Clinical features of 162 fatal cases of COVID-19: a multi-center, retrospective study

Xianlong Zhou

Emergency Center, Zhongnan Hospital of Wuhan University

Guoyong Ding

School of Public Health, Shandong First Medical University & Shandong Academy of Medical Sciences

Qing Fang

Qing Fang

Jun Guo

Intensive Care Unit, Huazhong University of Science and Technology Union Jiangbei Hospital

Luyu Yang

Intensive Care Unit, Wuhan Third Hospital

Ping Wang

School of Public Health, Shandong First Medical University & Shandong Academy of Medical Sciences

Shouzhi Fu

Intensive Care Unit, Wuhan Third Hospital

Ang Li

Emergency Center, Zhongnan Hospital of Wuhan University

Jian Xia

Emergency Center, Zhongnan Hospital of Wuhan University

Jiangtao Yu

Emergency Center, Zhongnan Hospital of Wuhan University

Jianyou Xia

Department of Urology, The General Hospital of PLA Central Theater Command

Min Ma

Intensive Care Unit, Huazhong University of Science and Technology Union Jiangbei Hospital

Zhuanzhuan Hu

Intensive Care Unit, Huazhong University of Science and Technology Union Jiangbei Hospital

Lei Huang

Intensive Care Unit, Huazhong University of Science and Technology Union Jiangbei Hospital

Ruining Liu

Emergency Center, Zhongnan Hospital of Wuhan University

Cheng Jiang

Emergency Center, Zhongnan Hospital of Wuhan University

Shaoping Li

Emergency Center, Zhongnan Hospital of Wuhan University

Mingxia Yu

Department of Clinical Laboratory, Zhongnan Hospital of Wuhan University

Xizhu Xu

School of Public Health, Shandong First Medical University & Shandong Academy of Medical Sciences

Yan Zhao

Emergency Center, Zhongnan Hospital of Wuhan University

Quan Hu (✉ huquan197799@sina.com)

Intensive Care Unit, The first people's Hospital of Jiangxia District

Weijia Xing (✉ wjxing@sdfmu.edu.cn)

School of Public Health, Shandong First Medical University & Shandong Academy of Medical Sciences

Zhigang Zhao (✉ drzhaozhigang@163.com)

Emergency Center, Zhongnan Hospital of Wuhan University

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Abstract

Understanding the epidemiological and clinical characteristics of fatal cases infected with SARS-CoV-2 is important to develop appropriate preventable intervention programs in hospitals. Demographic data, clinical symptoms, clinical course, co-morbidities, laboratory findings, CT scans, treatments and complications of 162 fatal cases were retrieved from electronic medical records in 5 hospitals of Wuhan, China. The median age was 69.5 years old (IQR: 63.0-77.25; range: 29-96). 112 (69.1%) cases were men. Hypertension (45.1%) was the most common co-morbidity, but 59 (36.4%) cases had no co-morbidity. At admission, 131 (81.9%) cases were assessed as severe or critical. However, 39 (18.1%) were assessed as moderate. Moderate cases had a higher prevalence of hypertension and chronic lung disease comparing with severe or critical cases ($P<0.05$, respectively). 126 (77.8%) and 132 (81.5%) cases received antiviral treatment and glucocorticoids, respectively. 116 (71.6%) cases were admitted to ICU and 137 (85.1%) cases received mechanical ventilation. Respiratory failure or acute respiratory distress syndrome (93.2%) was the most common complication. The young cases of COVID-19, without co-morbidity and in a moderate condition at admission could develop fatal outcome. We need to be more cautious in case management of COVID-19 for preventing the fatal outcomes.

Introduction

The coronavirus disease 2019 (COVID-19) had affected approximately 4 million people and causing more than 278,000 deaths to date¹. As COVID-19 is an outbreak caused by an emerging infectious disease, the clinical features and treatment methods are still under continuous study. Since the effectiveness of current antiviral treatments are uncertain, the management of COVID-19 cases are still essentially supportive and symptomatic². In most affected regions, the reported fatality rate for COVID-19 was approximately 5%, which is markedly lower than that of severe acute respiratory syndrome (SARS)^{3,4}. Recently, the fatality rate was excessively increased in highly endemic countries. Based on data up to April 15, the fatality rate in Italy and UK was 13.0% and 12.9%, respectively⁵. Although COVID-19 causes nearly 120,000 deaths around the world, but few data concerning fatal cases have been reported. Current evidence based on small series of fatal cases noted that men, elders, and patients with co-morbidities are potential risk factors for death^{6,7}. However, this was not quite sufficient to allow clinical physicians to improve the case management strategy and recognize the patients at risk of death in early stage. Therefore, we aimed to further analyze the epidemiological and clinical characteristics of 162 fatal cases admitted to 5 hospitals in Wuhan, China.

