Epidemiological 流行病學

Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study



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MuLBSTA: multilobular infiltration, hypo-lymphocytosis, bacterial coinfection, smoking history, hyper-tension and age.

Summary

Background In December, 2019, a pneumonia associated with the 2019 novel coronavirus (2019-nCoV) emerged in Wuhan, China. We aimed to further clarify the epidemiological and clinical characteristics of 2019-nCoV pneumonia.

retrospective. 回顧性的

Methods In this retrospective, single-centre study, we included all confirmed cases of 2019-nCoV in Wuhan Jinyintan Hospital from Jan 1 to Jan 20, 2020. Cases were confirmed by real-time RT-PCR and were analysed for epidemiological, demographic, clinical, and radiological features and laboratory data. Outcomes were followed up until Jan 25, 2020. demographic 人口統計 radiological 放射學的 chronic 慢性的

Findings Of the 99 patients with 2019-nCoV pneumonia, 49 (49%) had a history of exposure to the Huanan seafood market. The average age of the patients was 55·5 years (SD 13·1), including 67 men and 32 women. 2019-nCoV was detected in all patients by real-time RT-PCR. 50 (51%) patients had chronic diseases. Patients had clinical manifestations of fever (82 [83%] patients), cough (81 [82%] patients), shortness of breath (31 [31%] patients), muscle ache (11 [11%] patients), confusion (nine [9%] patients), headache (eight [8%] patients), sore throat (five [5%] patients), rhinorrhoea (four [4%] patients), chest pain (two [2%] patients), diarrhoea (two [2%] patients), and nausea and vomiting (one [1%] patient). According to imaging examination, 74 (75%) patients showed bilateral pneumonia, 14 (14%) patients showed multiple mottling and ground-glass opacity, and one (1%) patient had pneumothorax. 17 (17%) patients developed acute respiratory distress syndrome and, among them, 11 (11%) patients worsened in a short period of time and died of multiple organ failure.

Distribution

Community

Community

**Community*

Interpretation The 2019-nCoV infection was of clustering onset, is more likely to affect older males with comorbidities, and can result in severe and even fatal respiratory diseases such as acute respiratory distress syndrome. In general, characteristics of patients who died were in line with the MuLBSTA score, an early warning model for predicting mortality in viral pneumonia. Further investigation is needed to explore the applicability of the MuLBSTA score in predicting the risk of mortality in 2019-nCoV infection. Comorbidities 并發症

respiratory呼吸的

Funding National Key R&D Program of China.

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Introduction

Since Dec 8, 2019, several cases of pneumonia of unknown aetiology have been reported in Wuhan, Hubei province, China.¹⁻³ Most patients worked at or lived around the local Huanan seafood wholesale market, where live animals were also on sale. In the early stages of this pneumonia, severe acute respiratory infection symptoms occurred, with some patients rapidly developing acute respiratory distress syndrome (ARDS), acute respiratory failure, and other serious complications. On Jan 7, a novel coronavirus was identified by the Chinese Center for Disease Control and Prevention (CDC) from the throat swab sample of a patient, and was subsequently named 2019-nCoV by WHO.⁴

Coronaviruses can cause multiple system infections in various animals and mainly respiratory tract infections in humans, such as severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS).⁵⁻⁷ Most patients have mild symptoms and good prognosis.

comprehensive 全面 pulmonary oedema肺水腫

So far, a few patients with 2019-nCoV have developed severe pneumonia, pulmonary oedema, ARDS, or multiple organ failure and have died. All costs of 2019-nCoV treatment are covered by medical insurance in China.

At present, information regarding the epidemiology and clinical features of pneumonia caused by 2019-nCoV is scarce.¹⁻³ In this study, we did a comprehensive exploration of the epidemiology and clinical features of 99 patients with confirmed 2019-nCoV pneumonia admitted to Jinyintan Hospital, Wuhan, which admitted the first patients with 2019-nCoV to be reported on.

