

Clinical Features of 85 Fatal Cases of COVID-19 from Wuhan

A Retrospective Observational Study

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Abstract

Rationale: The global death toll from coronavirus disease (COVID-19) virus as of May 12, 2020, exceeds 286,000. The risk factors for death were attributed to advanced age and comorbidities but have not been accurately defined.

Objectives: To report the clinical features of 85 fatal cases of COVID-19 in two hospitals in Wuhan.

Methods: Medical records were collected of 85 fatal cases of COVID-19 between January 9, 2020, and February 15, 2020. Information recorded included medical history, exposure history, comorbidities, symptoms, signs, laboratory findings, computed tomographic scans, and clinical management.

Measurements and Main Results: The median age of the patients was 65.8 years, and 72.9% were male. Common symptoms were fever (78 [91.8%]), shortness of breath (50 [58.8%]), fatigue (50 [58.8%]), and dyspnea (60 [70.6%]). Hypertension, diabetes, and coronary heart

disease were the most common comorbidities. Notably, 81.2% of patients had very low eosinophil counts on admission. Complications included respiratory failure (80 [94.1%]), shock (69 [81.2%]), acute respiratory distress syndrome (63 [74.1%]), and arrhythmia (51 [60%]), among others. Most patients received antibiotic (77 [90.6%]), antiviral (78 [91.8%]), and glucocorticoid (65 [76.5%]) treatments. A total of 38 (44.7%) and 33 (38.8%) patients received intravenous immunoglobulin and IFN- α 2b, respectively.

Conclusions: In this depictive study of 85 fatal cases of COVID-19, most cases were males aged over 50 years with noncommunicable chronic diseases. The majority of the patients died of multiple organ failure. Early onset of shortness of breath may be used as an observational symptom for COVID-19 exacerbations. Eosinophilopenia may indicate a poor prognosis. A combination of antimicrobial drugs did not offer considerable benefit to the outcome of this group of patients.

Keywords: coronavirus disease 2019; severe acute respiratory syndrome coronavirus 2; fatal cases; eosinophilopenia; copathogen

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At a Glance Commentary

Scientific Knowledge on the

Subject: The global death toll from coronavirus disease (COVID-19) as of May 12, 2020, exceeds 286,000. The risk factors for death were attributed to advanced age and comorbidities but have not been accurately defined.

What This Study Adds to the Field:

This work will have value in helping clinicians identify patients with poor prognosis at an early stage by being aware of some of the alarming clinical characteristics presented by patients before they died from COVID-19, and help guide appropriate and effective management for future patients.

A new type coronavirus was discovered to be the cause of unexplained pneumonia cases in Wuhan, China, in late December, 2019 (1, 2). The virus belongs to the same genus as severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome (MERS)-CoV, and was thus named SARS-CoV-2 by the International Committee on Taxonomy of Viruses on February 11, 2020. However, SARS-CoV-2 is more infectious than SARS-CoV and MERS-CoV, with over 84,000 cases in China and over 4,200,000 cases worldwide reported as of May 12, 2020, according to the Center for Systems Science and Engineering at John Hopkins University (3). On February 11, 2020, the World Health Organization officially named the disease caused by the new coronavirus as coronavirus disease (COVID-19). SARS-CoV-2 is prone to transmit in family clusters (4, 5) or cause outbreaks in hospitals. Most patients with COVID-19 present with mild and moderate symptoms, but severe cases can present with acute respiratory distress syndrome (ARDS), multiple organ dysfunction syndrome, and even death. It has been reported that fatality rate of COVID-19 varies from 1.4% (6) to 4.3% (7) in different regions or hospitals. Mounting evidence has shown that this virus induces excessive and aberrant noneffective host immune responses associated with severe lung injury (1, 8). Higher rates of ARDS are seen in elderly patients with comorbidities (4). Previously published research has described clinical characteristics

of COVID-19 in Wuhan and other provinces, as well as SARS and MERS. Our current work includes the largest cohort of fatal cases of COVID-19 in the literature thus far.

As in patients with SARS and MERS, most patients with COVID-19 have a characteristic ground glass appearance on chest computed tomographic (CT) scans (9). Pathological characteristics of a patient with COVID-19, with biopsy samples from the lung, liver, and heart, show features similar to those seen in SARS-CoV and MERS-CoV infections (10). Along with ARDS, acute cardiac injury and acute kidney injury can also occur (1). Because COVID-19 is a new epidemic of SARS, the specific mechanisms and pathophysiology of the disease remain elusive. No effective vaccine or antiviral treatment is currently available. As of May 12, 2020, there have been a total of 286,835 reported COVID-19-related deaths worldwide (3), but no detailed analysis of this group has been reported. Here, we report on the characteristics of the largest series of fatal cases of COVID-19 in Wuhan city, the epicenter of the SARS-CoV-2 outbreak, and describe their clinical characteristics in the hope that this will help clinicians identify patients with poor prognosis at an early stage.