Results

General characteristics

In total, 162 fatal cases of COVID-19 from 5 hospitals in Wuhan before March 12, 2020 were included for analysis (Table 1). The median age was 69.5 years old (interquartile range [IQR]: 63.0–77.25; range: 29–96) and 80% of the cases were at least 61 years old (Figure 1). Nearly two thirds (112/162, 69.1%) of cases were men, the sex ratio between male and female cases was 2.2:1 (Table 1). Only 12 (7.4%) cases were current smokers, 146 (90.1%) cases had never smoked. 103 cases (63.6%) had coexisting disorders at admission, 43 (26.5%) with a single co-morbidity and 60 (37.0%) with two or more co-morbidities. However, 59 (36.4%) cases had no co-morbidity before severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Hypertension (45.1%) was the most frequent co-morbidity, followed by diabetes (19.1%), coronary heart disease (18.5%), renal failure (14.8%) and cerebrovascular disease (10.5%). The most common symptoms at illness onset were fever, cough or expectoration, chest distress or dyspnea, and fatigue (Table 1). A great proportion of cases (131, 80.9%) had been assessed as severe or critical at hospital admission, the remaining 29 (18.1%) cases had been assessed as moderate. The comparison of general characteristics by disease severity of cases was given in Supplementary Table S1. Moderate cases had a higher prevalence of hypertension and chronic lung disease as compared to severe or critical cases ($P<0.05$, respectively).

Table 1. General characteristics of COVID-19 fatal cases.

	Fatal cases (n=162)	
	number	(%)
Hospitals		
Zhongnan Hospital of Wuhan University (III-A) [†]	30	(18.5%)
The First People's Hospital of Jiangxia District (III-B) [†]	22	(13.6%)
Wuhan Third Hospital (III-A) [†]	26	(16.0%)
Union Jiangbei Hospital (II-A) [†]	33	(20.4%)
Wuhan No.7 Hospital (II-A) [†]	51	(31.5%)
Sex		
Female	50	(30.9%)
Male	112	(69.1%)
Smoker		
Never smoked	146	(90.1%)
Former smoker	4	(2.5%)
Current smoker	12	(7.4%)
Co-morbidities		
Hypertension	73	(45.1%)
Diabetes	31	(19.1%)
Coronary heart disease	30	(18.5%)
Renal insufficiency	24	(14.8%)
Cerebrovascular disease	17	(10.5%)
Chronic lung disease	12	(7.4%)
Malignant tumor	12	(7.4%)
Presence of co-morbidities		
0	59	(36.4%)
1	43	(26.5%)
2	36	(22.2%)
≥3	24	(14.8%)
Surgery history within 6 months	8	(4.9%)
Signs and symptoms		
Any	159	(98.1%)
Fever	128	(79.0%)
Highest temperature		
37.3-38.0°C	75	(46.3%)
38.1-39.0°C	74	(45.7%)
>39.0°C	13	(8.0%)
Duration of fever, median (IQR), d	7	(5-10)
Cough or sputum production	111	(68.5%)
Chest distress/dyspnea	101	(62.3%)
Fatigue	92	(56.8%)
Nausea or vomiting	23	(14.2%)
Diarrhea	22	(13.6%)
Disease severity at admission*		
Moderate	29	(18.1%)
Severe	51	(31.9%)
Critical	80	(50.0%)

Abbreviations: COVID-19, coronavirus disease 2019. Denominator used for calculating the percentage may not total number because of missing data.

[†]The grade of hospital was indicated in the brackets. The order of grade from the best was Grade III-A, Grade III-B, Grade II-A.

*Data were missing for two cases.

