

REVIEWS

Review of the Clinical Characteristics of Coronavirus Disease 2019 (COVID-19)

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In late December 2019, a cluster of cases with 2019 Novel Coronavirus pneumonia (SARS-CoV-2) in Wuhan, China, aroused worldwide concern. Previous studies have reported epidemiological and clinical characteristics of coronavirus disease 2019 (COVID-19). The purpose of this brief review is to summarize those published studies as of late February 2020 on the clinical features, symptoms, complications, and treatments of COVID-19 and help provide guidance for frontline medical staff in the clinical management of this outbreak.

KEY WORDS: COVID-19; SARS-CoV-2; coronavirus; pneumonia; Wuhan; review.

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INTRODUCTION

In December 31, 2019, hospitals reported a cluster of cases with pneumonia of unknown cause in Wuhan, Hubei, China, attracting great attention nationally and worldwide.¹ On January 1, 2020, Wuhan public health authorities shut down the Huanan Seafood Wholesale Market, where wild and live animals were sold, due to a suspected link with the outbreak. On January 7, 2020, researchers rapidly isolated a novel coronavirus (SARS-CoV-2, also referred to as 2019-nCoV) from confirmed infected pneumonia patients. Real-time reverse transcription polymerase chain reaction (RT-PCR) and next-generation sequencing were used to characterize it.² On January 23, 2020, owing to the large flow of people during the Chinese Spring Festival, public transport was suspended in Wuhan and, eventually, in all the cities in Hubei Province to reduce the risk of further transmission.

The number of RT-PCR–confirmed cases has increased rapidly. On January 30, 2020, the World Health Organization (WHO) declared COVID-19 (as it would be officially known as of February 11) to be a Public Health Emergency of International Concern (PHEIC) and declared an epidemic. As of February 24, 2020, 80,239 cases were confirmed worldwide

causing 2700 deaths. Mainland China, and especially Hubei Province, has borne the brunt of the epidemic, reporting 77,780 cases. Outside of mainland China, 33 countries have reported 2549 confirmed infections and 34 fatalities.³

We reviewed the published clinical features, symptoms, complications, and treatments of patients with COVID-19 to help health workers around the world combat the current outbreak.

We searched PubMed for all published articles regarding COVID-19 up to February 19, 2020. Keywords used were “COVID-19,” “2019 novel coronavirus,” “SARS-CoV-2,” “2019-nCoV,” “Wuhan coronavirus,” and “Wuhan seafood market pneumonia virus.” After careful screening, six published articles with confirmed cases were identified and included in this review. The summary of included clinical studies is shown in Table 1.

NATURAL HISTORY AND CLINICAL CHARACTERISTICS

Huang et al.⁴ first reported clinical features of 41 patients confirmed to be infected with COVID-19 on January 2, 2020, which include 13 ICU cases and 28 non-ICU cases. More than half of the cases (66%) had been exposed to the Huanan Seafood Wholesale Market. Almost all the patients had bilateral lung ground glass opacity on computed tomography imaging. The initial symptoms included fever (98%), cough (76%), dyspnea (55%), myalgia or fatigue (44%), sputum production (28%), headache (8%), hemoptysis (5%), and diarrhea (3%). Only one patient did not present fever in the early stage of disease. Twelve (29%) cases progressed to acute respiratory distress syndrome (ARDS), 5 (12%) had acute cardiac injury, 3 (7%) had acute kidney injury (AKI), and 3 (7%) had shock. At the data cutoff date, 28 (68%) patients were discharged and 6 (15%) had died.

