Clinical characteristics of a group of deaths with COVID-19 pneumonia in Wuhan, China: retrospective case series

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Abstract

Background: With the widespread outbreak of novel coronavirus diseases 2019(COVID-19), more and more death cases were reported, however, limited data are available for the patients who died. We aimed to explore the clinial characteristics of deaths with COVID-19 pneumonia

Methods: We abstracted and analyzed epidemiological, demographic, clinical, and laboratory data from 83 death cases with COVID-19 pneumonia in East hospital of Wuhan university Renmin hospital,between January 26, 2020, and February 28, 2020.

Results: Of the 83 deaths, none was the medical staff. The mean age was 71.8 years (SD 13.2; range, 34-97 years) and 53(63.9%) were male. The median from onset to admission was 10 days (IQR 7-14: range, 2-43 days), to death was 17days (IQR 14-21: range, 6-54 days). Most deaths (66[80%]) had underlying comorbid diseases, the most of which was hypertension [47(57%)]. The main initial symptoms of these 83 deaths were shortness of breath(98.8%), fever(94%) and myalgia or fatigue(90.4%). Laboratory analyses showed the lymphocytopenia in 69(83%) deaths, hypoalbuminemia in 77(93%) deaths, the elevation of lactate dehydrogenase in 79(95%) deaths, procalcitonin in 69(83%) deaths and C-reactive protein in 79(95%) deaths. All 83 patients received antiviral treatment, 81(97.6%) deaths received antibiotic therapy, and 54(65.1%) deaths received glucocorticoid therapy and 20(24.1%) patients received invasive mechanical ventilation.

Conclusion: Most of the deaths with COVID-19 pneumonia were elderly patients with underlying comorbid diseases, especially those over 70 years of age. The time of death was mostly 15-21 days after the onset of the disease. More care should be given to the elderly in the further prevention and control strategies of COVID-19.

Background

The novel coronavirus diseases 2019(COVID–19) first reported in Wuhan, Hubei province, China[1, 2]. It then spread widely to other regions of China and 24 other nations[3, 4]. With the widespread outbreak of COVID–19, more and more cases of death were reported[5–7]. As of February 11, 2020, China had confirmed 44672 cases of COVID–19, 1023 of them died (2.3%), according to a report by the Chinese CDC.[8]

At present, the early specific management of patients to reduce mortality has become an emergent issue confronting the current epidemic situation[9, 10]. The previous study has reported the features of severe cases admitted to ICU with COVID–19 pneumonia[11]. However, limited data are available until now for the patients who died, little is known about clinical features of deaths with COVID–19 pneumonia.

In this study, we retrospectively collected and described detailed epidemiological, demographic, clinical, and laboratory characteristics of 83 deaths with COVID–19 pneumonia who had been admitted to east

hospital Wuhan University Renmin Hospital, which was one of the first designated hospitals in Wuhan to admit severe patients with COVID–19.

Methods

Study design and patients

This is a single-center retrospective study. We reviewed all patients with COVID–19 pneumonia who were admitted to East Hospital of Wuhan University Renmin hospital as of February 28, 2020, and collected data on death cases in hospital. East Hospital of Wuhan University Renmin hospital located in Wuhan, Hubei Province, China, was designated as one of the first hospitals to admit severe adult patients with COVID–19 pneumonia by government. The diagnostic standard of COVID–19 pneumonia is based on the 4th edition protocole of the New Coronavirus Pneumonia Prevention and Control Program issued by the National Health Commission of Republic of China[12].

This study protocol complied with the Medical Ethical Committee of Wuhan University Renmin hospital (No.WDYR2020-k050). Written informed consent was waived due to the rapid emergence of this infectious disease.

Data collection

Several investigators reviewed the electronic medical record system of the hospital, and abstracted epidemiological, demographic, clinical, and laboratory data from death cases with COVID–19 pneumonia as of February 28, 2020. The other two researchers reviewed and checked the data collected. The investigators directly contacted their families to refine the data if some epidemiological date of patients were not available in the medical record.