Laboratory and radiological findings

Most cases experienced a normal vital sign at admission, including blood pressure (108, 67.9%), heart rate (116, 73.0%) and temperature (96, 59.3%) (Table 2). The decreased systolic blood pressure was observed in three (1.9%) cases, and 18 (11.3%) had a decreased diastolic blood pressure. The respiratory rate increased in 79 (50.6%) cases, and only 15 (9.6%) cases had a respiratory rate over 30 breaths/min. The decreased oxygen saturation was observed in 110 (67.9%) cases. Neutrophils increased in 76 (47.8%) cases and lymphocytopenia occurred in 119 cases (74.4%). We found increased procalcitonin and IL-6 in 51 (37.2%) and 12 (31.6%) cases, respectively. In addition, erythrocyte sedimentation rate (ESR) increased in 46 (60.5%) cases. 39 (24.1%) cases had a longer activated partial prothrombin time (APTT) and prothrombin time (PT). D-dimer was increased in 77 (64.7%) cases. At admission, 107 (80.5%) cases showed decreased partial pressure of oxygen (PaO₂), and 72 (67.3%) of them less than 60 mmHg. The disturbance of acid-base balance occurred in 79 (59.4%) cases and lactate increased in 92 (76.0%) cases. Radiological evidences of pneumonia were observed in all cases at admission. Bilateral pneumonia was observed in the majority of cases (155, 95.7%), and unilateral pneumonia was observed in seven cases (7, 4.3%). Moreover, 112 (69.1%) patients showed multiple mottling and ground-glass opacity.

Table 2. Vital signs, laboratory and radiological findings of COVID-19 fatal cases.

	Fatal cases (n=162)	
	number (%), median (IQR)	
Vital signs		
Systolic blood pressure (mmHg; normal range 90-140)	130	(119-141)
Increased	40	(25.2%)
Decreased	3	(1.9%)
Diastolic blood pressure (mmHg; normal range 60-90)	76	(66-82)
Increased	10	(6.3%)
Decreased	18	(11.3%)
Heart rate (beats per minute; normal range 60-100)	90	(80-101)
Increased	40	(25.2%)
Axillary temperature (°C; normal range 36.2-37.3)	36.8	(36.5-37.6)
Increased	50	(30.9%)
Respiratory rate (breaths per minute; normal range 12-20)	21	(20-25)
21-29	64	(41.0%)
≥ 30	15	(9.6%)
Oxygen saturation (%; normal range ≥ 94)	90	(83-95)
Decreased	110	(67.9%)
Laboratory findings		
Leucocytes (10 ⁹ /L; normal range 3.5-9.5)	7.2	(4.7-11.5)
Increased	60	(37.7%)
Decreased	13	(8.2%)
Neutrophils (10 ⁹ /L; normal range 1.8-6.3)	6.1	(3.6-10.3)
Increased	76	(47.8%)
Lymphocytes (10 ⁹ /L; normal range 1.1-3.2)	0.6	(0.4-1.0)
< 1.0	119	(74.4%)
≥ 1.0	41	(25.6%)
Erythrocyte (10 ¹² /L; normal range 4.3-5.8)	4.1	(3.7-4.6)
Decreased	93	(58.9%)
Haemoglobin (g/L; normal range 130-175)	125	(109-134)
Decreased	103	(64.8%)
Platelet count (10 ⁹ /L; normal range 125-350)	145	(104-191)
Decreased	58	(36.7%)
Procalcitonin (ng/mL; normal range < 0.5)	0.27	(0.11-0.92)
Increased	51	(37.2%)
IL-6 (pg/mL; normal range 0.0-7.0)	0	(0-45.4)
Increased	12	(31.6%)
ESR (mm/h; normal range 0.0-15.0)	27.5	(0-48.0)
Increased	46	(60.5%)
APTT (s, normal range 28.0-43.5)	41.2	(26.4-51.7)
Increased	39	(24.1%)
PT (s, normal range 11.0-16.0)	14.2	(8.7-19.6)
Increased	39	(24.1%)
D-dimer (ng/mL; normal range 0.0-500.0)	740	(364-4270)
Increased	77	(64.7%)
ALT (U/L; normal range 9.0-50.0)	31	(18-42)
Increased	28	(17.8%)
AST (U/L; normal range 15.0-40.0)	48.0	(31.3-71.5)
Increased	91	(58.0%)
TBLI (μmol/L; normal range 5.0-21.0)	11.4	(8.0-17.4)
Increased	25	(15.9%)
Albumin (g/L; normal range 40.0-55.0)	32.9	(29.5-35.7)
Decreased	148	(96.1%)
Creatinine (μmol/L; normal range 64.0-104.0)	78.0	(63.6-115.5)
Increased	50	(31.8%)
BUN (mmol/L; normal range 2.8-7.6)	7.9	(5.5-11.9)
Increased	80	(51.0%)
hs-cTnI (pg/mL; normal range 0.0-26.2)	0.07	(0.02-15.28)
Increased	14	(17.9%)
NT-proBNP (pg/mL; normal range 0.0-900.0)	125	(0-1190)
Increased	18	(27.7%)
Blood glucose (mmol/L; normal range 3.9-6.1)	8.3	(6.4-10.1)
Increased	43	(82.7%)
pH (normal range 7.35-7.45)	7.43	(7.35-7.48)
Increased	43	(32.3%)
Decreased	36	(27.1%)