On January 20, 2020, Chen et al.⁵ reported 99 cases with SARS-CoV-2–infected pneumonia. This case series revealed that older males with comorbidities as a result of weaker immune function were the most susceptible to COVID-19 incidence. The symptoms, complications, and treatments in this study were similar to the previous published study by Huang and colleagues.⁴ At the data cutoff date, 31 (31%) were discharged and 11 (11%) died, and 57 (58%) of the patients

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Table 1 Summary of included clinical studies to date

Author	Huang et al. ⁴	Chen et al. ⁵	Li et al. ⁶	Song et al. ⁷	Chen et al. ⁸	Wang et al. ⁹	
Study setting	Wuhan Jinyintan Hospital from Dec 16, 2019 to Jan 2, 2020	Wuhan Jinyintan Hospital from Jan 1 to Jan 20, 2020	Hospitals in Wuhan on Jan 22, 2020	Shanghai Public Health Clinical Center from Jan 20 to Jan 27, 2020	Tongji Hospital from Jan 14 to Jan 29, 2020	Zhongnan Hospital of Wuhan University from Jan 1 to Jan 28, 2020, follow-up to Feb 3, 2020	
City	Wuhan, China	Wuhan, China	Wuhan, China	Shanghai, China	Wuhan, China	Wuhan, China	
Total patients	41	99	425	51	29	138	
Age, mean (IQR) or mean ± SD, years	49 (41–58)	55.5 ± 13.1	56 (26–82)	49 ± 16	56 (26–79)	56 (42–68)	
Gender, male	30 (73%)	67 (68%)	31 (66%)	25 (49%)	21 (72%)	75 (54.3%)	
Exposure history, cases	27 (66%) exposed to Huanan Seafood Wholesale Market	49 (49%) exposed to Huanan Seafood Wholesale Market	26 (55%) exposed to Huanan Seafood Wholesale Market	50 (98%) exposed to Wuhan	2 (7%) exposed to Huanan Seafood Wholesale Market	12 (8.7%) exposed to Huanan Seafood Wholesale Market	
X-ray and CT findings, cases	Bilateral ground glass opacity, 40 (98%)	Multiple mottling and ground glass opacity, 14 (14%)	Radiographic evidence of pneumonia	Ground glass opacity, 39 (77%)	NA	Ground glass opacity, 138 (100%)	
Signs and symptoms	Fever, 40 (98%) Cough, 31 (76%) Myalgia or fatigue, 18 (44%) Sputum production, 11/39 (28%) Headache, 3/38 (8%) Hemoptysis, 2/39 (5%) Diarrhea, 1/38 (3%) Dyspnea, 22/40 (55%)	Fever, 82 (83%) Cough, 81 (82%) Shortness of breath, 31 (31%) Muscle ache, 11 (11%) Confusion, 9 (9%) Headache, 8 (8%) Sore throat, 5 (5%) Rhinorrhoea, 4 (4%) Chest pain, 2 (2%) Diarrhea, 2 (2%) Nausea and vomiting, 1 (1%)	Fever, with or without recorded temperature	Fever, 49 (96%) Cough, 24 (47%) Phlegm, 10 (20%) Myalgia or fatigue, 16 (31%) Headache and dizziness, 8 (16%) Dyspnea or chest pain, 7 (14%) Loss of appetite, 9 (18%) Diarrhea 5, (10%) Stuffy and runny nose, 2 (4%) Sore throat, 3 (6%) Nausea and vomiting, 3 (6%) NA	Fever, 28 (97%) Cough or expectoration, 21 (72%) Dyspnea, 17 (59%) Myalgia or fatigue, 12 (41%) Headache, 2 (7%) Diarrhea, 4 (14%)	Fever, 136 (98.6%) Fatigue, 96 (69.6%) Dry cough, 82 (59.4%) Anorexia, 55 (39.9%) Myalgia, 48 (34.8%) Dyspnea, 43 (31.2%) Expectoration, 37 (26.8%) Pharyngalgia, 24 (17.4%) Diarrhea, 14 (10.1%) Nausea, 14 (10.1%) Dizziness, 13 (9.4%) Headache, 9 (6.5%) Vomiting, 5 (3.6%) Abdominal pain, 3 (2.2%)	
Complications	ARDS, 12 (29%) RNAemia, 6 (15%) Acute cardiac injury, 5 (12%) Acute kidney injury, 3 (7%) Secondary infection, 4 (10%) Shock, 3 (7%) Antiviral, 38 (93%) Antibiotic, 41 (100%) Corticosteroid, 9 (22%) CRRT, 3 (7%) Nasal cannula, 27 (66%) Noninvasive ventilation or high-flow nasal cannula, 10 (24%) Invasive mechanical ventilation, 2 (5%)	ARDS, 17 (17%) Acute renal injury, 3 (3%) Acute respiratory injury, 8 (8%) Septic shock, 4 (4%) Ventilator-associated pneumonia, 1 (1%) Oxygen therapy, 75 (76%) Noninvasive ventilation, 13 (13%) Invasive ventilation, 4 (4%) CRRT, 9 (9%) ECMO, 3 (3%) Antibiotic, 70 (71%) Antifungal, 15 (15%) Antiviral, 75 (76%) Glucocorticoids, 19 (19%)	NA	NA	NA	Shock, 12 (8.7%) Acute cardiac injury, 10 (7.2%) Arrhythmia, 23 (16.7%) ARDS, 27 (19.6%) AKI, 5 (3.6%)	Antiviral, 124 (89.9%) Glucocorticoid, 62 (44.9%) CRRT, 2 (1.45%) Oxygen inhalation, 106 (76.81%) NIV, 15 (10.9%) IMV, 17 (12.32%) ECMO, 4 (2.9%)
Treatments							