Nasopharyngeal swabs were obtained from all patients at admission. All samples were processed at the Department of Clinical Laboratory of Wuhan university Renmin Hospital. COVID–19 was confirmed by Real-time polymerase chain reaction testing according to WHO guidelines for Laboratory testing[13]. Positive confirmed patients with COVID–19 infection were defined as at least 2 positive test results.

Statistical analysis

Continuous variables are expressed as the means ± standard deviations (SD) if they are normally distributed or medians (interquartile ranges, IQR) if they are not. Categorical variables are expressed as frequencies and percentages. All statistical analysis was performed with SPSS, version 25.0 (SPSS Inc., Chicago, IL, USA).

Results

As of February 28, 2020, 83(5.7%) of the 1439 patients with COVID–19 pneumonia admitted to the hospital, died in hospital. None of the 83 deaths were medical staff, and there was no definite exposure history of patients with suspected or confirmed COVID–19.

The mean age was 71.8 years (SD 13.2; range, 34–97 years), including 26 patients over 80 years (31%) and 2 patient under 40 years (2%). Among the deaths, 53(63.9%) were male. The initial symptoms of these 83 patients were shortness of breath(98.8%), fever(94%), myalgia or fatigue(90.4%), anorexia(82%), cough(60.2%), hemoptysis(6%), pharyngalgia(6%), headache(3.6%), nausea or vomiting(2.4%) and diarrhea(4.8%) *(Table 1).*

Onset-to-admission interval of the 83 deaths was between 2 and 43 days (median 10 days, IQR 7–14), most of them were 6–10 days (43%). Onset-to-death interval was between 6 and 54 days (median 17 days, IQR 14–21), and most of them were 15–21 days for 56% of women and 49% of men *(Table 2). Figure 1* showed the date distribution of illness onset in all 83 patients. As described in this figure, the most dates of illness onset are between January 20 and January 28, 2020.

Of the 83 deaths, 66 patients (80%) had chronic comorbidities, the most of which was hypertension(57%), followed by cardiovascular disease(31%), diabetes (26%), cerebrovascular disease(17%), chronic lung disease(19.3%), chronic renal disease (6%), malignancy (6%) and chronic liver disease (4%) *(Table 3).*

The main laboratory findings of the deaths on admission were shown in *Table 4.* The results of the blood count showed that white blood cell count in 5(6%) patients, lymphocyte count in 69(83%) patients, hemoglobin in 34(41%) patients, and platelets in 24(29%) patients were below the normal range. In addition, white blood cell count in 34(41%) patients, and monoclear leucocyte in 16(19%) patients were above the normal range.

On admission, many patients had an abnormal liver function and renal function. Aspartate aminotransferase in 57% patients, gamma-glutamyl transpeptidase in 49% patients, serum creatinine in 47% patients and blood urea nitrogen in 53% patients were above the normal range. Albumin was lower than the normal level in most patients 93%. Lactate dehydrogenase increased in 95% patients. Most patients have abnormal coagulation function, which showed the elevation of D-dimer in 94% patients, the extension of Prothrombin time in 43% patients and Activated partial thromboplastin time in 33% patients. Moreover, procalcitonin (83%) and C-reactive protein 95%) increased above the normal range in most patients.

Each patient performed a chest CT scan on admission, and pneumonia was confirmed in all 83 patients, and 71 patients were involved in the bilateral lung (Table 5). Multiple patchy ground-glass shadows were the main feature in the chest CT of most patients. The typical manifestation is the patchy ground-glass shadow in the lung CT.

In drug treatment, all 83 patients received antiviral therapy for 5–10 days, and all of them received abidole, 58 received oseltamivir, 16 received ribavirin, 4 received lopinavir and ritonavir. Of 83 patients,

81(97.6%) patients received antibiotics therapy, 54(65.1%) patients received glucocorticoid therapy and 39 patients received intravenous immunoglobulin therapy. In non-drug treatment, 6(7.3%) patients received continuous replacement therapy due to severe renal dysfunction, 20(24.1%) patients received invasive mechanical ventilation, 1(1.2%) patients were given extracorporeal membrane oxygenation treatment(ECOM). (*Table 5)*..