PaO ₂ (mmHg; normal range 80-100)	56	(44-72)
Decreased	107	(80.5%)
PaCO ₂ (mmHg; normal range 35-45)	35	(28-44)
Increased	29	(21.8%)
HCO ₃ ⁻ (mmol/L; normal range 21.4-27.3)	22.1	(18.7-26.0)
Increased	27	(20.6%)
Decreased	56	(42.7%)
Lactate (mmol/L; normal range 0.5-1.6)	2.2	(1.7-3.3)
Increased	92	(76.0%)
Radiological findings		
Unilateral pneumonia	7	(4.3%)
Bilateral pneumonia	155	(95.7%)
Multiple mottling and ground-glass opacity	112	(69.1%)

Data are median (IQR) and no. (%). Increased means over the upper limit of the normal range and decreased means below the lower limit of the normal range. Abbreviation: ALT, alanine aminotransferase; APTT, activated partial prothrombin time; AST, aspartate aminotransferase; BUN, blood urea nitrogen; COVID-19, coronavirus disease 2019; ESR, erythrocyte sedimentation rate; HCO₃⁻, bicarbonate concentration; hs-cTnI, high sensitivity troponin; IL-6, interleukin-6; IQR, interquartile range; NT-proBNP, N-terminal pro-brain natriuretic peptide; PaO₂, partial pressure of oxygen in artery; PaCO₂, partial pressure of carbon dioxide in artery; pH, potential-of-hydrogen; PT, prothrombin time; TBLI, total bilirubin. Denominator used for calculating the percentage may not be the total number because of missing data.

Treatments and complications

Among these 162 fatal cases, 126 cases (77.8%) received antiviral treatment, including oseltamivir (43.2%), ribavirin (29.6%), abidor (21.6%), interferon (13.6%) and Kaletra (4.3%). In addition, 81 of 162 (50.0%) cases received single antiviral drug and 45 (27.8%) were given combined antiviral therapy. Glucocorticoids treatment was applied in 132 (81.5%) cases. The median duration of glucocorticoids treatment was 5 days (IQR: 3–9; range: 1–26), with the median initial dose of 80 mg/qd (IQR: 40–80). Vasoactive drugs were prescribed in 104 (80.0%) cases, and immunoglobulin was used in 63 (38.9%) cases. Moreover, 17 (10.6%) cases received continuous renal replacement therapy (CRRT). Extracorporeal membrane oxygenation (ECMO) was applied in only 2 (1.2%) cases. Finally, 116 (71.6%) cases were admitted to the intensive care unit (ICU) and 137 (85.1%) cases received mechanical ventilation. Respiratory failure or acute respiratory distress syndrome (ARDS) (93.2%) was the most common complication, followed by acute cardiac injury (51.9%), sepsis (37.0%), acute kidney injury (32.1%), septic shock (30.2%) and acute liver injury (22.2%). In addition, 130 cases (80.2%) had multiple complications.

Time-delay distributions

The time-delay distribution was estimated on the basis of the best-fitting Weibull distribution (Figure 2A&B). The median of onset-to-admission interval was 8.0 days (95% CI: 7.1–8.9). The median of admission-to-ICU interval was 8.8 days (95% CI: 7.4–10.3) (Figure 2A). The median duration of admission-to-death and ICU-to-death were 10.4 days (95% CI: 9.2–11.8) and 2.7 days (95% CI: 2.2–3.3), respectively (Figure 2B&C). The duration of admission-to-death among the patients admitted in different hospitals was similar (Figure 2D). The observational time intervals between different events were shown in Supplementary Figure S1.