Methods

Study design and participants

For this retrospective, single-centre study, we recruited patients from Jan 1 to Jan 20, 2020, at Jinyintan Hospital in Wuhan, China. Jinyintan Hospital is a hospital for adults (ie, aged ≥14 years) specialising in infectious diseases. According to the arrangements put in place by

Lancet 2020; 395: 507-13

Published Online January 29, 2020 https://doi.org/10.1016/ S0140-6736(20)30211-7

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Research in context

Evidence before this study

We searched PubMed on Jan 25, 2020, for articles that describe the epidemiological and clinical characteristics of the 2019 novel coronavirus (2019-nCoV) in Wuhan, China, using the search terms "novel coronavirus" and "pneumonia" with no language or time restrictions. Previously published research discussed the epidemiological and clinical characteristics of severe acute respiratory syndrome coronavirus or Middle East respiratory syndrome coronavirus, and primary study for the evolution of the novel coronavirus from Wuhan. The only report of clinical features of patients infected with 2019-nCoV was published on Jan 24, 2020, with 41 cases included.

Added value of this study

We have obtained data on 99 patients in Wuhan, China, to further explore the epidemiology and clinical features of 2019-nCoV. This study is, to our knowledge, the largest case series to date of 2019-nCoV infections, with 99 patients who were transferred to Jinyintan Hospital from other hospitals all

interim 臨時

the Chinese Government, adult patients were admitted centrally to the hospital from the whole of Wuhan without selectivity. All patients at Jinvintan Hospital who were diagnosed as having 2019-nCoV pneumonia according to WHO interim guidance were enrolled in this study. All the data of included cases have been shared with WHO. The study was approved by Jinyintan Hospital Ethics Committee and written informed consent was obtained from patients involved before enrolment when data were collected retrospectively.

demographic人口統計 Procedures

We obtained epidemiological, demographic, clinical, laboratory, management, and outcome data from patients' medical records. Clinical outcomes were followed up to Jan 25, 2020. If data were missing from the records or clarification was needed, we obtained data by direct communication with attending doctors and other healthcare providers. All data were checked by two physicians (XD and YQ).

Laboratory confirmation of 2019-nCoV was done in four different institutions: the Chinese CDC, the Chinese Academy of Medical Science, Academy of Military Medical Sciences, and Wuhan Institute of Virology, Chinese Academy of Sciences. Throat-swab specimens from the upper respiratory tract that were obtained from all patients at admission were maintained in viral-transport medium. 2019-nCoV was confirmed by 即時反轉錄PCR real-time RT-PCR using the same protocol described previously.3 RT-PCR detection reagents were provided by the four institutions. Other respiratory viruses including influenza A virus (H1N1, H3N2, H7N9), influenza B parainfluenza副流感virus, respiratory syncytial virus, parainfluenza virus, adenovirus腺病毒<mark>adenovirus,</mark> SARS coronavirus (SARS-CoV), and MERS

over Wuhan, and provides further information on the demographic, clinical, epidemiological, and laboratory features of patients. It presents the latest status of 2019-nCoV infection in China and is an extended investigation of the previous report, with 58 extra cases and more details on combined bacterial and fungal infections. In all patients admitted with medical comorbidities of 2019-nCoV, a wide range of clinical manifestations can be seen and are associated with substantial

Implications of all the available evidence

The 2019-nCoV infection was of clustering onset, is more likely to affect older men with comorbidities, and could result in severe and even fatal respiratory diseases such as acute respiratory distress syndrome. Early identification and timely treatment of critical cases of 2019-nCoV are important. Effective life support and active treatment of complications should be provided to effectively reduce the severity of patients' conditions and prevent the spread of this new coronavirus in China and worldwide.

endotracheal aspirates氣管內抽取物 coronavirus (MERS-CoV) were also examined with realtime RT-PCR Sputum淡

Sputum or endotracheal aspirates were obtained at admission for identification of possible causative bacteria or fungi. Additionally, all patients were given chest x-rays or chest CT.

Outcomes symptoms症狀 pathogens病原體

We describe epidemiological data (ie, short-term [occasional visits] and long-term [worked at or lived near] exposure to Huanan seafood market); demographics; signs and symptoms on admission; comorbidity; laboratory results; co-infection with other respiratory pathogens; chest radiography and CT findings; treatment received for 2019-nCoV; and clinical outcomes.

Statistical analysis

We present continuous measurements as mean (SD) if they are normally distributed or median (IQR) if they are not, and categorical variables as count (%). For laboratory results, we also assessed whether the measurements were outside the normal range. We used SPSS (version 26.0) for all analyses.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

99 patients with 2019-nCoV were included in this study, two of whom were husband and wife. In total, 49 (49%)

cardiovascular心血管的 cerebrovascular腦血管的 septic shock敗血性休克

patients were clustered and had a history of exposure to the Huanan seafood market. Among them, there were 47 patients with long-term exposure history, most of whom were salesmen or market managers, and two patients with short-term exposure history, who were shoppers. None of the patients were medical staff. Most patients were men, with a mean age of 55.5 years (SD 13·1; table 1). 50 (51%) patients had chronic diseases, including cardiovascular and cerebrovascular diseases, endocrine system disease, digestive system disease, respiratory system disease, malignant tumour, and nervous system disease (table 1).