Discussion

This retrospective study described the epidemiological and clinical characteristics of 83 deaths with COVID–19 pneumonia. To my knowledge, our study is the first epidemiological investigation, whose subjects were all patients with COVID–19 pneumonia who died.

In this study, the median of the onset-to-admission interval was longer than that of patients in the previous two studies[11, 14]. Most patients were hospitalized more than 6 days after the onset of the disease, and the longest was 43 days. Two factors likely contributed to the interval. Fisrt some patients have no severe symptoms in the early stage and it took more for home isolation and community treatment. Second, due to the COVID–19 outbreak, the isolation ward of the hospital may have been under capacity in the initial. Most of the patients who died in the 15–21days after the onset of the disease, both male and female. This result indicate that the third week may be a period of high risk of death for critically ill patients with COVID–19.

Most of the deaths with COVID–19 pneumonia were elderly patients especially those over 70 years of age, and male patients. These are consistent with a recent study[10]. The cases of COVID–19 in pregnant women have been mentioned in previous studiy[15]. Of 29 pregnant women with COVID–19 in the hospital, there are no deaths so far.

The proportion of patients with comorbidities was higher than previous studies in patients with COVID–19[10, 11, 14, 16]. The most common comorbidities were hypertension in our study, which was diabetes in two previous cohort studies of Middle Eastern respiratory syndrome coronavirus (MRSE-Cov) infection and severe acute respiratory syndrome coronavirus(SARS-CoV) infection[17, 18]. We observed that the majority of patients who died were also geriatric patients and those suffering from chronic comorbidities. However, some healthy people(22%) died without complications, which were an indication of the high pathogenicity of COVID–19. The initial clinical symptoms of patients infected with COVID–19 were nonspecific. There were no significant differences in the types of initial symptoms between the deaths in our study and the recently published studies[[11, 14, 16, 19]. However, the first three symptoms in our study were shortness of breath, fever, Myalgia or fatigue. A small number of patients initially presented with gastrointestinal symptoms, such as anorexia, nausea, vomiting, and diarrhoea, which were mentioned in previous studies[14, 16].

Most of the patients in our study developed acute respiratory failure including ARDS, fatal infection, abnormal coagulation and eventually multiple organ failure, except for six who died of acute myocardial infarction. As a newly identified disease, litter is known about the pathogenic mechanism of COVID–19.

Most of the patients who died had abnormal coagulation. Increased inflammatory markers such as procalcitonin and C-reactive, lymphopenia were a common characteristic in the patients. This series of changes is a manifestation of the immune response and maybe be a factor in poor prognosis[11, 14, 18]. In a recent fatal case report, typical features of inflammation were observed in the pulmonary pathology of the patient, whose pathological section showed interstitial mononuclear inflammatory infiltrates, dominated by lymphocytes[20]. These pathological characteristics greatly resemble those of MRSE-Cov infection and SARS-CoV infection[20–22].

Until now, no drugs have been found to be specifically effective against coronaviruses. Of the 83 patients in our study, each patient received abidol, and some patients were treated with oseltamivir, ganciclovir, lopinavir and ritonavir, but none of them had a definite therapeutic effect. In addition, radcivir is an unlisted nucleotide drug whose broad-spectrum antiviral activity has been confirmed in animal models[23, 24]. It may be a potential effective drug for patients with COVID–19.[25] Two randomized controlled clinical trials (NCT04252664; NCT04257656) to assess the safety and efficacy of radcivir are is currently underway in patients hospitalized with COVID–19 pneumonia.