Table 3. Treatments and complications of COVID-19 fatal cases.

	Fatal cases (n=162)	
	n (%), median (IQR)	
Antiviral drugs		
Oseltamivir	70	(43.2%)
Ribavirin	48	(29.6%)
Abidor	35	(21.6%)
Interferon	22	(13.6%)
Kaletra	7	(4.3%)
Antiviral therapy	126	(77.8%)
Monotherapy	81	(50.0%)
Combined therapy	45	(27.8%)
Antibiotics	154	(95.1%)
Glucocorticoids	132	(81.5%)
Initial dose, median (IQR), mg/qd	80	(40-80)
Duration of therapy, median (IQR), d	5	(3-9)
Intravenous Immunoglobulin therapy	63	(38.9%)
Vasoactive drugs	104	(80.0%)
Oxygen therapy	155	(96.9%)
Non-invasive ventilation	76	(47.2%)
Invasive mechanical ventilation	92	(57.1%)
Duration of mechanical ventilation, median (IQR), d	6	(2-13)
ECMO	2	(1.2%)
CRRT	17	(10.6%)
ICU admission	116	(71.6%)
Length of stay, median (IQR), d	2	(1-5)
Complications		
Any	160	(98.8%)
ARDS or respiratory failure	151	(93.2%)
Acute cardiac injury	84	(51.9%)
Sepsis	60	(37.0%)
Acute kidney injury	52	(32.1%)
Septic shock	49	(30.2%)
Acute liver injury	36	(22.2%)
DIC	25	(15.4%)
Arrhythmia	24	(14.8%)
Gastrointestinal bleeding	13	(8.0%)
ACVD	7	(4.3%)

Data are no. (%) and median (IQR). Abbreviation: ACVD, acute cerebrovascular disease; ARDS, acute respiratory distress syndrome; COVID-19, coronavirus disease 2019; CRRT, continuous renal replacement therapy; DIC, disseminated intravascular coagulation; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; IQR, interquartile range. Denominator used for calculating the percentage may not total number because of missing data.

Discussion

The elderly and males who are vulnerable population of deaths caused by SARS-CoV-2 infection have been noted in some studies⁶⁻¹². In our study, we observed a greater number of men than women in the fatal cases with SARS-CoV-2 infection. The median age of the fatal cases was 69.5 years and the cases aged older than 60 years old accounted for more than 80%, which is consistent with the previous study⁸. Nevertheless, the 20% of fatal cases less than 60 years old can not be ignored, the death cause by COVID-19 might occurred in any age. Additionally, more than 60% of the fatal cases infected by COVID-19 had chronic underlying diseases, mainly hypertension, diabetes, coronary heart disease, and renal insufficiency, which is also in line with previous studies^{7,8,10,11}. Although co-morbidities are risk factors for poor outcome, we observed 59 cases (36.4%) who had died without any co-morbidity. Another important finding is that a total of 29 (18.1%) patients with a moderate condition at admission finally died during hospitalization. Compared to severe or critical cases, most of the moderate cases had the history of hypertension or chronic lung disease co-morbidities. Although it has been suggested that smoking history has strong predictive ability for mortality of viral pneumonia¹³, our study found that more than 90% of deaths were non-smokers. In a recent study, 85.4% of patients with COVID-19 were never smoked¹⁴. Therefore, the smoking history was not a typical risk factor for COVID-19 prognosis.

The most common laboratory abnormalities observed in the present study were hypoalbuminemia, hyperglycemia, hypoxemia, hyperlactacidemia, lymphocytopenia, hypohemoglobin, and increased D-dimer. These laboratory abnormalities are similar to those previously observed in patients with SARS-CoV-2 infection^{6-11,14-18}. In detail, we found that 96.1% of fatal cases had hypoalbuminemia, which has been proven to be associated with mortality in critical patients¹⁹. Lymphocytopenia occurred in more than 70% of patients in our study, a finding that was consistent with the results of recent reports^{6,7,10,11,14,15}. About 64.7% of patients with COVID-19 had increased D-dimer levels. High levels of D-dimer have a reported association with 28-day mortality in patients with infection or sepsis identified in the emergency department²⁰. Increased IL-16 may be related to cytokine storm induced by SARS-CoV-2 infection, but only a few cases had been tested for IL-6 expressions in this study. In the later stages of the disease, majority of patients (98.8%) died with pulmonary and extrapulmonary organ damage. Major critical complications during hospitalization included

respiratory failure or ARDS, acute cardiac injury, sepsis, acute kidney injury and septic shock in our study, which is slightly different from those reported in recent studies^{7,8,11}.

