Clinical Characteristics and Outcomes of Hypertensive Patients Infected with COVID-19: A Retrospective Study

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Background: Hypertension has been reported as the most prevalent comorbidity in patients with coronavirus disease 2019 (COVID-19). This retrospective study aims to compare the clinical characteristics and outcomes in COVID-19 patients with or without hypertension.

Methods: A total of 944 hospitalized patients with laboratory-confirmed COVID-19 were included from January to March 2020. Information from the medical record, including clinical features, radiographic and laboratory results, complications, treatments, and clinical outcomes, were extracted for the analysis.

Results: A total of 311 (32.94%) patients had comorbidity with hypertension. In COVID-19 patients with hypertension, the coexistence of type 2 diabetes (56.06% vs 43.94%), coronary heart disease (65.71% vs 34.29%), poststroke syndrome (68.75% vs 31.25%) and chronic kidney diseases (77.78% vs 22.22%) was significantly higher, while the coexistence of hepatitis B infection (13.04% vs 86.96%) was significantly lower than in COVID-19 patients without hypertension. Computed tomography (CT) chest scans show that COVID-19 patients with hypertension have higher rates of pleural effusion than those without hypertension (56.60% vs 43.40%). In addition, the levels of blood glucose [5.80 (IQR, 5.05–7.50) vs 5.39 (IQR, 4.81–6.60)], erythrocyte sedimentation rate (ESR) [28 (IQR, 17.1–55.6) vs 21.8 (IQR, 11.5–44.1), $P=0.008$], C-reactive protein (CRP) [17.92 (IQR, 3.11–46.6) vs 3.15 (IQR, 3.11–23.4), $P=0.013$] and serum amyloid A (SAA) [99.28 (IQR, 8.85–300) vs 15.97 (IQR, 5.97–236.1), $P=0.005$] in COVID-19 patients with hypertension were significantly higher than in patients without hypertension.

Conclusion: It is common for patients with COVID-19 to have the coexistence of hypertension, type 2 diabetes, coronary heart disease and so on, which may exacerbate the severity of COVID-19. Therefore, optimal management of hypertension and other comorbidities is essential for better clinical outcomes.

Keywords: COVID-19, coronavirus disease, hypertension, clinical characteristics, comorbidities

Introduction

The coronavirus disease (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has become a public health emergency worldwide. It typically presents with fever, cough, myalgia, and fatigue. As of July 22, 2021, there have been 191,773,590 confirmed cases and 4127,963 deaths, with the numbers still rising across 217 countries/regions worldwide.¹ Therefore, COVID-19 has been considered a pandemic.²

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Previous studies have suggested that the presence of comorbidities among COVID-19 may be associated with poor clinical outcomes.³ According to the latest reports, around 20–51% of patients with COVID-19 have at least one comorbidity,^{4–6} with hypertension (16.9%) and diabetes mellitus (8.2%) being the most prevalent comorbidities.⁷ A pooled analysis has indicated that hypertension may be related to a higher risk of severe or fatal COVID-19, especially in the elderly.⁸

The angiotensin-converting enzyme 2 (ACE2) has been discovered to be the receptor that allows the entry of SARS-CoV-2 into human cells.^{9,10} ACE2 converts angiotensin II to Ang-(1-7), transforming the vasoconstrictor into a vasodilator peptide, which promotes the release of nitric oxide, decreases the outflow of sympathetic nerves, increases baroreflex sensitivity, and ultimately reduces hypertension.¹¹ However, the relationship between COVID-19 and hypertension remains unclear.

The objective of this study was to elucidate the risk and severity of COVID-19 among patients with comorbid hypertension by investigating the clinical features, radiographic and laboratory results, complications, treatments, and clinical outcomes of COVID-19 patients with or without hypertension.

Materials and Methods

Data Sources

This was a retrospective study. We included 944 hospitalized COVID-19 patients from the Hubei Provincial Hospital of Integrated Traditional Chinese and Western Medicine from January 2020 to March 2020. All patients confirmed to have COVID-19 using a real-time reverse-transcriptase polymerase chain reaction (RT-PCR) assay of the sputum, throat swab, or lower respiratory tract secretion specimens were hospitalized for treatment. All patients were divided into hypertension group and non-hypertension group according to whether they had hypertension or not. Written informed consent was waived owing to the rapid emergence of this infectious disease and the urgent need to collect data.