The patients in this study were generally had associated with a secondary bacterial infection, followed by sepsis and septic shock. 97.6% of the patients were treated with antibiotics based on abnormal inflammatory markers and bacterial culture results. In patients with SARS and MERS, the effect of glucocorticoid therapy on prognosis is Controversial[26, 27]. However, severe patients with COVID–19 may be beneficial from glucocorticoid therapy to prevent ARDS development, based on recent studies[16, 20]. 65.1% of the patients in this study received glucocorticoid therapy. In the study, 63 patients did not receive invasive mechanical ventilation, 41 of them declined invasive mechanical ventilation, and the other 22 for unknown reasons.

Our study has several limitations. First of all, the study had a limited number of cases, with only 83 deaths. However, to our knowledge, very few case series of deaths have been reported, the data is a valuable demonstration of characteristics of deaths with COVID–19 pneumonia in the early period of exponential growth. Secondly, some data such as cytokines (eg, IL2, IL4, IL6, IL10, TNF, IFN γ) were absent in patients admitted early, which were related to lung injury in previous studies SARS-CoV and MERS-CoV[28, 29]. We will routinely observe the changes of cytokines of patients in further study. Thirdly, data on all patients with COVID–19 pneumonia in the hospital during the same period were not fully available at the time of our analysis. However, this is a series of study designs and the patients will continue to be followed up.

Conclusions

This single-center retrospective case series early shows the epidemiological and clinical characteristics of deaths with COVID–19 pneumonia. Most of the deaths with COVID–19 pneumonia were elderly patients with underlying comorbid diseases, especially those over 70 years of age. The time of death was mostly

15–21 days after the onset of the disease. More care should be given to the elderly in the further prevention and control strategies of COVID–19.

Abbreviations

novel coronavirus diseases: 2019(COVID–19); SD: standard deviations; IQR: interquartile ranges; CRRT: continuous renal replacement therapy; ECMO: extracorporeal membrane oxygenation; MRSE-Cov: Middle Eastern respiratory syndrome coronavirus; SARS-CoV: severe acute respiratory syndrome coronavirus; WHO: World health organization

Declarations

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Authors' contributions

TY, YG and QC contributed equally to this article. ZCL and ZHZ conceived and designed the study. YG, QC, YC, JSL, CPH, CH, JP, JJW, YQZ, JY, and JHT collected the data. YG, and QC performed the statistical analysis. BP took responsibility for obtaining ethical approval. TY were the main contributors in writing the first draft. YG and QC revised the final manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The data will be available from the corresponding author on a reasonable request. After the publication of this study, the participant data without names an identifiers will be made available after approval from the corresponding authors and Wuhan University Renmin Hospital.

Ethics approval and consent to participate

This study protocol complied with the Medical Ethical Committee of Wuhan University Renmin hospital (No.WDYR2020-k050). Written informed consent was waived due to the rapid emergence of this infectious disease with the permission of the Medical Ethical Committee.

Consent for publication

Not applicable.

Competing interests

We declare that we have no conflicts of interest.

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Tables

Table 1: Demographics and clinical characteristics of 83 deaths with COVID-19 pneumonia

Characteristics	Patients(n=83)
Demographic factors	
Age(years) Mean (SD) ,	71.8(13.2)
<40	2(2%)
40-49	3(4%)
50-59	10(12%)
60-69	15(18%)
70-79	27(33%)
³80	26(31%)
Sex	
Men	53(63.9%)
Women	30(36.1%)
Clinical Characteristics	
Signs and symptoms at onset	
Fever	78(94%)
Myalgia or fatigue	75(90.4%)
Cough	50(60.2%)
pharyngalgia	5(6%)
Headache	3(3.6%)
Haemoptysis	5(6%)
Shortness of breath	81(98.8%)
Anorexia	70(84.3%)
Nausea or Vomiting	2(2.4%)
Diarrhoea	4(4.8%)

