non-exposed) group is significantly higher than that in the exposure group, but there was no significant difference in the degree of illness (mild, severe, or critical) between the two groups. We compared the proportion of severe/critical type in younger (<60 years) between these two groups and found no significant difference. We also compared radiographic and laboratory findings of 788 COVID-19 patients with and without exposure to Wuhan, where only the differences in AST and LDH were statistically significant between the two groups. The differences in AST and LDH may be due to age differences between the groups since patients in the control group were older than those in the exposure group. Patients from Wuhan were diagnosed earlier because of a clear epidemiological history. In addition, patients with early onset had a history of Wuhan exposure and had a higher discharge rate. Therefore, from the perspective of epidemiological and clinical characteristics, no significant differences were found between COVID-19 patients with and without Wuhan exposure. The mortality rate of COVID-19 patients across the full range of Zhejiang Province is significantly lower than those directly in the city of Wuhan. The differences in mortality may be due to the early diagnosis and treatment of COVID-19 patients in Zhejiang Province, and the ICU-level care may be

more readily available in Zhejiang Province, contributing to the improved survival.

Our study has several limitations. First, the retrospective nature of this study may decrease its accuracy; a future cohort study could confirm our findings. Second, we compared groups only from the perspective of epidemiological and clinical characteristics without direct virologic evidence which would have provided more direct and reliable data. Third, the data regarding the outcomes of patients with COVID-19 need to be further investigated, as at the time of this study most patients were still under treatment in hospital.

Contributors

Yi-da YANG and Ji-fang SHENG designed the study and reviewed the manuscript prior to submission. Jiang-shan LIAN coordinated the work and took the lead in drafting the manuscript and interpreting. Huan CAI, Shao-rui HAO, and Xi JIN developed the statistical methods. Xiao-li ZHANG, Lin ZHENG, Hong-yu JIA, Jian-hua HU, Shan-yan ZHANG, Guo-dong YU, Jue-qing GU, Chan-yuan YE, Ci-liang JIN, and Ying-feng LU participated in the collection of experimental data. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. All authors have read and approved the final manuscript and, therefore, have full access to all the data in the study and take responsibility for the integrity and security of the data.

Acknowledgments

We thank the Health Commission of Zhejiang Province, China for coordinating data collection. We are grateful to all the front-line medical staffs of Zhejiang Province for their bravery and efforts in COVID-19 prevention and control.

Compliance with ethics guidelines

Jiang-shan LIAN, Huan CAI, Shao-rui HAO, Xi JIN, Xiao-li ZHANG, Lin ZHENG, Hong-yu JIA, Jian-hua HU, Shan-yan ZHANG, Guo-dong YU, Jue-qing GU, Chan-yuan YE, Ci-liang JIN, Ying-feng LU, Ji-fang SHENG, and Yi-da YANG declare that they have no conflict of interest.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5). Informed consent was obtained from all patients for being included in the study. Additional informed consent was obtained from all patients for whom identifying information is included in this article.

References

Chen NS, Zhou M, Dong X, et al., 2020. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study.

- Lancet*, 395(10223):507-513.
[https://doi.org/10.1016/S0140-6736\(20\)30211-7](https://doi.org/10.1016/S0140-6736(20)30211-7)
- Deng LH, Zeng YL, Feng P, et al., 2012. Clinical characteristics of critical patients with pandemic influenza A (H1N1) virus infection in Chengdu, China. *J Zhejiang Univ-Sci B (Biomed & Biotechnol)*, 13(1):49-55.
<https://doi.org/10.1631/jzus.B1100168>
- Goka EA, Valley PJ, Mutton KJ, et al., 2014. Mutations associated with severity of the pandemic influenza A(H1N1)pdm09 in humans: a systematic review and meta-analysis of epidemiological evidence. *Arch Virol*, 159(12):3167-3183.
<https://doi.org/10.1007/s00705-014-2179-z>
- Huang CL, Wang YM, Li XW, et al., 2020. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*, 395(10223):497-506.
[https://doi.org/10.1016/S0140-6736\(20\)30183-5](https://doi.org/10.1016/S0140-6736(20)30183-5)
- Li Q, Guan XH, Wu P, et al., 2020. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med*, 382:1199-1207.
<https://doi.org/10.1056/NEJMoa2001316>
- Otte A, Sauter M, Daxer MA, et al., 2015. Adaptive mutations that occurred during circulation in humans of H1N1 influenza virus in the 2009 pandemic enhance virulence in mice. *J Virol*, 89(14):7329-7337.
<https://doi.org/10.1128/JVI.00665-15>
- Vazquez-Perez JA, Isa P, Kobasa D, et al., 2013. A (H1N1) pdm09 HA D222 variants associated with severity and mortality in patients during a second wave in Mexico. *Virology*, 10:41.
<https://doi.org/10.1186/1743-422X-10-41>
- Wang DW, Hu B, Hu C, et al., 2020. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA*, 323(11):1061-1069.
<https://doi.org/10.1001/jama.2020.1585>
- WHO (World Health Organization), 2020. Clinical management of severe acute respiratory infection when COVID-19 is suspected: interim guidance. [https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-\(ncov\)-infection-is-suspected](https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected) [Accessed on Jan. 30, 2020].
- Wong G, He SH, Leung A, et al., 2019. Naturally occurring single mutations in Ebola virus observably impact infectivity. *J Virol*, 93(1):e01098-18.
<https://doi.org/10.1128/JVI.01098-18>
- Wu JT, Leung K, Leung GM, 2020. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study. *Lancet*, 395(10225):689-697.
[https://doi.org/10.1016/s0140-6736\(20\)30260-9](https://doi.org/10.1016/s0140-6736(20)30260-9)
- Wu ZY, McGoogan JM, 2020. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. *JAMA*, 323(13):1239-1242.
<https://doi.org/10.1001/jama.2020.2648>
- Xu LL, Bao LL, Li FD, et al., 2011. Adaption of seasonal H1N1 influenza virus in mice. *PLoS ONE*, 6(12):e28901.
<https://doi.org/10.1371/journal.pone.0028901>
- Yang XB, Yu Y, Xu JQ, et al., 2020. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med*, in press.
[https://doi.org/10.1016/s2213-2600\(20\)30079-5](https://doi.org/10.1016/s2213-2600(20)30079-5)
- Zhu N, Zhang DY, Wang WL, et al., 2020. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med*, 382(8):727-733.
<https://doi.org/10.1056/NEJMoa2001017>

中文概要

题目: 浙江省有无武汉暴露史新型冠状病毒肺炎患者的流行病学和临床特征的比较研究

目的: 调查浙江省有武汉暴露史和无武汉暴露史的新型冠状病毒肺炎患者的流行病学和临床特征。

创新点: 探索新型冠状病毒从武汉市向浙江省传播过程中是否会发生流行病学和临床特征的变化。

方法: 我们进行了一项回顾性研究。收集了2020年1月17日至2月7日浙江省确诊的新型冠状病毒肺炎患者的流行病学和临床资料，并比较分析了有武汉暴露史和无武汉暴露史患者的流行病学和临床特征。

结论: 从流行病学和临床特征的角度来看，有武汉暴露史和无武汉暴露史的新型冠状病毒肺炎患者之间没有显著差异。

关键词: 新型冠状病毒； SARS-CoV-2； 浙江省； 武汉