The demographics, clinical symptoms or signs, radiological and laboratory results, comorbidities, and treatment results were extracted from the electronic medical record system. All medical data reviews and collections were processed by experienced clinicians. We established a computerized database for data storage and verification. Missing or incomplete information was acquired by sending requests for clarification to the coordinators, who

subsequently contacted the attending clinicians. Major disagreements during the extraction process were resolved by consultation with the reviewers.

Finally, in accordance with the guidelines for prevention and treatment of hypertension in China (2018 Edition),¹² we divided the patients into two groups: the COVID-19 with hypertension group and the non-hypertensive group (Hypertension was defined as: clinic systolic BP $\geq$ 140 mmHg and/or diastolic BP $\geq$ 90 mmHg without the use of anti-hypertensive medications at three visits on different days; with a BP<140/90 mmHg but having hypertensive history and currently are taking anti-hypertensive medication).

Study Outcomes

To assess the severity of COVID-19 among the patients with hypertension, the primary clinical outcomes included admission to an intensive care unit (ICU), discharge from the hospital, duration of hospitalization, and death.¹³

Laboratory Confirmation

Laboratory confirmation of SARS-CoV-2 was performed in accordance with the protocol established by the World Health Organization using RT-PCR assays at Hubei Provincial Hospital of Integrated Traditional Chinese and Western Medicine. The laboratory confirmation processes were similar to the ones used in our previous study.¹⁴

Statistical Analysis

Continuous variables are described as mean and standard deviation, and categorical variables are expressed as frequencies and percentages. Continuous variables were analyzed using an independent sample *t*-test when normally distributed; otherwise, the Mann–Whitney test was used. Categorical variables were compared using the chi-square test or Fisher's exact test. All statistical analyses were performed using Statistical Package for the Social Sciences version 13.0 software (IBM; Chicago, Illinois, United States). Statistical significance was set at $P < 0.05$.

Results

Demographic and Clinical Characteristics

This study included 944 patients with confirmed COVID-19 from the Hubei Provincial Hospital of Integrated Chinese and Western Medicine from January 2020 to March 2020. As shown in [Tables 1](#), 311 (32.94%) patients had hypertension and 633 (67.06%) were non-hypertensive. The median age of the patients was 60