Methods

Study Design and Participants

This is a retrospective study conducted in two hospitals in Wuhan: Hannan Hospital and Wuhan Union Hospital. The study was approved by the ethics committees of both hospitals. All consecutive patients with severe, confirmed COVID-19 admitted to the two hospitals between January 9, 2020, and February 15, 2020, were enrolled. All patients were diagnosed based on the recommendations by the National Institute for Viral Disease Control and Prevention, China (fifth edition), which specifies that suspected cases who were from Hubei Province, of which Wuhan city is the capital, who have a contact history, and/or who present typical chest CT features may be diagnosed with COVID-19. A positive PCR test for SARS-CoV-2 is mandatory for patients located outside of Hubei province to make the diagnosis. Clinical outcomes (mortality) were monitored up to February 15, 2020, the final date of follow-up.

Data Collection

Epidemiological, clinical, laboratory, and radiological test results, as well as clinical

management data, were obtained using data collection forms from electronic medical records. The data were reviewed by physicians and scientists of the Wuhan-Beijing Medical Treatment Group for COVID-19. Data collected included demographics, medical history, exposure history, underlying comorbidities, symptoms, signs, laboratory findings, chest CT scans, and clinical management (i.e., antiviral therapy, corticosteroid therapy, respiratory support, intravenous immunoglobulin, and continuous renal replacement therapy). The date of disease onset was defined as the day symptoms (i.e., fever, shortness of breath, fatigue, dyspnea, anorexia, expectoration, dry cough, diarrhea, myalgia, headache, vomiting, abdominal pain, chest pain, and pharyngalgia) first appeared. ARDS was defined according to the Berlin definition. Acute kidney injury and cardiac injury were defined according to a previous study (7). The duration from onset of disease to hospital admission, and death, was also recorded.

We searched PubMed, Medline, and Google Scholar on March 25, 2020, for articles describing the clinical features of patients infected with SARS-CoV-2 (previously known as 2019 novel coronavirus [2019-nCoV]), using the search terms “novel coronavirus” or “2019-nCoV” and “fatal cases” or “COVID-19,” with no time restrictions. We also searched CNKI and Wanfang Data using the same terms in Chinese, with no time restrictions.

Statistical Analysis

Continuous measurements, such as mean (SD) and categorical variables, were reported as numbers and percentages (%). For laboratory results, we also assessed whether or not measurements fell within the normal range. We used SPSS (version 26.0) for all analyses.

Results

Presenting Characteristics

A total of 85 fatal cases with clinically diagnosed COVID-19 were included in this study; 33 (38.8%) patients had positive SARS-CoV-2 PCR tests. The median (SD) age was 65.8 (14.2) years (range, 14–86 yr), and 62 (72.9%) were male (Table 1). Three patients had a history of exposure to the Huanan seafood market.

Of the 85 patients, 58 (68.2%) had one or more comorbidities. Hypertension (32 [37.6%]), diabetes (19 [22.4%]), and coronary heart disease (10 [11.8%]) were the most common comorbidities. On admission, most patients had fever (78 [91.8%]) and dyspnea (60 [70.6%]), and two-thirds of the patients had shortness of breath (50 [58.8%]) and fatigue (50 [58.8%]). Almost one-half of the patients had anorexia, and more than one-third of the patients had expectoration

(32 [37.6%]). Other symptoms included dry cough, diarrhea, myalgia, headache, vomiting, abdominal pain, chest pain, and pharyngalgia. The mean (\pm SEM) duration from first symptoms to hospital admission and ARDS were 10.1 (\pm 6.2) days and 10.3 (\pm 6.6) days, respectively (Table 1). The mean duration from hospital admission to death was 6.35 (\pm 4.51) days (range, 1–21 d).

The most common cause of death in 81 of the 85 patients was respiratory failure (38 [46.91%]), followed by septic shock (16

[19.75%]), multiple organ failure (13 [16.05%]), and cardiac arrest (7 [8.64%]). Acute coronary syndrome, malignant arrhythmia, and disseminated intravascular coagulation were rare causes of death (Table 1).

Laboratory Findings

On admission, 69 (81.2%) patients had an eosinophil count below the normal range ($0.02\text{--}0.52 \times 10^9$ cells/L), and 10 (11.8%) and 38 (44.7%) patients had a white blood cell count below and above the normal range, respectively. Totals of 51 (60.0%) and 66 (77.6%) of the patients had neutrophils above and lymphocytes below the normal range, respectively. Platelet counts below and above the normal range were noted in 35 (41.2%) and 6 (7.1%) patients, respectively. Many patients had decreased Hb and hematocrit (Table 2). D-dimer was higher than the normal range in 56 (65.9%) patients. Many patients showed decreased activated partial prothrombin time (PT) and increased PT. A total of 67 (78.8%) patients had albumin below the normal range. Many patients had varying degrees of abnormal liver function with increased alanine aminotransferase or aspartate aminotransferase. Most patients had abnormal myocardial zymograms, characterized by increased creatine kinase in 31 (36.5%) and increased lactate dehydrogenase in 70 (82.4%) patients. A total of 48 (56.5%) patients had different degrees of impaired renal function with elevated blood urea nitrogen or serum creatinine, and 78 (91.8%) patients had C-reactive protein and 19 (22.4%) had procalcitonin levels above the normal ranges.