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Table 1. (continued)

Author	Huang et al. ⁴	Chen et al. ⁵	Li et al. ⁶	Song et al. ⁷	Chen et al. ⁸	Wang et al. ⁹
	Invasive mechanical ventilation and ECMO, 2 (5%) 28 (68%) 6 (15%)	Immunoglobulin, 27 (27%) 31 (31%) 11 (11%)	NA NA	NA NA	NA 2 (7%)	47 (34.1%) 6 (4.3%)

NA not applicable, AKI acute kidney injury, ARDS acute respiratory distress syndrome, CRRT continuous renal replacement therapy, ECMO extracorporeal membrane oxygenation, IMV invasive mechanical ventilation, NIV noninvasive ventilation

were still hospitalized. A study of Li et al.⁶ reported on 425 COVID-19 cases in Wuhan confirmed between January 1 and 22, 2020. The mean incubation period was 5.2 days, with the 95th percentile of the distribution at 12.5 days, though uncertainty remains.

Two subsequent studies confirmed the pattern of signs and symptoms.^{7, 8} At the time of this writing, the most recent published case series⁹ of 138 confirmed cases included 36 requiring intensive care by the data cutoff date of February 3, 2020. It also found the common presenting symptoms of fever (136, 99%), fatigue (96, 70%), and dry cough (82, 59%), though there were two patients who did not present any signs of fever at the onset of illness. A higher proportion of cases presented with gastrointestinal symptoms including diarrhea and nausea (14, 10%) than in previous series. Forty-seven (34%) were discharged while 6 (4%) died, while the remainder were still hospitalized. The organ failure complications were similar to the original studies.

Taken together, these studies indicate the main clinical manifestations of COVID-19 are fever (90% or more), cough (around 75%), and dyspnea (up to 50%). A small but significant subset has gastrointestinal symptoms. Preliminary estimates of case fatality, likely to fall as better early diagnostic efforts come into play, is about 2%, mostly due to ARDS, AKI, and myocardial injury.

