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Epidemiologic and clinical characteristics of 42 deaths caused by SARS-CoV-2 infection in Wuhan, China: A retrospective study

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ABSTRACT

This study described the epidemiologic and clinical characteristics of patients who died from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, and pointed out the potential risk factors associated with fatal outcomes. Retrospective data from 42 death cases due to SARS-CoV-2 infection at Tongji Hospital Affiliated to Huazhong University of Science and Technology, Wuhan, China was analyzed. Demographics, clinical detection, laboratory findings, and treatments of the deceased were collected and analyzed. The average time between onset of symptoms and admission to the hospitals was 11 ± 5 days of hospitalization. Among the deceased, 60% were with co-morbidities. All of them were having fever and bilateral pneumonia on computed tomography, abnormal infection-related biomarkers, and renal impairment. Abnormal blood coagulation parameters that appeared in more than half of them, were consistent with disseminated intravascular coagulation. All of the patients were treated in the ICU. Based on the fact that SARS-CoV-2 infection carries a risk of mortality, we may infer a few older male patients with underlying comorbidities are likely to have the increased risk. Impaired consciousness level, markers of renal impairment and coagulation abnormalities may be poor prognostic factors.

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1. Introduction

In December 2019, novel cases of pneumonia appeared in China, with its etiology known as SARS-CoV-2 [1–5], predominantly were transmitted from human-to-human [6,7] and clinical syndrome termed as "coronavirus disease 2019 (COVID-19)", by the World Health Organization (WHO). As of 25 February 2020, there had been 78,064 laboratory-confirmed cases with 2715 fatalities caused by COVID-19, as reported in China [8]. The overall mortality rate was estimated as 3.4%, while that of critically ill patients, was 61,5% [9]. It seemed necessary to analyze the COVID-19 caused deaths and to understand the potential risk factors associated with the fatal outcomes.

In this retrospective study, we described the epidemiologic and clinical characteristics of 42 patients who died of COVID-19 infection. Hopefully, the epidemiologic data could help physicians better understand the COVID-19 infection, take appropriate actions on severe pneumonia, and reduce fatality, accordingly.

2. Materials and methods

2.1. Participants and data collection

All the patients enrolled were confirmed of being infected by COVID-19. The data of the 42 confirmed COVID-19 fatalities was collected from Jan. 21 to Feb. 14, 2020. The data includes, demographics, clinical symptoms, laboratory findings, and treatment. All the patients were treated at Tongji Hospital Affiliated with HUST. SARS-CoV-2 infection was confirmed in accordance with the WHO interim guidelines. Data including age, gender, underlying diseases, clinical signs and symptoms, virus detection, computed tomography (CT) findings, treatments, routine blood and biochemistry, coagulation function, infection-related biomarkers, and routine urine etc., was gathered. Respiratory syncytial virus, adenovirus, and bacteria that caused pneumonia were also tested.

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HIGHLIGHTS

Scientific question

COVID-19 is a highly contagious viral infection, large outbreaks have occurred by human-to-human transmission. Epidemiological and clinical characteristics of death cases with COVID-19 can contribute to a alerting physicians to the implications of severe pneumonia, and reducing mortality.

Evidence before this study

Prior to conducting this study, we searched PubMed for articles up to 25 February 2020, using the keywords "2019 novel coronavirus", "2019-nCoV", or "COVID-19" and "epidemiologic and clinical characteristics" or "death", with no time restrictions. We found one previously published article that discussed the clinical course and outcomes of critically ill patients with COVID-19. The study did not focus on the potential risk factors associated with a fatal outcome.

New findings

The mean time to admission from symptom onset was 11±5 days, the mean hospital stay was 5±4 days. Among the 42 patients, 71% were male, 60% had ≥1 co-morbidity. All patients had fever and bilateral pneumonia on computed tomography, abnormal infection-related biomarkers, and renal impairment. Abnormal blood coagulation parameters seen in more than half of patients may be consistent with disseminated intravascular coagulation. All these patients were treated in the ICU.

Significance of the study

This study demonstrated that COVID-19 carries a risk of mortality; based on this case series older men with underlying co-morbidities are likely at increased risk. Impaired consciousness level, markers of renal impairment and coagulation abnormalities may be poor prognostic factors.

2.2. Statistical analysis

Descriptive analyses were performed to display potential factors that might be associated with mortality related to the COVID-19 infection. SPSS (version 22.0) software was used. Continuous data were summarized as mean ± standard deviation (SD), or median (IQR, or interquartile range), with categorical data expressed in proportions.