On admission, copathogens were tested in a subset of patients (Table 3). Most testing was serological analysis of blood samples. *Mycoplasma* IgM antibodies were detected in 9 of 34 (26.5%) patients that were tested, and *Chlamydia* was positive in 12 out of 35 (34.1%) patients tested. Two patients out of 22 patients (9.1%) tested were influenza A positive, and 1 out of 19 patients (5.3%) tested was influenza B positive. Three of nine (33.3%) patients tested positive for respiratory syncytial virus. There were no patients positive for parainfluenza virus, adenovirus, coxsackievirus, tuberculosis, rickettsia, or legionella. With regard to sputum cultures, no bacterial cultures were positive in 12 patients tested, but 3 patients had positive fungal cultures.

Table 1. Clinical Characteristics of Patients with COVID-19

Clinical Characteristics, Symptoms, or Signs	n (%) or Mean \pm SD (n = 85)
Age, yr	65.8 \pm 14.2
Age groups, yr	
0–14	1 (1.2)
15–49	8 (9.4)
50–64	24 (28.2)
\geq 65	52 (61.2)
Sex	
Female	23 (27.1)
Male	62 (72.9)
Exposure to Huanan seafood market	3 (3.53)
Comorbidities	
Any	58 (68.2)
Hypertension	32 (37.6)
Diabetes	19 (22.4)
Coronary heart disease	10 (11.8)
Cerebrovascular diseases	7 (8.2)
Chronic liver disease	5 (5.9)
Malignancy	6 (7.1)
Chronic kidney disease	3 (3.5)
Chronic obstructive pulmonary disease	2 (2.4)
Signs and symptoms on admission	
Fever	78 (91.8)
Short of breath	50 (58.8)
Fatigue	50 (58.8)
Dyspnea	60 (70.6)
Anorexia	48 (56.5)
Expectoration	32 (37.6)
Dry cough	19 (22.4)
Diarrhea	16 (18.8)
Myalgia	14 (16.5)
Headache	4 (4.7)
Vomiting	4 (4.7)
Abdominal pain	3 (3.5)
Chest pain	2 (2.4)
Pharyngalgia	2 (2.4)
Days onset of symptom to:	
Hospital admission	10.1 \pm 6.2
Acute respiratory distress syndrome	10.3 \pm 6.6
Days onset of hospital admission to death	6.35 \pm 4.51
Cause of death	
Respiratory failure	38/81 (46.91)
Multiple organ failure	13/81 (16.05)
Septic shock	16/81 (19.75)
Cardiac arrest	7/81 (8.64)
Acute coronary syndrome	4/81 (4.94)
Malignant arrhythmia	2/81 (2.47)
Disseminated intravascular coagulation	1/81 (1.23)

Definition of abbreviation: COVID-19 = coronavirus disease.

Table 2. Laboratory Findings of Patients with COVID-19 on Admission to Hospital

	<i>n</i> (%) or Mean ± SD (<i>n</i> = 85)
White blood cell count, ×10 ⁹ /L; normal range, 3.5–9.5	10.121 ± 6.266
Increased	38 (44.7)
Decreased	10 (11.8)
Neutrophil count, ×10 ⁹ /L; normal range, 1.8–6.3	8.765 ± 6.181
Increased	51 (60.0)
Decreased	11 (12.9)
Lymphocytes, ×10 ⁹ /L; normal range, 1.1–3.2	0.729 ± 0.419
Decreased	66 (77.6)
Eosinophils, ×10 ⁹ /L; normal range, 0.02–0.52	0.013 ± 0.025
Decreased	69 (81.2)
Basophils, ×10 ⁹ /L; normal range, <0.06	0.018 ± 0.035
Increased	4 (4.7)
Monocytes, ×10 ⁹ /L; normal range, 0.1–0.6	0.413 ± 0.305
Increased	16 (18.8)
Decreased	7 (8.2)
Platelets, ×10 ⁹ /L; normal range, 125–350	162.6 ± 108.9
Increased	6 (7.1)
Decreased	35 (41.2)
Neutrophil:lymphocyte ratio	15.17 ± 13.67
Eosinophil:lymphocyte ratio	0.027 ± 0.056
Eosinophil:neutrophil ratio	0.003 ± 0.014
Hemoglobin, g/L; normal range, 130–175	129.1 ± 25.4
Decreased	41 (48.2)
Hematocrit, %; normal range, 40–50	38.05 ± 7.10
Increased	5 (5.9)
Decreased	53 (62.4)
D-dimer, μg/L; normal range, 0.0–1.5	5.159 ± 4.679
Increased	56 (65.9)
Activated partial prothrombin time, s; normal range, 28.0–43.5	39.22 ± 9.26
Increased	22 (25.9)
Decreased	4 (4.7)
Prothrombin time, s; normal range, 11.0–16.0	15.41 ± 3.32
Increased	22 (25.9)
Decreased	1 (1.2)
Fibrinogen, g/L; normal range, 2.0–4.0	6.321 ± 18.349
Increased	40 (47.1)
Decreased	19 (22.4)
Albumin, g/L; normal range, 35.0–55.0	30.95 ± 9.85
Decreased	67 (78.8)
Alanine aminotransferase, U/L; normal range, 21–72	72.9 ± 199.5
Increased	14 (16.5)
Aspartate aminotransferase, U/L; normal range, 17–59	94.4 ± 263.3
Increased	28 (32.9)
Total bilirubin, μmol/L; normal range, 5.1–19.0	18.44 ± 13.61
Increased	30 (35.3)
Blood urea nitrogen, mmol/L; normal range, 3.2–7.1	9.368 ± 7.360
Increased	42 (49.4)
Serum creatinine, μmol/L; normal range, 58–110	113.73 ± 149.70
Increased	16 (18.8)
Creatine kinase, U/L; normal range, 55–170	298.0 ± 401.8
Increased	31 (36.5)
Lactate dehydrogenase, U/L; normal range, 109–245	645.8 ± 596.9
Increased	70 (82.4)
Glucose, mmol/L; normal range, 4.1–5.9	9.383 ± 5.099
Increased	67 (78.8)
Decreased	3 (3.5)
Procalcitonin, μg/L; normal range, <0.5	3.650 ± 13.398
Increased	19 (22.4)
C-reactive protein, mg/L; normal range, <8.0	107.259 ± 117.215
Increased	78 (91.8)