On admission, most patients had fever or cough and a third of patients had shortness of breath (table 2). Other symptoms included muscle ache, headache,

Patients (n=99) Age, years Mean (SD) 55.5 (13.1) Range 10 (10%) ≤39 40-49 22 (22%) 50-59 30 (30%) 60-69 22 (22%) ≥70 15 (15%) Sex Female 32 (32%) Male 67 (68%) Occupation Agricultural worker 2 (2%) Self-employed 63 (64%) Employee 15 (15%) Retired 19 (19%) Exposure to Huanan seafood market* 49 (49%) Long-term exposure history 47 (47%) Short-term exposure history 2 (2%) Chronic medical illness 50 (51%) Cardiovascular and cerebrovascular diseases 40 (40%) Digestive system disease 11 (11%) Endocrine system disease† 13 (13%) Malignant tumour 1 (1%) Nervous system disease 1 (1%) Respiratory system disease 1 (1%) Admission to intensive care unit 23 (23%) Clinical outcome Remained in hospital 57 (58%) Discharged 31 (31%) 11 (11%) Data are n (%) unless specified otherwise. 2019-nCoV=2019 novel coronavirus. *Long-term exposure is having worked at or lived in or around Huanan seafood market, whereas short-term exposure is having been to Huanan seafood market occasionally, †12 were diabetic.

Table 1: Demographics, baseline characteristics, and clinical outcomes of 99 patients admitted to Wuhan Jinyintan Hospital (Jan 1-20, 2020) with 2019-nCoV pneumonia

confusion, chest pain, and diarrhoea (table 2). Many patients presented with organ function damage, including 17 (17%) with ARDS, eight (8%) with acute renal腎的 respiratory injury, three (3%) with acute renal injury, four (4%) with septic shock, and one (1%) with ventilator-associated pneumonia (table 2). leucocytes白血球

On admission, leucocytes were below the normal range in nine (9%) patients and above the normal range in 24 (24%) patients (table 3). 38 (38%) patients had neutrophils above the normal range. Lymphocytes and Lymphocytes淋巴 haemoglobin were below the normal range in many

haemoglobin血紅蛋白

	Patients (n=99)
Signs and symptoms at admission	
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%)
Diarrhoea	2 (2%)
Nausea and vomiting	1 (1%)
More than one sign or symptom	89 (90%)
Fever, cough, and shortness of breath	15 (15%)
Comorbid conditions	
Any	33 (33%)
ARDS	17 (17%)
Acute renal injury	3 (3%)
Acute respiratory injury	8 (8%)
Septic shock	4 (4%)
Ventilator-associated pneumonia	1 (1%)
Chest x-ray and CT findings	
Unilateral pneumonia	25 (25%)
Bilateral pneumonia	74 (75%)
Multiple mottling and ground-glass opacity	14 (14%)
Treatment	
Oxygen therapy	75 (76%)
Mechanical ventilation	
Non-invasive (ie, face mask)	13 (13%)
Invasive	4 (4%)
CRRT	9 (9%)
ECMO	3 (3%)
Antibiotic treatment	70 (71%)
Antifungal treatment	15 (15%)
Antiviral treatment	75 (76%)
Glucocorticoids	19 (19%)
Intravenous immunoglobulin therapy	27 (27%)
2019-nCoV=2019 novel coronavirus. ARDS=acute r ECMO=extracorporeal membrane oxygenation. CRF replacement therapy.	