3. Results

3.1. Epidemiologic characteristics and underlying diseases

All the 42 patients who died from COVID-19, including 30 males (30/42, 71%) were included in this study (Table 1), with age distribution appeared as 69 ± 13 y (33–95 y). Of the 42 deaths, 25 (25/42, 60%) had more than one underlying known comorbidities, including 9 (9/42, 21%) with diabetes and 7 (7/42, 17%) with hypertension, 5 (5/42, 12%) with chronic cardiac or pulmonary disease, 3 (3/42, 7%) with chronic kidney disease, and 2 (2/42, 5%) with mild liver disease.

3.2. Symptoms and CT examination

The most common symptoms appeared as fever (42/42, 100%), cough (32/42, 76%), dyspnea (32/42, 76%), shortness of breath (30/42, 71%), fatigue (16/42, 38%), chest pain (14/42, 33%), expectoration (13/42, 31%) and disturbance of consciousness (12/42, 29%). However, myalgia (6/42, 14%), arthralgia (4/42, 10%), headache (3/42, 7%), respiratory distress (3/42, 7%), hemoptysis (3/42, 7%), and rhinorrhea (1/42, 2%) appeared less frequently. All patients had undergone CT examinations and all of them presented bilateral pneumonia. Three patients were concurrently tested flu-positive.

Table 1
Baseline characteristics and treatments of 42 patients with COVID-19 infection *

Characteristic	All patients
Age, y	69 ± 13 (33–95)
Gender	
Male	30 (71)
Female	12 (29)
Underlying diseases	
Diabetes	9 (21)
Hypertension	7 (17)
Chronic cardiac disease	5 (12)
Chronic pulmonary disease	5 (12)
Chronic kidney disease	3 (7)
Mild liver disease	2 (5)
Signs and symptoms	
Temperature, °C	37.7 ± 1.1 (36.0–41.0)
Heart rate, bpm	104 ± 32 (61–189)
Respiratory rate, breaths/min	26 ± 8 (12–49)
Systolic pressure	127 ± 25 (80–180)
Diastolic pressure	74 ± 18 (30 − 120)
Fever	42 (100)
Cough	32 (76)
Dyspnea	32 (76)
Shortness of breath	30 (71)
Fatigue	16 (38)
Chest pain	14 (33)
Expectoration	13 (31)
Conscious disturbance	12 (29)
Myalgia	6 (14)
Arthralgia	4 (10)
Headache	3 (7)
Respiratory distress	3 (7)
Hemoptysis	3 (7)
Rhinorrhea	1 (2)
Virus detection	
Novel coronavirus	42 (100)
Influenza	3 (7)
CT findings	
Bilateral pneumonia	42 (100)
ICU	
Oxygen therapy	40 (95)
Non-invasive ventilation	34 (81)
Tracheotomy and intubation	13 (31)
Invasive ventilation	4 (10)
Extracorporeal life support	2 (5)
Renal replacement therapy	1 (2)

* Reported as mean ± standard deviation (minimum-maximum), or N (%), unless indicated otherwise.

3.3. Laboratory findings

Upon admission of these patients, counts on blood cells (15 (15/39, 38%) with leucocytes, 23 (23/40, 58%) with neutrophils, 8 (8/40, 20%) with monocytes and 33 (33/40, 83%) with eosinophils) were above the normal ranges, respectively (Table 2). In 36 (36/39, 92%), 23 (23/40, 58%), 39 (39/41, 95%) and 12 (12/39, 31%) of the patients, lymphocytes, hemoglobin, albumin/globulin and platelets appeared below the normal ranges. All patients showed elevated levels of alkaline phosphatase (ALP). Higher levels of aspartate aminotransferase (AST) was seen in 51% but γ-glutamyl transpeptidase (GGT) appeared low in 49%, of the patients. However, elevated alanine aminotransferase (ALT) appeared less common.

Most patients showed elevated levels of infection-related biomarkers, specifically on erythrocyte sedimentation rate (ESR) (88% of cases), serum ferritin (96%), C-reactive protein (100%), and serum procalcitonin (100%) (Table 2). In most patients, concentrations of interleukin (IL)-2R, IL-10, and tumor necrosis factor alpha (TNF) also showed an increase

Table 2
Laboratory findings of patients infected with COVID-19 on admission.