Definition of abbreviation: COVID-19 = coronavirus disease.

Increased means over the upper limit of the normal range, and decreased means below the lower limit of the normal range.

Chest CT Findings

Chest CT scan was done in 80 patients on admission: 78 (97.5%) patients showed bilateral pneumonia, and only 2 patients had unilateral pneumonia. A total of 61 (76.3%) patients showed multiple mottling and ground-glass opacities (Figure 1 and Table 4).

Complications and Treatment

Patients presented with functional damage involving multiple vital organs, including respiratory failure (80 [94.1%]), shock (69 [81.2%]), ARDS (63 [74.1%]), arrhythmia (51 [60.0%]), acute myocardial injury (38 [44.7%]), acute liver injury (30 [35.3%]), and sepsis (28 [32.9%]) (Table 5).

Most patients received antibiotics (77 [90.6%]), antiviral treatment (78 [91.8%]), and glucocorticoids (65 [76.5%]). Totals of 38 (44.7%) and 33 (38.8%) patients received intravenous infusions of immunoglobulin and recombinant human IFN-α2b; 11 patients received antifungal treatment; two-thirds of the patients had oxygen therapy; and 44 and 18 patients received noninvasive and invasive mechanical ventilation, respectively. Continuous renal replacement therapy was given to eight patients, one patient received plasma from a patient who had recovered from COVID-19, and no patients received extracorporeal membrane oxygenation as rescue therapy (Table 5).

On admission, the median (SD) CURB-65 was 1.9 (1.1; range: 0–5); 8 (9.4%) patients had a CURB-65 (confusion, urea, respiratory rate, blood pressure, age ≥65 years) score of 0, 27 (31.8%) patients had a score of 1, and 25 (29.4%) patients had a score of 2. These were classified as mild according to the CURB-65 guidelines. Only 25 patients were classified as severe on admission, of whom 20 (23.5%) patients had a score of 3, 3 (3.5%) had a score of 4, and 2 (2.4%) had a score of 5 (Table 6). Procalcitonin appears to increase with higher CURB-65 admission scores (Table 6). There was a 3.35 (95% confidence interval, 0.17–6.53) increase in procalcitonin level for each increase in CURB-65 level ($P=0.0451$).

Discussion

In this retrospective study, we report what is, to date, the largest series of patients who

Table 3. Copathogens of Patients with Fatal COVID-19

Copathogens	n (%)
Blood sample	
<i>Mycoplasma</i>	9/34 (26.5)
<i>Chlamydia</i>	12/35 (34.1)
Respiratory syncytial virus	1/3 (33.3)
Adenovirus	0/3 (0)
Coxsackievirus	0/2 (0)
Influenza A virus	2/22 (9.1)
Influenza B virus	1/19 (5.3)
Parainfluenza virus	0/18 (0)
Tuberculosis	0/9 (0)
<i>Rickettsia</i>	0/1 (0)
<i>Legionella</i>	0/1 (0)
Sputum culture	
Bacterial culture	0/12 (0)
Fungal culture	3/9 (33.3)

Definition of abbreviation: COVID-19=coronavirus disease.

have died from COVID-19, providing detailed clinical characteristics of this cohort of patients from two Wuhan hospitals. The 85 fatal cases of COVID-19 reported here

account for 2.7% of the total mortality due to SARS-CoV-2 infection in Hubei province. Although the symptoms of the majority of patients in other provinces have been

comparatively mild (11), the number of deaths from SARS-CoV-2 infection continues to increase, with more cases and fatalities occurring now in other provinces, countries, and regions. As of May 12, 2020, there have been 4,643 fatalities and 84,450 confirmed cases of COVID-19 in China, according to the World Health Organization (12). Early diagnosis and timely treatment to reduce mortality is of crucial importance. It is hoped that this work will have value in helping clinicians identify patients with poor prognosis at an early stage by being aware of some of the alarming clinical characteristics presented by patients before they died from COVID-19, and help guide appropriate and effective management for future patients.