Table 2: Clinical characteristics and treatment of patients with

2019-nCoV pneumonia

	Patients (n=99)
Blood routine	
Leucocytes (×10° per L; normal range 3·5–9·5)	7.5 (3.6)
Increased	24 (24%)
Decreased	9 (9%)
Neutrophils (× 10° per L; normal range 1·8-6·3)	5.0 (3.3–8.1)
Increased	38 (38%)
Lymphocytes (×10° per L; normal range 1·1–3·2)	0.9 (0.5)
Decreased	35 (35%)
Platelets (×10° per L; normal range 125·0–350·0)	213.5 (79.1)
Increased	4 (4%)
Decreased	12 (12%)
Haemoglobin (g/L; normal range 130·0–175·0)	129.8 (14.8)
Decreased	50 (51%)
Coagulation function	
Activated partial thromboplastin time (s; normal range $21\cdot0$ – $37\cdot0$)	27·3 (10·2)
Increased	6 (6%)
Decreased	16 (16%)
Prothrombin time (s; normal range 10·5–13·5)	11.3 (1.9)
Increased	5 (5%)
Decreased	30 (30%)
D-dimer (μg/L; normal range 0·0–1·5)	0.9 (0.5-2.8)
Increased	36 (36%)
Blood biochemistry	
Albumin (g/L; normal range 40·0–55·0)	31.6 (4.0)
Decreased	97 (98%)
Alanine aminotransferase (U/L; normal range 9·0-50·0)	39.0 (22.0–53.0)
Increased	28 (28%)
Aspartate aminotransferase (U/L; normal range 15-0-40-0)	34.0 (26.0–48.0)
Increased	35 (35%)
Total bilirubin (µmol/L; normal range 0·0-21·0)	15.1 (7.3)
Increased	18 (18%)
Blood urea nitrogen (mmol/L; normal range 3·6–9·5)	5.9 (2.6)
Increased	6 (6%)
Decreased	17 (17%)
Serum creatinine (µmol/L; normal range 57·0–111·0)	75.6 (25.0)
Increased	3 (3%)
Decreased	21 (21%)
Creatine kinase (U/L; normal range 50·0–310·0)	85.0 (51.0-184.0)
Increased	13 (13%)
Decreased	23 (23%)
Lactate dehydrogenase (U/L; normal range 120·0–250·0)	336-0 (260-0-447-0
Increased	75 (76%)
Myoglobin (ng/mL; normal range 0·0–146·9)	49.5 (32.2-99.8)
	15 (15%)
Increased	12 (12 10)
Increased Glucose (mmol/L; normal range 3·9–6·1)	7.4 (3.4)

(Table 3 continues in next column)

(Continued from previous column)	
Infection-related biomarkers	
Procalcitonin (ng/mL; normal range 0·0–5·0)	0.5 (1.1)
Increased	6 (6%)
Interleukin-6 (pg/mL; normal range 0·0–7·0)	7-9 (6-1-10-6)
Increased	51 (52%)
Erythrocyte sedimentation rate (mm/h; normal range 0·0–15·0)	49.9 (23.4)
Increased	84 (85%)
Serum ferritin (ng/mL; normal range 21·0–274·7)	808-7 (490-7)
Increased	62 (63%)
C-reactive protein (mg/L; normal range 0·0–5·0)*	51.4 (41.8)
Increased	63/73 (86%)
Co-infection	
Other viruses	0
Bacteria	1 (1%)
Fungus	4 (4%)
oata are n (%), n/N (%), mean (SD), and median (IQR). Ipper limit of the normal range and decreased means be the normal range. 2019-nCoV=2019 novel coronavirus 3 patients.	elow the lower limit o

patients (table 3). Platelets were below the normal range in 12 (12%) patients and above the normal range in four (4%). 43 patients had differing degrees of liver function abnormality, with alanine aminotransferase (ALT) or aspartate aminotransferase (AST) above the normal range (table 3); one patient had severe liver function damage (ALT 7590 U/L, AST 1445 U/L). Most patients had abnormal myocardial zymogram, which showed the elevation of creatine kinase in 13 (13%) patients and the elevation of lactate dehydrogenase in 75 (76%) patients, one of whom also showed abnormal creatine kinase (6280 U/L) and lactate dehydrogenase (20740 U/L). Seven (7%) patients had different degrees of renal function damage, with elevated blood urea nitrogen or serum creatinine. Regarding the infection index, procalcitonin was above the normal range in six (6%) patients. Most patients had serum ferritin above the normal range (table 3). 73 patients were tested for C-reactive protein, most of whom had levels above the normal range (table 3).

All patients were tested for nine respiratory pathogens and the nucleic acid of influenza viruses A and B. Bacteria and fungi culture were done at the same time. We did not find other respiratory viruses in any of the patients. Acinetobacter baumannii, Klebsiella pneumoniae, and Aspergillus flavus were all cultured in one patient. A baumannii turned out to be highly resistant to antibiotics. One case of fungal infection was diagnosed as Candida glabrata and three cases of fungal infection were diagnosed as Candida albicans.