Laboratory findings	Normal range	N / N (%)	Mean (SD)	Median (IQR)
Blood routine				
Leucocytes, $\times 10^9$/L	3.50–9.50	39	11.97 (13.69)	8.07 (5.56–12.89)
Increased		15 (38.46)	20.86 (19.16)	16.75 (12.23–21.67)
Neutrophils, $\times 10^9$/L	1.8–6.3	40	8.69 (5.45)	7.33 (4.52–11.38)
Increased		23 (57.50)	12.01 (4.99)	10.20 (8.00–17.40)
Lymphocytes, $\times 10^9$/L	1.1–3.2	39	1.94 (8.30)	0.63 (0.46–0.80)
Increased		1 (2.56)	52.42 (—) [a]	52.42 (—) [a]
Decreased		36 (92.31)	0.58 (0.22)	0.59 (0.45–0.75)
Monocytes, $\times 10^9$/L	0.1–0.6	40	1.26 (5.31)	0.38 (0.20–0.55)
Increased		8 (20.00)	5.07 (11.67)	0.88 (0.81–1.31)
Eosinophils, $\times 10^9$/L	0.02–0.52	40	0.02 (0.07)	0.00 (0.00–0.01)
Increased		33 (82.50)	0.00 (0.00)	0.00 (0.00–0.00)
Red blood cell, $\times 10^{12}$/L	4.3–5.8	40	4.12 (0.66)	4.14 (3.66–4.64)
Decreased		22 (55.00)	3.62 (0.39)	3.68 (3.26–3.98)
Hemoglobin, g/L	130.01 rang	40	120.48 (25.10)	119.00 (107.25–140.75)
Decreased		23 (57.50)	104.43 (21.05)	110.00 (96.00–117.00)
PCV, %	40–50	40	0.36 (0.06)	0.36 (0.32–0.41)
Decreased		27 (67.50)	33.37 (3.96)	34.10 (30.40–35.90)
Platelets, $\times 10^9$/L	125.01 rang	39	162.31 (66.06)	159.00 (117.00–182.00)
Increased		1 (2.56)	392.00 (—) [a]	392.00 (—) [a]
Decreased		12 (30.77)	97.83 (27.05)	109.50 (82.75–116.00)
Blood chemistry				
AST, U/L	≤40	41	70.27 (120.59)	41.00 (24.00–72.50)
Increased		21 (51.22)	112.00 (158.96)	70.00 (49.50–91.50)
ALT, U/L	≤41	41	31.34 (19.75)	24.00 (18.00–41.05)
Increased		10 (24.39)	58.71 (21.19)	49.50 (46.00–68.00)
GGT, U/L	7–50	41	66.07 (87.44)	42.00 (24.50–58.00)
Increased		6 (14.63)	234.67 (135.94)	161.00 (137.00–389.00)
Decreased		20 (48.78)	23.00 (8.28)	24.50 (14.50–27.00)
ALP, U/L	45.0–135.0	41	82.90 (43.97)	70.00 (55.50–100.00)
Increased		41 (100.00)	82.90 (43.97)	70.00 (55.50–100.00)
Total protein, g/L	60–80	41	64.80 (7.08)	65.40 (59.25–69.45)
Decreased		17 (41.46)	57.98 (4.03)	57.20 (55.70–61.45)
BUN, mmol/L	3.1–8.0	37	13.58 (12.06)	10.50 (5.56–18.00)
Increased		20 (54.05)	20.72 (12.51)	16.55 (11.04–24.08)
Decreased		2 (5.41)	2.20 (—) [a]	2.20 (—) [a]
sCr, μmol/L	59.0–104.0	37	131.76 (144.95)	89.00 (68.00–124.00)
Increased		13 (35.14)	238.85 (207.53)	140.00 (124.00–289.50)
Decreased		5 (13.51)	42.80 (11.84)	45.00 (31.00–53.50)
Albumin, g/L	35.0–52.0	41	29.50 (5.08)	29.90 (24.95–34.15)
Decreased		34 (82.93)	28.05 (4.26)	28.05 (24.03–31.40)
Globulin, g/L	20.0–35.0	41	35.44 (5.97)	36.40 (31.50–39.30)
Increased		21 (51.22)	40.21 (2.90)	39.20 (38.05–43.35)
Albumin/Globulin	1.5–2.5:1	41	0.87 (0.25)	0.83 (0.71–0.97)
Decreased		39 (95.12)	0.83 (0.20)	0.83 (0.69–0.92)
Total bilirubin, μmol/L	3.4–17.1	41	15.70 (18.66)	10.30 (7.60–15.95)
Increased		7 (17.07)	43.84 (33.65)	25.50 (22.20–78.80)
Glucose, mmol/L	4.11–6.05	38	10.31 (5.87)	7.54 (6.14–13.35)
Increased		31 (81.58)	11.46 (5.86)	8.87 (6.94–14.66)
Decreased		1 (2.63)	1.00 (—) [a]	1.00 (—) [a]
Calcium, mmol/L	2.25–2.75	41	2.05 (0.15)	2.08 (1.92–2.14)
Increased		1 (2.44)	2.56 (—) [a]	2.56 (—) [a]
Decreased		32 (78.05)	2.00 (0.11)	2.02 (1.89–2.10)
Phosphorus, mmol/L	0.97–1.6	8	0.99 (0.27)	0.98 (0.75–1.27)
Decreased		2 (25.00)	0.65 (—) [a]	0.65 (—) [a]
Coagulation function				
APTT[b], s	29.0e rma	40	43.49 (8.63)	41.85 (35.80–50.63)
Increased		19 (47.50)	50.97 (5.85)	51.00 (44.90–55.30)
Prothrombin time[b],s	11.5–14.5	40	16.42 (3.28)	15.55 (14.58–17.40)
Increased		30 (75.00)	17.30 (3.34)	15.80 (15.28–17.90)
INR[b]	0.8–1.2	40	1.32 (0.35)	1.21 (1.14–1.41)
Increased		21 (52.50)	1.50 (0.39)	1.40 (1.23–1.53)
Prothrombin activity[b], %	75–125	40	71.23 (17.40)	74.00 (58.50–80.75)
Increased		22 (55.00)	59.59 (13.39)	60.00 (54.50–73.00)
Fibrinogen[b]. g/L	2–4	40	5.16 (2.61)	5.45 (3.72–6.23)
Increased		27 (67.50)	6.36 (2.23)	5.98 (5.43–6.75)
Decreased		4 (10.00)	1.22 (0.46)	1.34 (0.74–1.59)
Infection-related biomarkers				
ESR, mm/h	Men, 0–15 Women, 0–20	34	44.32 (23.31)	39.50 (27.75–62.00)
Increased		30 (88.24)	48.90 (20.74)	43.00 (34.25–62.25)
Serum ferritin, ng/mL	30–400	28	2,129.74 (2,344.26)	1,330.85 (751.70–2,148.48)
Increased		27 (96.43)	2,198.91 (2,359.62)	1,396.40 (872.00–2,183.00)
Reactive protein, mg/L	0.0 g/L	25	129.73 (76.37)	114.10 (64.70–185.90)