A recent study by Zhou and colleagues (13) of 191 patients, of whom 54 died, found that older age, high sequential organ failure assessment score, and D-dimer $>1 \mu\text{g/ml}$ could assist in the early identification of patients who may have a poorer prognosis. In our study, the median age of nonsurvivors was 65.8 years, which is similar to the median age reported in nonsurvivors, but higher than that of the survivors (52 yr), reported in the previous study. Furthermore, our study found that the median (SD) level of D-dimer in nonsurvivors was 5.159 (4.679) $\mu\text{g/ml}$ (range, 0.27–26 $\mu\text{g/ml}$), and 70.6% of our patients had a D-dimer $>1 \mu\text{g/ml}$, which was also consistent with the previous study. The sequential organ failure assessment score was not included in our study. However, we found that 29.4% of patients had a CURB-65 score >3 , which was similar to the previous study (28% in nonsurvivors) (13). In our study, about one-quarter of patients who died had an elevated procalcitonin level, which was consistent with the previous study, but Zhou and colleagues' study also found that an elevated procalcitonin level >0.5 was associated with a 93% chance of death. In a non-COVID-19 study of patients with pneumonia, the CURB-65 score on admission correlated with mortality risk (14).

It was difficult to find age- and sex-matched control subjects for our study. In comparing our data to the previous study mentioned here, which did include survivors, we found that the hospital length of stay was the same in nonsurvivors between the two studies, but almost double the survivor length of stay (12 d) in the

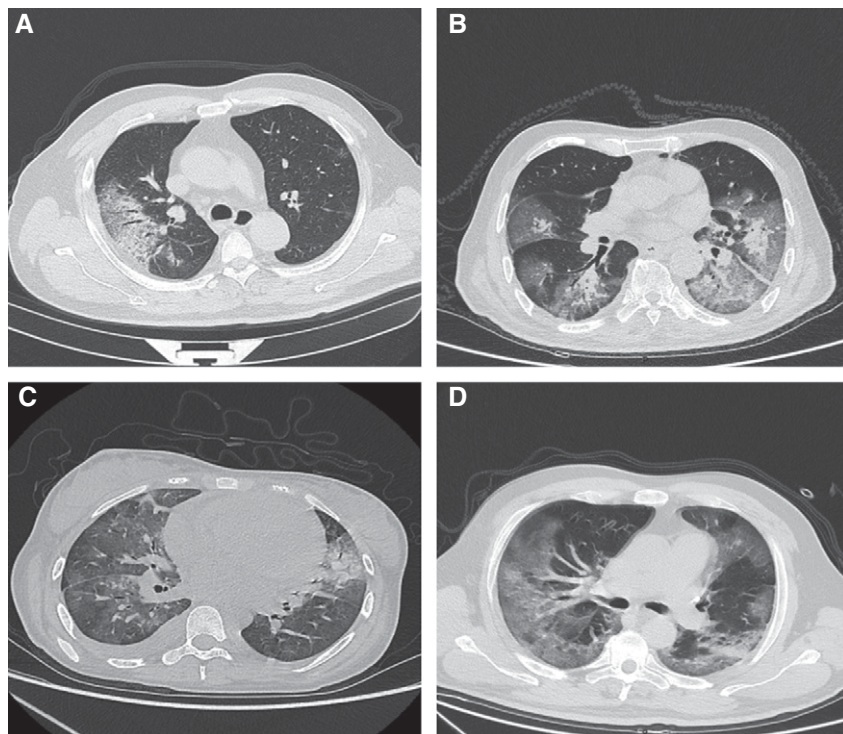


Figure 1. (A) Chest computed tomographic (CT) images of a 55-year-old male patient with coronavirus disease (COVID-19) taken on January 27, 2020, showing unilateral pneumonia. (B) Chest CT images of an 85-year-old male patient with COVID-19 taken on February 4, 2020, showing ground-glass opacity in both lungs. (C) Chest CT images of a 23-year-old female patient with COVID-19 taken on January 24, 2020, showing diffuse ground-glass opacity. (D) Chest CT images of a 72-year-old male patient with COVID-19 taken on January 30, 2020, showing bilateral pneumonia.

Table 4. Chest CT Findings of Patients with COVID-19

CT Finding	n (%) (n = 80)
Unilateral pneumonia	2 (2.5)
Bilateral pneumonia	78 (97.5)
Multiple mottling and ground-glass opacity	61 (76.3)

Definition of abbreviations: COVID-19 = coronavirus disease; CT = computed tomographic. A total of 80 patients were available.