According to chest x-ray and CT, 74 (75%) patients showed bilateral pneumonia (75%) with just 25 (25%)

Platelets血小板 liver肝

alanine aminotransferase 丙氨酸轉氨酶

myocardial 心肌的

creatine kinase肌酸激酶

lactate dehydrogenase 乳酸脫氫酶

urea nitrogen尿素氮
serum creatinine血清肌酐
procalcitonin降鈣素原
serum ferritin血清鐵蛋白

Klebsiella pneumoniae 肺炎克雷伯菌

Acinetobacter baumannii 鮑曼不動桿菌

cultured 養成的

Candida glabrata 光滑念珠菌

Aspergillus flavus 黃曲霉

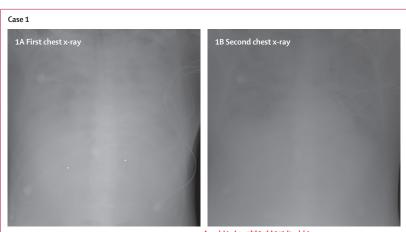
Candida albicans 白色念珠菌 patients showing unilateral pneumonia (table 2). 14 (14%) patients showed multiple mottling and ground-glass opacity (table 2; figure). Additionally, pneumothorax occurred in one (1%) patient.

All patients were treated in isolation. 75 (76%) patients received antiviral treatment, including oseltamivir (75 mg every 12 h, orally), ganciclovir (0·25 g every 12 h, intravenously), and lopinavir and ritonavir tablets (500 mg twice daily, orally). The duration of antiviral treatment was 3–14 days (median 3 days [IQR 3–6]).

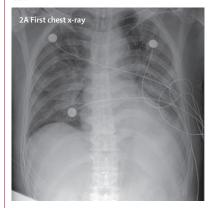
Most patients were given antibiotic treatment (table 2); 25 (25%) patients were treated with a single antibiotic and 45 (45%) patients were given combination therapy. The antibiotics used generally covered common pathogens and some atypical pathogens; when secondary bacterial infection occurred, medication was administered according to the results of bacterial culture and drug sensitivity. The antibiotics used were cephalosporins, quinolones, carbapenems, tigecycline against methicillin-resistant *Staphylococcus aureus*, linezolid, and antifungal drugs. The duration of antibiotic treatment was 3–17 days (median 5 days [IQR 3–7]). 19 (19%) patients were also treated with methylprednisolone sodium succinate, methylprednisolone, and dexamethasone for 3–15 days (median 5 [3–7]). invasive 受入性的

13 patients used non-invasive ventilator mechanical 通風 ventilation for 4–22 days (median 9 days [IQR 7–19]). Four patients used an invasive ventilator to assist ventilation for 3–20 days (median 17 [12–19]). The ventilator adopted P-SIMV mode, the inhaled oxygen concentration was 35–100%, and the positive endexpiratory pressure was 6–12 cm H₂O. All four patients were still using ventilators at data cutoff. Moreover, nine (9%) patients received continuous blood purification due to renal failure and three (3%) patients were treated with extracorporeal membrane oxygenation (ECMO; table 2). 葉克膜

By the end of Jan 25, 31 (31%) patients had been discharged and 11 (11%) patients had died; all other patients were still in hospital (table 1). The first two deaths were a 61-year-old man (patient 1) and a 69-year-old man (patient 2). They had no previous chronic underlying disease but had a long history of smoking. Patient 1 was transferred to Jinvintan Hospital and diagnosed with severe pneumonia and ARDS. He was immediately admitted to the intensive care unit (ICU) and given an 插管的 intubated ventilator-assisted breathing therapy. Later, the patient, having developed severe respiratory failure, heart 敗血症 failure, and sepsis, experienced a sudden cardiac arrest on the 11th day of admission and was declared dead. Patient 2 had severe pneumonia and ARDS after admission. The patient was transferred to the ICU and given ventilator-assisted breathing, and received antiinfection and ECMO treatment after admission. The patient's hypoxaemia remained unresolved. On the ninth day of admission, the patient died of severe pneumonia, septic shock, and respiratory failure. The intervals