Table 2: Key Epidemiologic Variables of 83 deaths with COVID-19 pneumonia

Variable	Patients(n=83)
Onset-to-admission interval	10(7-14)
1-5 d	11(13%)
6-10d	36(43%)
10-15 d	25(30%)
³16 d	11(13%)
Onset-to-death interval	17(14-21)
Women	16(14-20)
1-7d	1(3%)†
8-14 d	8(27%)†
15-21d	15(50%)†
22-28 d	4(13%)†
³29 d	2(7%)†
Men	18(14-23)
1-7d	2(4%)□
8-14 d	13(25%)□
15-21d	24(45%)□
22-28 d	11(21%)□
³29 d	3(6%)□

†, Proportion of women; □, Proportion of men

Table 3: Characteristics of comorbidity of 83 deaths with COVID-19 pneumonia

	death, n(%)
Comorbidities	66(80)
Hypertension	47(57)
Diabetes	14(26)
Cardiovascular	26(31)
Cerebrovascular disease	14(17)
Malignancy	5(6)
Chronic lung disease	16(19.3)
Chronic renal disease	5(6)
Chronic liver disease	3(4)
Number of comorbidities	
1.00	28(34)
2.00	17(21)
3.00	14(17)
4.00	6(7)
5.00	1(1)

Table 4: Laboratory findings of 83 deaths with COVID-19 pneumonia

	Normal Range	Patients(n=83)
White blood cell count,× 10⁹/L	3.5-9.5	9.1(4.7)
Decreased		5(6%)
Increased		34(41%)
Neutrophil count,× 10⁹/L	1.8-6.3	6.9(4.4-11.5)
Increased		49(59%)
Lymphocyte count, × 10⁹/L	1.1-3.2	0.6 (0.4-0.9)
Decreased		69(83%)
Mononuclear leucocyte, × 10⁹/L	0.1-0.6	0.4(0.3-0.5)
Increased		16(19%)
Haemoglobin ,g/L	Men：130.0-175.0；Women：115-150	116 (104-121)
Decreased		34(41%)
Platelets ,× 10⁹/L	125.0-350.0	166(72)
Decreased		24(29%)
Total bilirubin ,μmol/L	0.0-23.0	14.1(9.8-19.9)
Increased		16(19%)
Direct bilirubin, μmol/L	0.0-8.0	5.6(4.2-9.3)
Increased		29(35%)
Aspartate aminotransferase ,U/L	15.0-40.0	43(28-62)
Increased		47(57%)
Alanine aminotransferase ,U/L	7.0-40.0	25(19-49)
Increased		25(30%)
Alkaline phosphatase, U/L	50-135	76(59-105)
Increased		12(14%)
Gamma-glutamyl transpeptidase, U/L	7-45	44(23-75)
Increased		41(49%)
Albumin, g/L	40-55	33.7(4.1)
Decreased		77(93%)
Globulin, g/L	20-40	25.6(22.6-29.0)

Decreased		4(5%)
Increased		2(2%)
Lactate dehydrogenase ,U/L	120-250	493(362-682)
Increased		79(95%)
serum creatinine ,μmol/L	41-81	77(55-113)
Increased		39(47%)
Blood urea nitrogen ,mmol/L	3.1-8.8	9.36(5.50-16.00)
Increased		44(53%)
Prothrombin time ,s	9.0-13.0	12.9(12.2-14.2)
Increased		36(43%)
Activated partial thromboplastin time ,s	25.0-31.3	29.1(27.1-32.5)
Increased		27(33%)
D-dimer ,mg/L	0.0-0.55	4.68(1.09-18.00)
Increased		78(94%)
Procalcitonin ,ng/mL	0.0-0.1	0.23(0.12-0.94)
Increased		69(83%)
C-reactive protein ,mg/mL	0.0-10.0	85(47-180.0)
Increased		79(95%)

Table 5: Chest CT findings and treatment of 83 deaths with COVID-19 pneumonia

	Patients, n(%)
Chest CT characteristics	
Unilateral pneumonia	12(14.5)
Bilateral pneumonia	71(85.5)
Treatment	
Antifungal therapy	2(2.4)
Antibiotic therapy	81(97.6)
Glucocorticoid therapy	54(65.1)
Intravenous immunoglobulin therapy	54(65.1)
CRRT	6(7.3)
Invasive mechanical ventilation	20(24.1)
ECMO	1(1.2)

Abbreviation: CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation.