Table 2 (*continued*)

Laboratory findings	Normal range	N / N (%)	Mean (SD)	Median (IQR)
Increased		25 (100.00)	129.73 (76.37)	114.10 (64.70–185.90)
Serum procalcitonin, μg/L	< 0.5	27	2.13 (5.64)	0.60 (0.18–1.31)
Increased		27 (100.00)	2.13 (5.64)	0.60 (0.18–1.31)
Interleukin-2R, U/mL		27	1,108.93 (550.63)	1,006.00 (712.00–1,301.00)
Increased		21 (77.78)	1,279.05 (503.32)	1,179.00 (960.50–1,456.50)
Interleukin-6, pg/mL	0.0–7.0	27	109.26 (118.55)	71.96 (23.15–162.90)
Increased		27 (100.00)	109.26 (118.55)	71.96 (23.15–162.90)
Interleukin-10, pg/mL		27	12.89 (8.95)	10.90 (6.60–17.40)
Increased		16 (59.26)	18.13 (7.86)	16.80 (11.63–23.75)
TNF, fmol/mL	< 30	27	12.07 (10.55)	8.40 (6.70–11.60)
Increased		15 (55.56)	16.35 (12.74)	10.40 (9.30–22.20)
Urine routine				
PH		15	5.93 (0.42)	6.00 (5.50–6.00)
Red cell + (%)		13 (92.86)		
Urinary protein + (%)		14 (93.33)		

[a] Standard deviation and quartile cannot be calculated due to the small number of cases; [b] Ca^{2+} ALP, alkaline phosphatase; ALT, alanine aminotransferase; APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; BUN, blood urea nitrogen; ESR, erythrocyte sedimentation rate; GGT, γ-glutamyl transpeptidase; INR, international normalized ratio; IQR, interquartile range; PCV, packed cell volume; sCr, serum creatinine; SD, standard deviation; TNF, tumor necrosis factor-α.

in plasma and IL-6 was elevated in all the cases. Moreover, biochemical changes were consistent with renal impairment including microscopic proteinuria (93%) and hematuria (93%), hypocalcemia (78%), hyperphosphatemia, acidosis, elevated blood urea nitrogen (54%), and serum creatinine (35%) that appeared in many of the patients. More than half of the patients presented coagulation abnormality, including elevated activated partial thromboplastin time (APTT; 48%), prothrombin time (75%), decreased prothrombin activity (55%), and/or international normalized ratio (INR; 53%). The data suggested that disseminated intravascular coagulation (DIC) was associated with the outcomes of death, in patients with COVID-19 infection.