Table I Clinical Characteristics of the Study Patients with COVID-19

Characteristic	No. (%)			P value
	Total	Hypertension	Non-Hypertension	
	944 (100)	311 (32.94)	633 (67.06)	
Female sex - no. /total no. (%)	338 (35.81)	161 (32.26)	338 (67.74)	0.6377
Age, Median (IQR) - year	60 (50–69)	67 (58–74)	56 (46–65)	<0.0001
Fever on admission (IQR) - °C	36.7 (36.5–37.0)	36.7 (36.4–37.0)	36.7 (36.5–37.0)	0.8626
Highest temperature during hospitalization (IQR) - °C	37.2 (36.9–37.9)	37.2 (36.9–38.0)	37.2 (36.9–37.9)	0.2767
Systolic pressure on admission - mmHg	125 (110–135)	130 (120–144)	120 (110–131)	<0.0001
Diastolic pressure on admission - mmHg	80 (71–90)	82 (75–90)	80 (70–90)	<0.0001
Symptoms – no, %				
Chill	75 (7.94)	26 (34.67)	49 (63.33)	0.7409
Cough	535 (56.67)	171 (31.96)	364 (68.04)	0.4627
Sputum production	202 (21.40)	66 (32.67)	136 (67.33)	0.9262
Hemoptysis	6 (0.64)	3 (50)	3 (50)	0.4018
Sore throat	29 (3.07)	9 (31.03)	20 (68.97)	0.8241
Dry throat	18 (2.54)	7 (38.89)	11 (61.11)	0.3985
Itchy throat	6 (0.82)	1 (16.67)	5 (83.33)	0.4774
Nasal congestion	9 (0.95)	2 (22.22)	7 (77.78)	0.4916
Headache	35 (3.71)	12 (34.29)	23 (65.71)	0.8634
Shortness of breath	272 (28.81)	99 (36.40)	173 (63.60)	0.1511
Dyspnea	32 (4.35)	9 (28.13)	23 (71.88)	0.8234
Conjunctival congestion	4 (0.42)	1 (25.00)	3 (75.00)	0.7248
Chest tightness	172 (23.37)	54 (31.40)	118 (68.60)	0.6226
Chest pain	22 (2.99)	7 (31.82)	15 (68.18)	0.8411
Palpitation	32 (4.35)	4 (12.50)	28 (87.50)	0.0280
Nausea or vomiting	41 (4.34)	12 (29.27)	29 (70.73)	0.6086
Diarrhea	69 (7.31)	27 (39.13)	42 (60.87)	0.2562
Myalgia or arthralgia	125 (13.24)	47 (37.60)	78 (62.40)	0.2345
Mental fatigue	414 (56.25)	124 (29.95)	290 (70.05)	0.9676
Loss of appetite	451 (61.28)	141 (31.26)	310 (68.74)	0.3062
Sleep disorder	435 (59.10)	135 (31.03)	300 (68.97)	0.4154
Fatigue	604 (63.98)	198 (32.78)	406 (67.22)	0.8868
Coexisting disorder - no. (%)				
Type 2 diabetes	132 (13.98)	74 (56.06)	58 (43.94)	<0.0001
Coronary heart disease	70 (7.42)	46 (65.71)	24 (34.29)	<0.0001
Poststroke syndrome	32 (3.39)	22 (68.75)	10 (31.25)	<0.0001
Malignant tumor	26 (2.75)	5 (19.23)	21 (80.77)	0.1304
Chronic kidney disease	9 (0.95)	7 (77.78)	2 (22.22)	0.007
Chronic obstructive pulmonary disease	13 (1.38)	4 (30.77)	9 (69.23)	0.8665
Asthma	6 (0.82)	3 (50)	3 (50)	0.28
Heart failure	6 (0.82)	3 (50)	3 (50)	0.28
Arrhythmia	18 (2.54)	9 (50)	9 (50)	0.06
Bronchiectasis	2 (0.27)	1 (50)	1 (50)	0.5088
Hepatitis B infection*	23 (2.44)	3 (13.04)	20 (86.96)	0.0431

Notes: *The presence of hepatitis B infection was defined as a positive result upon testing for the hepatitis B surface antigen, with or without elevated levels of alanine or aspartate aminotransferase. Arrhythmias refers to atrial fibrillation, frequent ventricular premature beats, and nodal tachycardia.

years (IQR, 50–69 years). A total of 35.81% of the participants were female. Fever (body temperature $\geq 37.5^{\circ}\text{C}$) was present in 7.85% of the patients on admission, increasing to 33.16% during hospitalization. The most common symptoms were fatigue (63.98%), loss of appetite (61.28%), poor sleep quality (59.10%), cough (56.67%), and mental fatigue (56.25%). Among the overall population, 29.13% had at least one coexisting illness, including diabetes, poststroke syndrome, malignant tumor, and chronic kidney disease.

The mean age of the hypertensive patients was higher than that of the non-hypertensive patients (67 years [IQR, 58–74] vs 56 years [IQR, 46–65], $P<0.001$), consistent with previous reports.¹⁵ Furthermore, the systolic (130 mmHg [IQR, 120–144] vs 120 mmHg [IQR, 110–131], $P<0.001$) and diastolic blood pressures (82 mmHg [IQR, 75–90] vs 80 mmHg [IQR, 70–90], $P<0.001$) were significantly higher among patients with hypertension than among those without. Palpitation (12.50% vs 87.50%, $P=0.028$) was the only symptom that was statistically different between the two groups. It is possible that hypertensive patients were more likely to regularly take antihypertensive medication, making them less sensitive to palpitations.

Table 1 also shows significant differences in the comorbidities between COVID-19 patients with and without hypertension, including diabetes mellitus (56.06% vs 43.94%, $P<0.001$), coronary heart disease (65.71% vs 34.29%, $P<0.001$), poststroke syndrome (68.75% vs 31.25%, $P<0.001$), chronic kidney disease (77.78% vs 22.22%, $P=0.007$), and hepatitis B infection (13.04% vs 86.96%, $P=0.043$). However, malignant tumors, chronic obstructive pulmonary disease, asthma, heart failure, arrhythmia, and bronchiectasis were similar between the two groups.