Staphylococcus aureus金黃色葡萄球菌





case 3 inhaled吸入



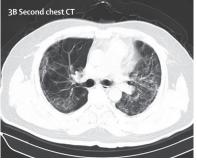


Figure: Chest x-rays and chest CTs of three patients

Case 1: chest x-ray was obtained on Jan 1 (1A). The brightness of both lungs was diffusely decreased, showing a large area of patchy shadow with uneven density. Tracheal intubation was seen in the trachea and the heart shadow outline was not clear. The catheter shadow was seen from the right axilla to the mediastinum. Bilateral diaphragmatic surface and costal diaphragmatic angle were not clear, and chest x-ray on Jan 2 showed worse status (1B). Case 2: chest x-ray obtained on Jan 6 (2A). The brightness of both lungs was decreased and multiple patchy shadows were observed; edges were blurred, and large ground-glass opacity and condensation shadows were mainly on the lower right lobe. Tracheal intubation could be seen in the trachea. Heart shadow roughly presents in the normal range. On the left side, the diaphragmatic surface is not clearly displayed. The right side of the diaphragmatic surface was light and smooth and rib phrenic angle was less sharp. Chest x-ray on Jan 10 showed worse status (2B). Case 3: chest CT obtained on Jan 1 (3A) showed mass shadows of high density in both lungs. Bright bronchogram is seen in the lung tissue area of the lesion, which is also called bronchoinflation sign. Chest CT on Jan 15 showed improved status (3B).

cardiac arrest心臟驟停 hypoxaemia低氧血症 體或體內器官的 損傷

lymphopenia 淋巴細胞減少症 hypertension

civets麝香貓 dromedary camels 單峰駱駝 virions病毒體

intravenous 靜脈

exacerbations惡化

susceptibility

between the onset of symptoms and the use of ventilatorassisted breathing in the two patients were 3 days and 10 days, respectively. The course of the disease and lung lesions progressed rapidly in both patients, with both developing multiple organ failure in a short time. The deaths of these two patients were consistent with the MuLBSTA score, an early warning model for predicting mortality in viral pneumonia.8

Of the remaining nine patients who died, eight patients had lymphopenia, seven had bilateral pneumonia, five were older than 60 years, three had hypertension, and one was a heavy smoker.

Discussion

This is an extended descriptive study on the epidemiology and clinical characteristics of the 2019-nCoV, including data on 99 patients who were transferred to Jinyintan Hospital from other hospitals across Wuhan. It presents the latest status of the 2019-nCoV infection in China and adds details on combined bacterial and fungal infections.

Human coronavirus is one of the main pathogens of respiratory infection. The two highly pathogenic viruses, SARS-CoV and MERS-CoV, cause severe respiratory syndrome in humans and four other human coronaviruses (HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-HKU1) induce mild upper respiratory disease. The major SARS-CoV outbreak involving 8422 patients occurred during 2002-03 and spread to 29 countries globally.9,10 MERS-CoV emerged in Middle Eastern countries in 2012 but was imported into China. 11,12 The sequence of 2019-nCoV is relatively different from the six other coronavirus subtypes but can be classified as betacoronavirus. SARS-CoV and MERS-CoV can be transmitted directly to humans from civets and dromedary camels, respectively, and both viruses originate in bats, but the origin of 2019-nCoV needs further investigation.¹³⁻¹⁵ 2019-nCoV also has enveloped virions that measure approximately 50-200 nm in diameter with a single positive-sense RNA genome. 16 Club-shaped glycoprotein spikes in the envelope give the virus a crown-like or coronal appearance. Transmission rates are unknown for 2019-nCoV; however, there is evidence of human-to-human transmission. None of the 99 patients we examined were medical staff, but 15 medical workers have been reported with 2019-nCoV infection, 14 of whom are assumed to have been infected by the same patient.17 The mortality of SARS-CoV has been reported as more than 10% and MERS-CoV at more than 35%. 5,18 At data cutoff for this study, mortality of the 99 included patients infected by 2019-nCoV was 11%, resembling that in a previous study.3 However, additional deaths might occur in those still hospitalised.

We observed a greater number of men than women in the 99 cases of 2019-nCoV infection. MERS-CoV and SARS-CoV have also been found to infect more males than females. 19,20 The reduced susceptibility of females to viral infections could be attributed to the protection

adaptive immunity innate先天

innate 无大 適應性免疫 from X chromosome and sex hormones, which play an important role in innate and adaptive immunity.21 Additionally, about half of patients infected by 2019-nCoV had chronic underlying diseases, mainly cardiovascular and cerebrovascular diseases and diabetes; this is similar to MERS-CoV.19 Our results suggest that 2019-nCoV is more likely to infect older adult males with chronic comorbidities as a result of the weaker immune functions of these patients.19-22