The efficacy of antiviral treatment for SARS-CoV-2 infection is still under evaluation^{21,22}. In our study, 126 (77.8%) patients received antiviral treatment, including oseltamivir (43.2%), ribavirin (29.6%), abidor (21.6%), interferon (13.6%), and kaletra (4.3%). Nearly two-thirds of the patients were treated with a single antiviral drug, and more than a third of patients received combined antiviral therapy. In addition, the efficacy of corticosteroids for the treatment of COVID-19 pneumonia is still uncertain²³. Some experts recommended short courses of corticosteroids at low-to-moderate dose, used prudently, for critically ill patients with COVID-19 pneumonia²⁴. In this study, most patients (81.5%) were given glucocorticoids treatment. In addition, our study showed that most patients received treatments of vasoactive drugs and oxygen therapy, and the proportion of intravenous Immunoglobulin therapy was relatively small, which is slightly different from those in the recent reports^{7,8,11}.

The median time interval between the hospital admission to mechanical ventilation was 3 days. Nevertheless, 50% of cases was admitted to ICU in 8 days after hospital admission. The big time lag between mechanical ventilation and ICU admission might represent the shortage of beds in ICU. A previous study that was conducted in the beginning of COVID-19 outbreak showed a median duration from ICU admission to death was 7 days¹⁰. However, our study showed this median duration was much shorter using estimation of Weibull distribution, only 2.7 days. This shorter median duration of ICU stay for COVID-19 cases before death also confirmed the shortage of ICU beds with the dramatical increase of COVID-19 incidence. The patients could not be timely admitted to ICU for a best case management in the early stage of the serious deterioration. A recent study by Du *et al.* of 85 fatal cases showed the median duration from hospital admission to death was 5 days⁷. A longer duration of hospital stay for COVID-19 cases before death was observed in our study. Additionally, the survival time of COVID-19 cases in different levels of hospitals were similar. This could be explained by the standardized care for COVID-19 cases following NHC guideline in these hospitals. Moreover, the assistance of medical team and medical instruments from other cities may minimized the differences in human resources and equipments between hospitals.

Our study has some limitations. First, this study is only based on the fatal cases of COVID-19. A further study including the survival and non-survival cases of COVID-19 with a large simple size will provide more evidences for case management. Second, the patients who died at the hospital after a long stay had a lower probability to be observed at the date of last follow-up (i.e. March 10, 2020), especially those who were admitted shortly before the date of last follow-up. Therefore, the delays reported relating to Figure 2 are somehow under-estimated. Third, we found in our descriptive analyses that the fatal outcome was occurred in moderate cases, younger cases, even in the cases without co-morbidity. A case-control or cohort study should be conducted in the future to better identify the predictive factors for recognizing the patients at high risk of death in early stage of hospital admission.

In conclusion, a considerable part of young cases of COVID-19 without co-morbidity and in a moderate condition at admission developed also the fatal outcome. With our limited knowledge on COVID-19, it is a big challenge for the clinical physicians to early recognize the patients at high risk of death. In addition, a standard case management strategy might guarantee the same treatment effectiveness of COVID-19 cases who admitted in different levels of hospital.

Methods

Study design, setting and participants

This is a retrospective study conducted in five following hospitals in Wuhan, China: Zhongnan Hospital of Wuhan University, the First People's Hospital of Jiangxia District, Wuhan Third Hospital, Union Jiangbei Hospital, and Wuhan No.7 Hospital. All these hospitals were designated for COVID-19 treatment. We included the fatal cases of COVID-19 from these hospitals between Dec 30, 2019 and Mar 12, 2020 for analysis. The case of COVID-19 was diagnosed according to the guidelines of the National Health Commission (NHC) of China²⁵. This study was approved by the Medical Ethics Committee of the five hospitals.

Data Collection

The demographic data, signs and symptoms, vital signs, smoking history, date of illness onset, date of hospital and ICU admission, co-morbidities, laboratory findings, CT scans, treatments and complications of fatal cases were retrieved from the electric medical records.

Data were documented on a pre-designed data collection form. All data were checked by two independent physicians, and a third expert made a final decision when disagreements occurred.