BASIC VIROLOGY

Coronaviruses are widespread in humans and several other vertebrates and cause respiratory, enteric, hepatic, and neurologic diseases. Notably, the severe acute respiratory syndrome coronavirus (SARS-CoV) in 2003 and Middle East respiratory syndrome coronavirus (MERS-CoV) in 2012 have caused human epidemics. Comparison with the current virus shows several significant differences and similarities. Both MERS-CoV and SARS-CoV have much higher case fatality rates (40% and 10%, respectively). Though the current SARS-CoV-2 shares 79% of its genome with SARS-CoV, it appears to be much more transmissible.¹⁰

Both SARS-CoVs enter the cell via the angiotensin-converting enzyme 2 (ACE2) receptor.^{11, 12} The SARS-Cov-2 first predominantly infects lower airways and binds to ACE2 on alveolar epithelial cells. Both viruses are potent inducers of inflammatory cytokines. The “cytokine storm” or “cytokine cascade” is the postulated mechanism for organ damage. The virus activates immune cells and induces the secretion of inflammatory cytokines and chemokines into pulmonary vascular endothelial cells.

TRANSMISSION DYNAMICS AND PROTECTIVE MEASURES

The preliminary estimate of R0 (the expected number of cases directly produced by one person in a population susceptible to

infection) for COVID-19 is 2.2 (95% CI, 1.4 to 3.9).⁶ Fomites are suspected as the main source of infectious particles, though some uncertainty remains. Other coronaviruses have been shown to persist for days on uncleaned surfaces.¹⁰ Additionally, SARS-CoV-2 RNA was detected in the stool specimen in a person who had symptoms while the serum specimen tested negative.¹³ Recently, SARS-Cov-2 was isolated from a swab sample of a confirmed patient's feces by Chinese researchers,¹⁴ indicating the potential for fecal-oral transmission. Studies have shown effective person-to-person transmission of 2019-nCoV even in the presence of isolation efforts in medical facilities.^{15, 16} A case series of nine infected pregnant women did not reveal evidence of third trimester vertical transmission after cesarian section.¹⁷ Transmission in health settings is a very serious threat. The most recent case series reported 57 (41%) of 138 patients were infected hospital settings, including 40 (29%) medical staff.⁹ While further study is needed, it appears that asymptomatic persons are also potential sources of 2019-nCoV infection.^{18, 19}

Handwashing is the mainstay of viral control. Contact isolation gear such as masks, gowns, and gloves are also recommended. Transmission via ocular surface is possible,²⁰ so eye protection should also be used.

VACCINES AND TREATMENTS

Several efforts to develop vaccines are underway, but the WHO estimates it will take 18 months for the COVID-19 vaccines to be available.²¹ At present, most treatment is symptomatic and supportive, though anti-inflammatory and antiviral treatments have been employed. Supportive treatment for complicated patients has included continuous renal replacement therapy (CRRT), invasive mechanical ventilation, and even extracorporeal membrane oxygenation (ECMO). No specific antiviral drugs have been confirmed effective. The first reported patient with 2019-nCoV infection in the USA was treated with remdesivir,¹³ and others have used antiretrovirals like ritonavir, with trials of both in progress.²² A recent study conducted by the "front-line" health care providers combating COVID-19 in Wuhan indicated that systemic corticosteroid treatment did not show significant benefit.²³ Baricitinib has been suggested as a potential drug for the treatment in the hope that it might reduce the process of both virus invasion and inflammation.²⁴

CONCLUSION

Despite some diversity in initial symptoms, most COVID-19 patients have fever and respiratory symptoms. For now, travel history to epidemic areas is important to the diagnosis and should be obtained on all patients with flu-like syndromes. If positive, timely referral to the public health authorities for testing is crucial. Frontline medical staff are at risk and should employ protective measures. Treatment is mainly supportive

and symptomatic, though trials of vaccines and antivirals are underway. Healthcare providers should follow subsequent reports as the situation will likely change rapidly.

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Authors' Contributions F. J. and Z. X. planned the work. F. J. drafted the manuscript. Z. X. revised the manuscript. L. D., L. Z., Y. C., and C. W. C. participated in the literature search and discussion. All authors read and approved the final manuscript. Editor's note: Several of the authors are natives of Hubei Province.

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Compliance with Ethical Standards:

Conflict of Interest: The authors declare that they do not have a conflict of interest.

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