Table 5. Complications and Management of Patients with COVID-19

	n (%) (n = 85)
Complications	
Respiratory failure	80 (94.1)
Shock	69 (81.2)
ARDS	63 (74.1)
Arrhythmia	51 (60)
Acute cardiac injury	38 (44.7)
Acute liver injury	30 (35.3)
Sepsis	28 (32.9)
Treatment	
Oxygen therapy	57 (67.1)
Noninvasive mechanical ventilation	61 (71.8)
Invasive mechanical ventilation	18 (21.2)
Kidney replacement therapy	8 (9.4)
ECMO	0
Antibiotic treatment	77 (90.6)
Antifungal treatment	11 (12.9)
Antiviral treatment	78 (91.8)
Glucocorticoids	65 (76.5)
IFN	33 (38.8)
Intravenous immunoglobulin therapy	38 (44.7)
COVID-19 recovery patient plasma treatment	1 (1.2)
Antiinfection treatment	
Antibiotics	
Meropenem	38 (44.7)
Imipenem/cilastatin	1 (1.2)
Moxifloxacin	40 (47.1)
Levofloxacin	4 (4.7)
Linezolid	18 (21.2)
Vancomycin	2 (2.4)
Teicoplanin	2 (2.4)
Tigecycline	2 (2.4)
Piperacillin/tazobactam	9 (10.6)
Ceftriaxone sodium	3 (3.5)
Cefoperazone/sulbactam	2 (2.4)
Ceftazidime tazobactam	2 (2.4)
Antiviral	
Arbidol hydrochloride capsules	51 (60)
Lopinavir and ritonavir tablets	11 (12.9)
Osetamivir	9 (10.6)
Paramivir	6 (7.1)
Ganciclovir	5 (5.9)
Ribavirin	4 (4.7)
Antifungal	
Caspofungin	2 (2.4)
Voriconazole	8 (9.4)
Fluconazole	3 (3.5)

Definition of abbreviations: ARDS = acute respiratory distress syndrome; COVID-19 = coronavirus disease; ECMO = extracorporeal membrane oxygenation.

previous study. Interestingly, the use of intravenous immunoglobulin was higher in nonsurvivors in both the previous study and our study (36% and 38%, respectively), but much lower in survivors (10%) in the previous study. The increased use of intravenous immunoglobulin may be due to the severity of illness but also raises the question of whether intravenous immunoglobulin may be ineffective in severely ill patients. The use of corticosteroids was higher in our cohort of 85 patients than in the above-mentioned study (65% vs. 48% in nonsurvivors and 30% in survivors, respectively). Lymphopenia was identified as a risk factor for death in the previous study, but eosinopenia was not mentioned.

Previous studies found that nearly half of patients with COVID-19 are over the age of 50 years, and that men are more likely to be infected than women (15). The mortality rate in males is higher than that in females. In patients who develop SARS, advanced age is an independent predictor for an adverse outcome, but sex is not (16). In this report, we observed that, among the 85 deaths, there were 76 (89.3%) patients over the age of 50 years and 62 (72.9%) were male.

The most common comorbidities of the patients with COVID-19 in our cohort are hypertension and diabetes, which is similar to findings of previous studies (4, 7). However, the most common comorbidities in the patients with SARS were diabetes (16 [11%]) and cardiac disease (12 [8%]) (17). The increased prevalence of hypertension in China may play a role in COVID-19-related deaths.

Common clinical features of patients with COVID-19 include fever (83%), cough (82%), shortness of breath (31%), and muscle ache (11%) (4). For SARS, the common clinical features included fever (99%), cough (69%), myalgia (49%), and dyspnea (42%) (17). It is worth noting that the overall rates of shortness of breath in our cohort were higher than that in patients with SARS (4). We suggest that early onset of shortness of breath may be indicative of poor prognosis.

We found that the absolute eosinophil count in peripheral blood was reduced in almost all patients who died. The number of patients with reduced eosinophil count in patients with nonsevere and severe COVID-19 who survived has been reported elsewhere to be 39/82 (47.6%) and 34/56

Table 6. CURB-65 of Patients with Fatal COVID-19

CURB-65	n (%) (n = 85)*	Procalcitonin Level [†] (Mean ± SEM) (n = 85)	Data from Zhou and Colleagues (n = 54)** [n (%)]
Mean CURB-65 ± SEM	1.9 ± 1.1	—	—
Grades			
0	8 (9.4)	1.00 ± 1.61	16 (30)
1	27 (31.8)	0.87 ± 1.81	
2	25 (29.4)	1.10 ± 1.91	23 (43)
3	20 (23.5)	4.19 ± 8.52	15 (28)
4	3 (3.5)	29.44 ± 50.22	
5	2 (2.4)	1.58 ± n.a.	

Definition of abbreviations: COVID-19 = coronavirus disease; CURB-65 = confusion, urea, respiratory rate, blood pressure, age ≥65 years; n.a. = not applicable.

*A total of 85 patients from our study compared to 54 patients from the study by Zhou and colleagues.

[†]P = 0.656, calculated using the Kruskal-Wallis H test for comparing multiple groups.