Fever was defined as axillary temperature of at least 37.3°C. ARDS was determined according to the Berlin Definition²⁶. Sepsis and septic shock were diagnosed according to the 2016 Third International Consensus Definition for Sepsis and Septic Shock²⁷. Acute kidney injury was diagnosed according to the KDIGO clinical practice guidelines²⁸, and acute cardiac injury was diagnosed by increased serum cardiac biomarkers. Disseminated intravascular coagulation (DIC) was defined according to the guidelines of the Scientific Subcommittee on Disseminated Intravascular Coagulation of the International Society on Thrombosis and Haemostasis²⁹. The disease severity of COVID-19 case at hospital admission was defined as mild, moderate, severe and critical according to the guidelines of the NHC of China (trial version 6.0)²⁵. The date of illness onset was defined as the first day in which symptoms (e.g., fever, cough, chest distress, fatigue, etc.) appeared.

Laboratory testing for SARS-CoV-2

SARS-CoV-2 laboratory test assays were based on the recommendation of WHO³⁰. The throat swabs were collected from the suspected cases of COVID-19 and immediately placed into sterile tubes containing 3 ml of viral transport media. Throat swabs RNA was extracted and tested by real-time reverse-transcription-polymerase-chain-reaction (RT-PCR) with SARS-CoV-2 specific primers and probes. Two target genes, including open reading frame 1ab (ORF1ab) and nucleocapsid protein (N), were simultaneously amplified and tested during the real-time RT-PCR. The real-time RT-PCR assay was performed using a SARS-CoV-2 nucleic acid detection kit according to the manufacturer's instructions (DAAN Gene Co., Ltd of Sun Yat-Sen University, Guangzhou, China) as previously described¹⁵.

Statistical Analysis

Median and IQR were used to describe the characteristics of the continuous variables. The number and percentage were used for describing the categorical variables. We used the survival analysis techniques to estimate time-delay distributions, including illness onset to hospital admission, illness onset to ICU admission, hospital admission to ICU admission, illness onset to death, hospital admission to death, and ICU admission to death. We compared alternative parametric distributions, including gamma, Weibull and lognormal distributions, with non-parametric estimates, and selected the best parametric distribution on the basis of Chi-Squared Goodness-of-Fit test. Kaplan-Meier analysis performed for survival time from the illness onset, hospital admission or ICU admission. The Kruskal-Wallis test was used to compare the time intervals between the different events to death, and the time intervals between the hospital admission to death in different hospitals. The Kruskal-Wallis test was also adopted to examine the difference among different disease severity at admission for continuous and ranked variables. Frequency rates for categorical variables were compared using the Chi-square test. All the analyses were performed with the use of R software (version 3.6.3, R Foundation for Statistical Computing).

Declarations

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Authors' contributions

Z.Z., W.X., Q.H. and Y.Z. conceived and designed the study. Q.F., J.G., L.Y., S.F., A.L., J.X., M.M. and Z.H. performed data extraction from the electric medical records system. G.D., R.L., J.Y., S.L., M.Y., P.W., X.X. and X.Z. performed data analysis and figure illustration. X.Z., G.D. and W.X. discussed the data and wrote the manuscript. Q.H., Y.Z. and Z.Z. supervised the study. All authors approved the final draft for submission.

Competing interests

The authors declare no competing interests.

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Additional Information

Supplementary information

Table S1. General characteristics of COVID-19 fatal cases in different disease severity at admission.

Figure S1. Timeline of COVID-19 fatal cases since onset of illness. The appropriate number of cases were given under the corresponding event. CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; IQR, interquartile range.

Figures

Figure 1

Age distribution of COVID-19 fatal cases. COVID-19, coronavirus disease 2019.

Figure 2

Time-delay distributions and Kaplan-Meier analysis of time-delay for fatal cases of COVID-19. The estimated distributions of times from illness onset to hospital or ICU admission, and from hospital admission to ICU admission are shown in Panel A. The estimated distributions of times from illness onset, hospital or ICU admission to death are shown in Panel B. The Kaplan-Meier analysis of time from illness onset, hospital or ICU admission to death are shown in Panel C. The Kaplan-Meier analysis of time from hospital admission to death by different hospitals in which the cases admitted are shown in Panel D. The shades correspond to the 95% confidence intervals of each curve. COVID-19, coronavirus disease 2019.

Supplementary Files

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