Some patients, especially severely ill ones, had coinfections of bacteria and fungi. Common bacterial cultures of patients with secondary infections included A baumannii, K pneumoniae, A flavus, C glabrata, and C albicans.8 The high drug resistance rate of A baumannii can cause difficulties with anti-infective treatment, leading to higher possibility of developing septic shock.²³ For severe mixed infections, in addition to the virulence factors of pathogens, the host's immune status is also one of the important factors. Old age, obesity, and presence of comorbidity might be associated with increased mortality.24 When populations with low immune function, such as older people, diabetics, people with HIV infection, people with long-term use of immunosuppressive agents, and pregnant women, are infected with 2019-nCoV, prompt administration of antibiotics to prevent infection and strengthening of immune support treatment might reduce complications and mortality.

In terms of laboratory tests, the absolute value of lymphocytes in most patients was reduced. This result suggests that 2019-nCoV might mainly act on lymphocytes, especially T lymphocytes, as does SARS-CoV. Virus particles spread through the respiratory mucosa and infect other cells, induce a cytokine storm in the body, generate a series of immune responses, and cause changes in peripheral white blood cells and immune cells such as lymphocytes. Some patients progressed rapidly with ARDS and septic shock, which was eventually followed by multiple organ failure. Therefore, early identification and timely treatment of critical cases is of crucial importance. Use of intravenous immunoglobulin is recommended to enhance the ability of anti-infection for severely ill patients and steroids (methylprednisolone 1-2 mg/kg per day) are recommended for patients with ARDS, for as short a duration of treatment as possible. Some studies suggest that a substantial decrease in the total number of lymphocytes indicates that coronavirus consumes many immune cells and inhibits the body's cellular immune function. Damage to T lymphocytes might be an important factor leading to exacerbations of patients.25 The low absolute value of lymphocytes could be used as a reference index in the diagnosis of new coronavirus infections in the clinic.

In general, the characteristics of patients who died were in line with the early warning model for predicting mortality in viral pneumonia in our previous study: the MuLBSTA score.8 The MuLBSTA score system contains six indexes, which are multilobular infiltration, lymphopenia, bacterial

comprehensive 全面的 applicability 適用性

co-infection, smoking history, hypertension, and age. Further investigation is needed to explore the applicability of the MuLBSTA score in predicting the risk of mortality in 2019-nCoV infection.

This study has several limitations. First, only 99 patients with confirmed 2019-nCoV were included; suspected but undiagnosed cases were ruled out in the analyses. It would be better to include as many patients as possible in Wuhan, in other cities in China, and even in other countries to get a more comprehensive understanding of 2019-nCoV. Second, more detailed patient information, particularly regarding clinical outcomes, was unavailable at the time of analysis; however, the data in this study permit an early assessment of the epidemiological and clinical characteristics of 2019-nCoV pneumonia in Wuhan, China.

In conclusion, the infection of 2019-nCoV was of clustering onset, is more likely to infect older men with comorbidities, and can result in severe and even fatal respiratory diseases such as ARDS.

Contributors

NC, XD, FG, YH, YQ, JW, YL, YW, JX, TY, and LZ collected the epidemiological and clinical data and processed statistical data. NC and MZ drafted the manuscript. JQ and XZ revised the final manuscript. XZ is responsible for summarising all data related to the virus. LZ is responsible for summarising all epidemiological and clinical data.

Declaration of interests

We declare no competing interests.

Acknowledgments

This study was funded by the National Key R&D Program of China (number 2017YFC1309700). We thank all patients involved in the study.

References

- Lu H, Stratton CW, Tang YW. Outbreak of pneumonia of unknown etiology in Wuhan China: the mystery and the miracle. J Med Virol 2020; published online Jan 16. DOI:10.1002/jmv.25678.
- 2 Hui DS, I Azhar E, Madani TA, et al. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health the latest 2019 novel coronavirus outbreak in Wuhan, China. Int J Infect Dis 2020: 91: 264–66.
- 3 Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020; published online Jan 24. https://doi.org/10.1016/S0140-6736(20)30183-5.
- 4 WHO. Clinical management of severe acute respiratory infection when Novel coronavirus (nCoV) infection is suspected: interim guidance. Jan 11, 2020. https://www.who.int/internalpublications-detail/clinical-management-of-severe-acute-respiratoryinfection-when-novel-coronavirus-(ncov)-infection-is-suspected (accessed Jan 20, 2020).
- Yin Y, Wunderink RG. MERS, SARS and other coronaviruses as causes of pneumonia. Respirology 2018; 23: 130–37.
- 6 Drosten C, Günther S, Preiser W, et al. Identification of a novel coronavirus in patients with severe acute respiratory syndrome. N Engl J Med 2003; 348: 1967–76.