Radiologic and Laboratory Findings

The radiologic indices (Table 2) showed that 767 (81.25%) of the patients had radiological abnormalities, including

572 cases (64.41%) with ground-glass opacity, 76 (8.56%) with local patchy shadowing, 521 (58.67%) with bilateral patchy shadowing, and 53 (5.97%) with pleural effusion, which are the typical features of an organizing pneumonia pattern of a lung injury.¹⁶ Compared with non-hypertensive patients, hypertensive patients had higher rates of pleural effusion (56.60% vs 43.40%, $P<0.001$), which may have resulted from bacterial superinfection or another cause among the hypertensive COVID-19 patients.

Table 3 shows the laboratory findings on admission. Blood glucose levels (5.80 mmol/L [IQR, 5.05–7.50] vs 5.39 mmol/L [IQR, 4.8–6.60]) in COVID-19 patients with hypertension were significantly higher than those in patients without hypertension ($P=0.007$). The hypertensive patients did not have disorders in glucose metabolism because the HbA1c levels were within the normal range. On admission, the white cell count (5.97 g/L [IQR, 4.74–7.67] vs 5.48 g/L [IQR, 4.30–6.82]) in COVID-19 patients with hypertension were significantly higher than that in those without hypertension ($P<0.001$), while the hemoglobin count was higher in COVID-19 patients without hypertension (125.6 g/L [IQR, 114.5–136] vs 127 g/L [IQR, 116–138]; $P=0.0316$). However, since the parameters were within the normal range, no clinically significant effects were noted.

The levels of the inflammatory markers, including the erythrocyte sedimentation rate (28 mm/h [IQR, 17.1–55.6] vs 21.8 mm/h [IQR, 11.5–44.1], $P=0.008$) and C-reactive protein level (17.92 mg/L [IQR, 3.11–46.6] vs 3.15 mg/L [IQR, 3.11–23.4], $P=0.013$), were elevated, but there were no significant differences between the groups. This suggests that COVID-19 patients with hypertension were more likely to develop more severe infections. Meanwhile, the pro-inflammatory cytokines, such as procalcitonin, tumor necrosis factor, and interleukins, did not change in either COVID-19 group. The levels of immunity parameters showed that the serum concentrations of IgE (50.15 g/L [IQR, 18.5–142.5] vs 38.7 g/L [IQR, 18.3–95.8]) were

Table 2 Radiographic Examination Results

Variable- No./Total No. (%)	Total	Hypertension	Non-Hypertension	P value
	944 (100)	311 (32.94)	633 (67.06)	
Abnormalities on chest CT				
Ground-glass opacity	572 (64.41)	195 (34.09)	377 (65.91)	0.3026
Local patchy shadowing	76 (8.56)	25 (32.89)	51 (67.11)	0.9982
Bilateral patchy shadowing	521 (58.67)	183 (35.12)	338 (64.88)	0.0902
Pleural effusion	53 (5.97)	30 (56.60)	23 (43.40)	0.0002