^{**}Grades grouped into three: 0–1, 2, and 3–5.

(60.7%), respectively (18). Previous studies have reported that there is a rapid and persistent decrease in the numbers of circulating eosinophils in acute infection or inflammation (19, 20). A study on 30-day mortality and eosinopenia showed that eosinopenia is an independent predictor of death in patients with pneumonia, but without chronic respiratory disease (21). This effect was not related to steroid use. In the case of COVID-19, this may be related to CD8 T-cell depletion and eosinophil consumption caused by SARS-CoV-2. IL-5, produced by CD8 T cells, contributes to eosinophil proliferation and activation in blood (22–24). Lower numbers of CD8 T cells has been found in patients infected with SARS-CoV-2 (25). Moreover, ECP and EDN, two eosinophil granule proteins, can neutralize viruses

(20, 26, 27). Therefore, the decrease of eosinophils in patients with COVID-19 may be related to a higher viral load of SARS-CoV-2 and SARS-CoV-2-triggered eosinophil granule protein consumption.

We thus speculate that eosinophilopenia may be used as a prognostic indicator for patients with COVID-19. In addition, the ratio of neutrophil to eosinophil counts may be another measure that can minimize variability in absolute eosinophil counts from different hospitals. Another laboratory abnormality found in this study was decreased total lymphocytes, which is consistent with the conclusions of existing research indicating that lymphocytopenia is more often seen in nonsurvivors of SARS-CoV-2 infection (7).

Similarly, prolonged PT and elevated lactate dehydrogenase were noted in our

cohort, whereas a previous study found that 13% of patients had creatine kinase and 3% of patients had serum creatinine above the normal ranges at the time of admission (4). Wang and colleagues (7) reported that the levels of blood urea and creatinine, as measured by dynamic profiling of laboratory data, progressively increased before death. We observed that 56.5% of our patients had renal dysfunction, as indicated by the increased levels of blood urea or creatinine at the time of admission. Therefore, we suggest that an increased level of creatinine and urea nitrogen may also indicate poor prognosis.

Copathogens of patients with COVID-19 have not been previously reported in the literature. Testing for copathogens was done in some, but not all, patients in our cohort, and we found that <10% of tested patients were positive for influenza A virus, influenza B virus, and parainfluenza virus. It is worth noting that the antibody-positive rate of mycoplasma and *Chlamydia* were relatively high.

The initial admission CURB-65 score of most patients was not high, and yet the outcome of all the patients was death. This indicates that the clinical course of COVID-19 develops rapidly, so the CURB-65 at the beginning of admission cannot be used as a guide of severity. Patients with COVID-19 need to be closely monitored after admission. A Kaplan-Meier curve is illustrated in Figure 2.

From a practical standpoint, doctors equipped with protective suits and helmets have great difficulties in closely examining patients with standard techniques, such as auscultation and observing for signs of shortness of breath. Therefore, laboratory findings and chest CT scan become critical in monitoring disease progress and treatment outcome. We determined that the presence of bilateral pneumonia and progressive radiographic deterioration on follow-up CT scan may be risk factors for poor prognosis (26). It should be noted that the administration of multiple antibiotics did not change the outcome of the disease in our series. Rational use of antibiotics should thus be exercised. It is also not known if any of the therapies used in COVID-19, such as steroids, may actually be counterproductive and lead to increased morbidity or mortality.

This study has some limitations. First, only fatal cases of COVID-19 were included. A prospective study including patients with

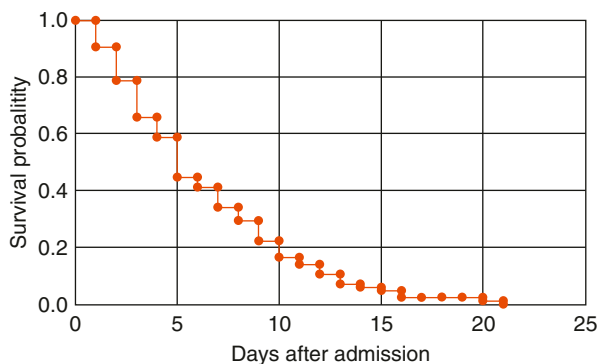


Figure 2. A Kaplan-Meier survival curve from the time of admission with coronavirus disease (COVID-19) to time of death.

fatal and nonfatal disease will provide more conclusive and valuable data. Second, pathological findings were not available. Third, although eosinophilopenia was found in almost all patients in this series, it can also occur in many patients with nonfatal severe and moderate disease, based on our clinical observations (unpublished results). Therefore, additional studies are needed to confirm the prognostic value of eosinophilopenia in patients with COVID-19.