- 7 Zaki AM, van Boheemen S, Bestebroer TM, Osterhaus AD, Fouchier RA. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. N Engl J Med 2012; 367: 1814–20.
- 8 Guo L, Wei D, Zhang X, et al. Clinical features predicting mortality risk in patients with viral pneumonia: the MuLBSTA score. Front Microbiol 2019; 10: 2752.
- 9 Hu B, Zeng LP, Yang XL, et al. Discovery of a rich gene pool of bat SARS-related coronaviruses provides new insights into the origin of SARS coronavirus. PLoS Pathog 2017; 13: e1006698.
- 10 Song HD, Tu CC, Zhang GW, et al. Cross-host evolution of severe acute respiratory syndrome coronavirus in palm civet and human. Proc Natl Acad Sci USA 2005; 102: 2430–35.
- 11 Haagmans BL, Al Dhahiry SH, Reusken CB, et al. Middle East respiratory syndrome coronavirus in dromedary camels: an outbreak investigation. *Lancet Infect Dis* 2014; 14: 140–45.
- 12 Azhar EI, El-Kafrawy SA, Farraj SA, et al. Evidence for camel-to-human transmission of MERS coronavirus. N Engl J Med 2014; 370: 2499–505.
- 13 Tao Y, Shi M, Chommanard C, et al. Surveillance of bat coronaviruses in Kenya identifies relatives of human coronaviruses NL63 and 229E and their recombination history. J Virol 2017; 91: e01953–16.
- 14 Cui J, Li F, Shi ZL. Origin and evolution of pathogenic coronaviruses. Nat Rev Microbiol 2019; 17: 181–92.
- 15 Zhou P, Fan H, Lan T, et al. Fatal swine acute diarrhoea syndrome caused by an HKU2-related coronavirus of bat origin. *Nature* 2018; 556: 255–58.
- 16 Xu XT, Chen P, Wang JF, et al. Evolution of the novel coronavirus from the ongoing Wuhan outbreak and modeling of its spike protein for the risk of human transmission. Sci China Life Sci 2020; published online Jan 21. DOI:10.1007/s11427-020-1637-5.
- 17 Chinese Academy of Sciences. Wuhan coronavirus has strong ability to infect humans. Press release. Jan 21, 2020. https://view. inews.qq.com/w2/20200121A0M08X00?tbkt=F&strategy=&openid= 004IBALMrLyGDxbWNOPoDM1IfG-s&uid=&refer=wx_hot (accessed Jan 29, 2020).
- 18 Song Z, Xu Y, Bao L, et al. From SARS to MERS, thrusting coronaviruses into the spotlight. Viruses 2019; 11: 59.
- 19 Badawi A, Ryoo SG. Prevalence of comorbidities in the Middle East respiratory syndrome coronavirus (MERS-CoV): a systematic review and meta-analysis. *Int J Infect Dis* 2016; 49: 129–33.
- 20 Channappanavar R, Fett C, Mack M, Ten Eyck PP, Meyerholz DK, Perlman S. Sex-based differences in susceptibility to severe acute respiratory syndrome coronavirus infection. *J Immunol* 2017; 198: 4046–53.
- 21 Jaillon S, Berthenet K, Garlanda C. Sexual dimorphism in innate immunity. Clin Rev Allergy Immunol 2019; 56: 308–21.
- 22 Dryden M, Baguneid M, Eckmann C, et al. Pathophysiology and burden of infection in patients with diabetes mellitus and peripheral vascular disease: focus on skin and soft-tissue infections. Clin Microbiol Infect 2015; 21 (suppl 2): S27–32.
- 23 Gao HN, Lu HZ, Cao B, et al. Clinical findings in 111 cases of influenza A (H7N9) virus infection. N Engl J Med 2013; 368: 2277–85.
- 24 Wang XF, Shi GC, Wan HY, et al. Clinical features of three avian influenza H7N9 virus-infected patients in Shanghai. Clin Respir J 2014; 8: 410–16.
- 25 Liu WJ, Zhao M, Liu K, et al. T-cell immunity of SARS-CoV: implications for vaccine development against MERS-CoV. Antiviral Res 2017; 137: 82–92.