3.4. Treatment

Different forms of treatment (Table 1) were provided to the 42 patients at the Intensive Care Unit (ICU) of the hospital. The treatment included oxygen therapy (40/42, 95%), non-invasive ventilation (34/42, 81%), tracheotomy and intubation (13/42, 31%), invasive ventilation (4/42, 10%), extracorporeal life support (2/42, 5%), and renal replacement therapy (1/42, 2%). None of the patients ever received any experimental antiviral therapies of potential benefits during the treatment of COVID-19 infection. Patients with Flu-positive were treated with Zanamivir.

4. Discussion

SARS-CoV-2 has been the seventh identified coronavirus, and ranking the third potentially lethal one, after SARS-CoV and MERS-CoV [1,10–13]. The present retrospective study aimed to analyze the demographic and clinical characteristics of patients who died of SARS-CoV-2 infection.

Forty-two patients died of confirmed COVID-19 infection were included in this study. In the previous studies, characteristics and fatalities of the COVID-19 infection were summarized [3,14]. The average survival time before death was within 1–2 weeks after admission to the ICU. Patients at older age (>65 years), with underlying diseases or ARDS were at higher risks of death [9]. Du et al. [15] identified four predictors including age ≥ 65 years, preexisting concurrent cardiovascular or cerebrovascular diseases, $CD3^+CD8^+$ T cells ≤75 cell/μL, and cardiac troponin $I \geq 0.05$ ng/mL etc. were related to the fatality of COVID-19. In our cohort, more than half of the deaths occurred in older men with underlying diseases, especially diabetes and hypertension. However, still 40% of the deceased did not have any known underlying co-morbidity with COVID-19 infection. Common symptoms as fever, cough, expectoration, chest pain, dyspnea were all similar to reports from other researchers. However, 29% of these patients presented disturbance of consciousness, which to our knowledge, had not been mentioned in previous reports and may serve a marker for the poor outcome. Among all the patients, 3 were co-infected of flu and COVID-19, confirmed by nucleic acid testings. All the patients showed signs of bilateral pneumonia on CT examination. As for laboratory findings, lymphocytopenia appeared in more than 90% of the deaths with COVID-19 infection, suggesting that the severity of lymphocytopenia might reflect the severity of COVID-19 infection. Elevated levels of infection-related biomarkers occurred in most of the patients while the elevated level of IL-6 was observed in all the cases. Moreover, many patients showed renal impairment to some degrees. It is noteworthy that patients with abnormal blood coagulation may indicate the presence of DIC, hence increasing the risk of mortality. In terms of treatments involved, more than half of these patients received oxygen therapy and non-invasive ventilation, with a quarter of them underwent tracheotomy.

5. Conclusions

Potential risk factors associated with COVID-19 fatalities include being male and those with underlying comorbidities. However, 40% of the patients were without any known underlying comorbidities. Lymphopenia, ALP, high serum ferritin, hypoalbuminaemia/globulinaemia, C-reactive protein, serum levels of procalcitonin, IL-6, and markers of renal dysfunction appeared common in these patients. It must also be mentioned that more than half of the patients presented clotting abnormalities, which might serve as a marker for poor prognosis.

We hope that the information we have provided could highlight those conditions related to early warning on the risk of the COVID-19 fatalities, so as to reduce both the incidence of critical illness and mortality.

Ethics statement

Ethical approval was granted by the Ethics Commission of the First Hospital of Jilin University (2020–235), with a waiver of informed consent from the participants of the study.

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Conflict of interest statement

The authors declare that there are no conflicts of interest.

Author contributions

G. Wang and H. Xu conceived and designed this study. N. Zhang collected the data. D. Zhang, J. Pan, E. Peng, J. Huang, Y. Zhang, X. Xu, and G. Tian did literature search. H. Yao analyzed the data and wrote the paper, with contributions from all authors.

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