Conclusions

In summary, most cases of death from COVID-19 were males over 50 years of age with noncommunicable chronic diseases, such as hypertension, diabetes, and coronary heart diseases. The patients mainly died of multiple organ failure. Early onset of shortness of breath might be predictive of demise, and eosinophilopenia may indicate a poor prognosis. The use of a combination of more than three antimicrobial drugs

appears to offer no benefit to the outcome of this group of patients. ■

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References

- Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, *et al.* Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395:497–506.
- Carlos WG, Dela Cruz CS, Cao B, Pasnick S, Jamil S. Novel Wuhan (2019-nCoV) coronavirus. *Am J Respir Crit Care Med* 2020;201:P7–P8.
- Center for Systems Science and Engineering, John Hopkins University. COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) [accessed 2012 May 12]. Available from: <https://www.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6>.
- Chen N, Zhou M, Dong X, Qu J, Gong F, Han 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.
- Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, *et al.* A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet* 2020;395:514–523.
- Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, *et al.* Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* [online ahead of print] 28 Feb 2020; DOI: 10.1056/NEJMoa2002032.
- Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, *et al.* Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* [online ahead of print] 7 Feb 2020; DOI: 10.1001/jama.2020.1585.
- Hui DSC, Zumla A. Severe acute respiratory syndrome: historical, epidemiologic, and clinical features. *Infect Dis Clin North Am* 2019;33: 869–889.
- Azhar EI, Hui DSC, Memish ZA, Drosten C, Zumla A. The Middle East Respiratory Syndrome (MERS). *Infect Dis Clin North Am* 2019;33: 891–905.
- Wu F, Zhao S, Yu B, Chen YM, Wang W, Song ZG, *et al.* A new coronavirus associated with human respiratory disease in China. *Nature* 2020;579:265–269.
- Xu XW, Wu XX, Jiang XG, Xu KJ, Ying LJ, Ma CL, *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.
- World Health Organization. Coronavirus disease (COVID-19). Situation report - 112 [accessed 2020 May 12]. Available from: https://www.who.int/docs/default-source/coronavirus/situation-reports/20200511-covid-19-sitrep-112.pdf?sfvrsn=813f2669_2.
- Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, *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. [Published erratum appears in *Lancet* 395:1038.]
- Lim WS, van der Eerden MM, Laing R, Boersma WG, Karalus N, Town GI, *et al.* Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. *Thorax* 2003;58:377–382.
- Yang Y, Lu Q, Liu M, Wang Y, Zhang A, Jalali N, *et al.* Epidemiological and clinical features of the 2019 novel coronavirus outbreak in China [preprint]. medRxiv. 2020 [accessed 2020 Feb 21]. Available from: <https://www.medrxiv.org/content/10.1101/2020.02.10.20021675v2>.
- Lee N, Hui D, Wu A, Chan P, Cameron P, Joynt GM, *et al.* A major outbreak of severe acute respiratory syndrome in Hong Kong. *N Engl J Med* 2003;348:1986–1994.
- Booth CM, Matukas LM, Tomlinson GA, Rachlis AR, Rose DB, Dwosh HA, *et al.* Clinical features and short-term outcomes of 144 patients with SARS in the greater Toronto area. *JAMA* 2003;289: 2801–2809.
- Zhang JJ, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ, *et al.* Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. *Allergy* [online ahead of print] 19 Feb 2020; DOI: 10.1111/all.14238.
- Bass DA, Gonwa TA, Szejda P, Cousart MS, DeChatelet LR, McCall CE. Eosinopenia of acute infection: production of eosinopenia by chemotactic factors of acute inflammation. *J Clin Invest* 1980;65: 1265–1271.
- Gleich GJ. Mechanisms of eosinophil-associated inflammation. *J Allergy Clin Immunol* 2000;105:651–663.
- Echevarria C, Hartley T, Nagarajan T, Tedd H, Steer J, Gibson GJ, *et al.* 30 day mortality and eosinopenia in patients with pneumonia. *Eur Res J* 2014;44:P2550.
- Schwarze J, Hamelmann E, Bradley KL, Takeda K, Gelfand EW. Respiratory syncytial virus infection results in airway hyperresponsiveness and enhanced airway sensitization to allergen. *J Clin Invest* 1997;100: 226–233.
- Schwarze J, Cieslewicz G, Hamelmann E, Joetham A, Shultz LD, Lamers MC, *et al.* IL-5 and eosinophils are essential for the development of airway hyperresponsiveness following acute respiratory syncytial virus infection. *J Immunol* 1999;162:2997–3004.
- Schwarze J, Cieslewicz G, Joetham A, Ikemura T, Hamelmann E, Gelfand EW. CD8 T cells are essential in the development of respiratory syncytial virus-induced lung eosinophilia and airway hyperresponsiveness. *J Immunol* 1999;162:4207–4211.
- Liu Y, Yang Y, Zhang C, Huang F, Wang F, Yuan J, *et al.* Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury. *Sci China Life Sci* 2020;63: 364–374.
- Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J, *et al.* Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. *The Lancet Infectious Diseases* 2020;20: P425–P434.
- Hamann KJ, Ten RM, Loegering DA, Jenkins RB, Heise MT, Schad CR, *et al.* Structure and chromosome localization of the human eosinophil-derived neurotoxin and eosinophil cationic protein genes: evidence for intronless coding sequences in the ribonuclease gene superfamily. *Genomics* 1990;7:535–546.