Table 3 Laboratory Findings

Variable- No./Total No. (%)	No. (%)			P value
	Total	Hypertension	Non-Hypertension	
	944 (100)	311 (32.94)	633 (67.06)	
Blood glucose and lipids				
Random blood glucose - mmol/L	5.53 (4.88–6.94)	5.80 (5.05–7.50)	5.39 (4.81–6.60)	0.0066
HbA1c - %	2 (2–5.2)	2 (2–3)	2 (2–5.3)	0.4810
TC - mmol/L	4.22 (3.64–4.81)	4.19 (3.64–4.73)	4.23 (3.66–4.67)	0.7850
TG - mmol/L	1.30 (0.94–1.72)	1.33 (0.95–1.81)	1.27 (0.93–1.70)	0.3223
LDL-C - mmol/L	1.79 (1.46–2.17)	1.77 (1.50–2.18)	1.80 (1.42–2.17)	0.8271
HDL-C - mmol/L	1.10 (0.93–1.30)	1.12 (0.89–0.23)	1.10 (0.95–1.30)	0.3518
Hematologic				
White cell count - g/L	5.61 (4.47–7.09)	5.97 (4.74–7.67)	5.48 (4.3–6.82)	0.0008
Lymphocyte count - g/L	1.32 (0.88–1.77)	1.28 (0.83–1.72)	1.36 (0.91–1.82)	0.2339
Platelet count - g/L	220 (169–277)	221 (164–288)	218.5 (171–272)	0.2809
Hemoglobin - g/L	127 (116–137)	125.6 (114.5–136)	127 (116–138)	0.0316
Inflammatory				
ESR - mm/h	25 (13.5–48.1)	28 (17.1–55.6)	21.8 (11.5–44.1)	0.0083
TNF - fmol/mL	9.3 (6.8–12.7)	9.9 (7.03–14.2)	9.3 (6.49–12.1)	0.7094
IL-1 β - pg/mL	5 (5–5.8)	5 (5–5.8)	5 (5–5.72)	0.3926
IL-10 - pg/mL	5 (5–7.2)	5 (5–7.8)	5 (5–6.6)	0.1855
IL-6 - pg/mL	5.3 (2.6–16.1)	6.02 (3.02–18.2)	4.95 (2.49–14.8)	0.2482
PCT - ng/mL	0.03 (0.02–0.07)	0.04 (0.02–0.08)	0.03 (0.02–0.06)	0.5126
CRP - mg/L	5.85 (3.11–37.1)	17.92 (3.11–46.6)	3.15 (3.11–23.4)	0.0131
Immune				
IgA - g/L	2.19 (1.84–2.7)	2.22 (1.85–2.79)	2.18 (1.84–2.61)	0.1964
IgM - g/L	0.99 (0.79–1.28)	0.89 (0.68–1.15)	1.03 (0.85–1.34)	<0.0001
IgG - g/L	11.7 (10.3–13.3)	11.9 (10.8–13.2)	11.7 (10.2–13.4)	0.4699
IgE - g/L	40.6 (18.3–115.0)	50.15 (18.50–142.5)	38.7 (18.3–95.8)	0.0363
C3 - g/L	1.18 (1.03–1.33)	1.22 (1.11–1.37)	1.16 (0.98–1.29)	0.5755
C4 - g/L	0.26 (0.21–0.33)	0.27 (0.24–0.34)	0.25 (0.20–0.32)	0.0196
Total T lymphocytes - %	68.1 (59.79–74.2)	66.43 (57.09–73.05)	69.14 (61.04–74.65)	0.0633
Total T lymphocytes count	618 (372–821)	546 (282–787)	662.5 (421–838)	0.0364
Cytotoxic T lymphocytes - %	23.30 (17.2–29.8)	20.66 (15.86–28.16)	24.32 (18.36–30.33)	0.0580
Cytotoxic T lymphocytes count	205 (118–299)	170 (100–266)	211.5 (134–313)	0.1275
Helper T cells - %	40.76 (33.52–48.18)	41.54 (32.94–48.82)	40.04 (34.03–47.91)	0.6426
Helper T cells count	364 (225–512)	345.5 (167–508)	372 (241–514)	0.2946
B lymphocytes - %	13.68 (9.88–19.22)	13.50 (9.40–19.32)	13.7 (10.08–19.04)	0.8565
B lymphocytes count	112 (77–172.5)	103 (64.5–151.5)	116 (83.5–183.5)	0.0445
K cells - %	13.85 (8.88–20.34)	15.66 (9.94–22.75)	13.26 (8.50–19.44)	0.0120
K cells count	112 (65.5–181.5)	116 (65.5–187.5)	110.5 (65.5–178)	0.5853
Lymphocytes count	908 (609–1167)	851 (530–1122)	951 (678–1199)	0.1020
Helper/Cytotoxic T lymphocytes ratio	1.78 (1.26–2.54)	2.10 (1.38–2.66)	1.64 (1.19–2.32)	0.2465
Coagulation				
Fibrinogen - g/L	2.91 (2.32–3.88)	3.03 (2.44–3.97)	2.84 (2.25–3.83)	0.0116
PT - s	12.1 (11.3–13.1)	12.1 (11.2–13.1)	12.1 (11.3–13.1)	0.4645
INR	1.01 (0.94–1.10)	1.01 (0.94–1.09)	1.01 (0.95–1.10)	0.3082
PAP	99 (94–104)	99 (94–104)	99 (94–103.8)	0.1569
APTT - s	30.00 (27.7–32.2)	29.45 (27.3–32.2)	30.1 (27.9–32.2)	0.5937
TT - s	15.75 (14.85–17.01)	15.8 (14.9–17.1)	15.7 (14.8–17.0)	0.3625
D-dimer - mg/L	0.48 (0.32–0.97)	0.59 (0.38–1.30)	0.43 (0.29–0.89)	0.3873

(Continued)

Table 3 (Continued).