Figures

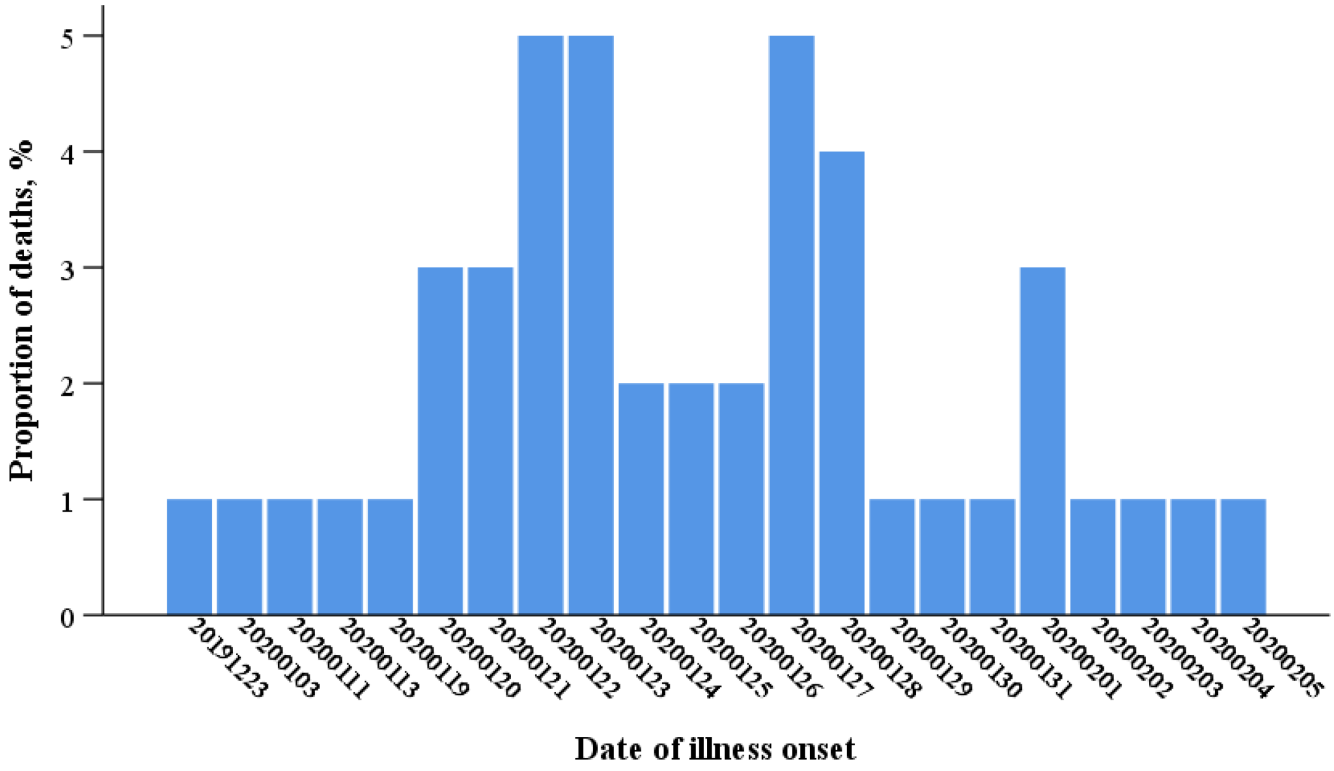

Figure 1. Date of illness onset of 83 deaths with COVID-19 pneumonia

Figure 1

Date of illness onset of 83 deaths with COVID-19 pneumonia