Variable- No./Total No. (%)	No. (%)			P value
	Total	Hypertension	Non-Hypertension	
	944 (100)	311 (32.94)	633 (67.06)	
Biochemical				
BNP - pg/mL	26 (10–64)	37.5 (13–91)	23 (10–50.5)	0.0042
ALT - IU/L	20 (11–35)	20 (12–35)	20 (11–35.5)	0.4357
AST - IU/L	22 (16–32)	23 (16–35)	21 (16–31)	0.3370
TP- g/L	63.6 (59.5–67.5)	63.75 (60.1–67.9)	63.45 (59.3–67.1)	0.3625
ALB- g/L	37.85 (34.3–41.2)	37.4 (34.0–40.3)	38.1 (34.5–41.4)	0.1262
PA- g/L	153.7 (106.2–211.5)	154.7 (103.1–219.2)	153.6 (107.7–206.5)	0.5847
GLB- g/L	25.8 (22.4–29.01)	26.1 (23.3–29.5)	25.5 (22.01–28.8)	0.6356
Cys-C - mg/L	0.79 (0.66–0.98)	0.90 (0.74–1.16)	0.75 (0.64–0.89)	<0.0001
TBIL - μ mol/L	11 (8.2–14.6)	11.5 (8.4–15.8)	10.9 (8.2–14.1)	0.0578
CRE - μ mol/L	66.3 (56.8–81.3)	72.75 (60.4–86.4)	64 (55.2–78.2)	<0.0001
BUN- mmol/L	4.76 (3.76–6.01)	5.16 (4.08–6.65)	4.53 (3.67–5.72)	0.0741
UA- mmol/L	269.7 (219.7–340.1)	290.3 (237.4–365.8)	260.5 (213.5–321.7)	<0.0001
Creatinine - μ mol/L	63 (39–104.5)	64 (42–105)	62 (38–103)	0.9357
LDH - U/L	210 (170.5–278.0)	219 (180–298)	204 (168–266)	0.3137
SAA- mg/L	22.18 (6.02–254.04)	99.28 (8.85–300)	15.97 (5.97–236.1)	0.0050
Blood Gas Analysis				
PH	7.45 (7.42–7.48)	7.45 (7.42–7.48)	7.45 (7.42–7.48)	0.5964
P _{CO2} - mmHg	36 (33–41)	35 (33–41)	37 (32.5–41)	0.6320
P _{O2} - mmHg	94 (69–123)	85 (70–113)	98.5 (68.5–134)	0.0264
Minerals				
Sodium - mmol/L	139.7 (137.4–141.3)	139.5 (137–141.3)	139.8 (137.5–141.3)	0.2377
Potassium - mmol/L	3.82 (3.51–4.21)	3.77 (3.42–4.21)	3.85 (3.55–4.20)	0.1796
Chloride - mmol/L	106 (103.6–107.7)	105.7 (102.8–107.4)	106.0 (103.7–107.8)	0.0488

Abbreviations: HbA1c, glycosylated hemoglobin A1; TC, total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; PCT, procalcitonin; TNF, tumor necrosis factor; IL, interleukin; BUN, blood urea nitrogen; PT, prothrombin time; INR, international normalized ratio; APTT, activated partial thromboplastin time; PAP, prothrombin activation percentage; TT, thrombin time; LDH, lactic dehydrogenase; Ig, immunoglobulin; C3, complement 3; C4, complement 4; AST, aspartate aminotransferase; ALT, alanine aminotransferase; SAA, serum amyloid A; PH, pondus hydrogenii.

increased ($P=0.036$), whereas the serum levels of complement 4 (0.27 g/L [IQR, 0.24–0.34] vs 0.25 g/L [IQR, 0.20–0.32]) were decreased ($P=0.020$) in the hypertensive COVID-19 patients when compared with the non-hypertensive COVID-19 patients. The level of complement 4 was decreased in both groups, indicating viral infection. The IgM level, total T lymphocyte count, B lymphocyte count, and percentage of K cells showed positive changes, but no clinical manifestations were observed.

Compared to the COVID-19 group without hypertension, the COVID-19 group with hypertension had a higher level of fibrinogen, though its level was within the normal range in both groups. The levels of D-dimer, activated partial thromboplastin time, thrombin time, etc. were within the laboratory ranges, suggesting a more or less normal blood coagulation function. Serum amyloid A levels were higher in the

hypertensive group than in the non-hypertensive group (99.28 mg/L [IQR, 8.85–300] vs 15.97 mg/L [IQR, 5.97–236.1], $P=0.005$), suggesting acute infection. The level of the brain natriuretic peptide showed a positive change, but it was clinically irrelevant. Although cystatin C, creatinine, and uric acid levels of both the hypertensive and non-hypertensive groups were within normal range, the hypertensive patients had higher cystatin C (0.90 mg/L [IQR, 0.74–1.16] vs 0.75 mg/L [IQR, 0.64–0.89], $P < 0.001$), creatinine, and uric acid levels than the non-hypertensive patients, possibly indicating renal function injury. No abnormalities were noted in the levels of alanine aminotransferase, aspartate aminotransferase, and blood urea nitrogen. Compared to the non-hypertensive patients, the hypertensive patients had much lower PO₂ (85 mmHg [IQR, 70–113] vs 98.5 mmHg [IQR, 68.5–134], $P=0.026$). This may be related to the ACE2 levels,

as it has been previously reported that hypoxia could decrease ACE2 expression in the lung tissues of rats.¹⁷

Clinical Outcomes

As shown in Table 4, 86 patients were admitted to the ICU and 904 patients were discharged from the hospital. There were no significant differences in the incidence of ICU admission and hospital discharge between the two groups. No deaths were observed during the entire study. The median duration of hospitalization was 14 days (median, 9–20 days). Patients with hypertension had significantly longer hospital stays (14 [IQR, 9–21] vs 13 [IQR, 8–19], $P=0.022$) than those without hypertension.

Treatment and Complications

All COVID-19 patients received symptomatic treatment. The majority of the patients (77.67%) received antiviral

therapy, while 61.5% received intravenous antibiotic therapy. Furthermore, 31.31% received systemic glucocorticoids, and 1.44% received antifungal medication. The majority (89.62%) received oxygen therapy, while only a few required invasive (1.52%) and noninvasive mechanical ventilation (7.16%). In addition, 83.93% received traditional Chinese medicine treatment, 69.92% received Chinese patent medicine treatment, and 16.68% received acupuncture or ear acupoint therapy. There were no significant differences in the above treatment measures between the COVID-19 patients with and without hypertension. Anti-hypertensive drugs and lipid-lowering drugs were administered more to patients with hypertension than to those without (62.12% vs 37.88%, $P<0.001$ and 44.00% vs 56.00%, $P<0.036$, respectively), whereas antidiabetic drugs were used less frequently in hypertensive patients (44.00% vs 56.00%, $P=0.036$) (Table 4).

Table 4 Complications, Treatments, and Clinical Outcomes

Variable	No. (%)			P value
	Total	Hypertension	Non-Hypertension	
	944 (100)	311 (32.94)	633(67.06)	
Complications				
Septic shock - no. (%)	10 (1.07)	2 (20.00)	8 (80.00)	0.3922
Heart failure - no. (%)	14 (1.50)	8 (57.14)	6 (42.86)	0.0799
Acute respiratory distress syndrome - no. (%)	48 (5.15)	15 (31.25)	33 (68.75)	0.8356
Acute kidney injury - no. (%)	10 (1.07)	5 (50)	5 (50)	0.2385
Disseminated intravascular coagulation - no. (%)	2 (0.21)	1 (50)	1 (50)	0.5467
Rhabdomyolysis - no. (%)	1 (0.11)	0 (0.00)	1 (100.00)	1.0000
Treatments				
Anti-hypertensive medication - no. (%)	264 (35.87)	164 (62.12)	100 (37.88)	<0.0001
Antidiabetic medication - no. (%)	50 (6.79)	22 (44.00)	28 (56.00)	0.0362
Lipid-lowering medication - no. (%)	65 (8.83)	40 (61.54)	25 (38.46)	<0.0001
Intravenous antibiotics - no. (%)	567 (61.50)	192 (33.86)	375 (66.14)	0.2780
Antifungal medication - no. (%)	13 (1.44)	6 (46.15)	7 (53.85)	0.2747
Antiviral medication - no. (%)	714 (76.77)	243 (34.03)	471 (65.97)	0.0561
Systemic glucocorticoids - no. (%)	284 (31.31)	98 (34.51)	186 (65.49)	0.2912
Oxygen therapy- no. (%)	798 (85.62)	267 (33.46)	531 (66.54)	0.1816
Invasive mechanical ventilation - no. (%)	14 (1.52)	6 (42.86)	8 (57.14)	0.3940
Noninvasive mechanical ventilation - no. (%)	66 (7.16)	28 (42.42)	38 (57.58)	0.0754
Intravenous immunoglobulin- no. (%)	227 (24.57)	78 (34.36)	149 (65.64)	0.4336
Traditional Chinese Medicine - no. (%)	781 (83.93)	245 (31.37)	536 (68.63)	0.1052
Chinese Patent Medicine - no. (%)	651 (69.92)	214 (32.87)	437 (67.13)	0.7029
Acupuncture or ear acupoint - no. (%)	154 (16.68)	59 (38.31)	95 (61.69)	0.0856
Clinical outcomes at data cutoff				
Admission to intensive care unit - no. (%)	86 (9.12)	32 (37.21)	54 (62.79)	0.3815
Discharge from hospital	904 (95.76)	294 (32.52)	610 (67.48)	0.1889
Median length of hospital stay (IQR) - days	13 (9–20)	14 (9–21)	13 (8–19)	0.0216

During hospital admission, patients were diagnosed with acute respiratory distress syndrome (5.15%), acute heart failure (1.50%), septic shock (1.07%), acute kidney injury (1.07%), disseminated intravascular coagulation (DIC) (0.21%), and rhabdomyolysis (0.11%). However, all the above-mentioned diagnoses showed similar incidences in the two groups.

Discussion

Compared to the diseases associated with previous coronavirus epidemics, such as the Severe Acute Respiratory Syndrome and the Middle East Respiratory Syndrome, COVID-19 is more severe and has a faster spread.¹⁸ SARS-CoV-2 enters cells through the ACE2 receptor, considered the functional receptor for this coronavirus.¹⁹ Additionally, ACE2 is regarded as a potent modulator of blood pressure, and its deficiency leads to hypertension.²⁰ Due to the interaction between SARS-CoV-2 and ACE2, it is believed that hypertension may be related to the pathogenesis of COVID-19 by working directly as a previous clinical predictor of disease severity or by leading to late deterioration in the disease process.⁸

Hypertension, diabetes, chronic obstructive pulmonary disease, cardiovascular disease, and cerebrovascular disease are risk factors for COVID-19.^{21–25} In this retrospective cohort study, we focused on hypertension as it was the most prevalent comorbidity among patients with COVID-19. The median age of the COVID-19 patients was 60 years, and the prevalence rate of hypertension was 32.94%. We found no difference in the patients' sex distribution, but the patients with hypertension were older and had higher blood pressures, consistent with a previous study.²⁶ This may be due to the higher median age of the patients we included. Normally, the frequency of palpitation is higher in patients with hypertension. However, in our study, the incidence of palpitations was lower in the hypertensive group, which could have resulted from the small number of patients with palpitation or the presence of drug interventions in hypertensive patients. Our study indicated that hypertensive COVID-19 patients had more comorbidities, such as diabetes mellitus, coronary heart disease, pleural effusion, and chronic kidney disease.

Chest CT images proved that patients with hypertension had higher rates of pleural effusion than those without hypertension, indicating that the former had more severe lung pathologies.²⁷ Furthermore, the levels of the inflammatory markers, such as the erythrocyte sedimentation

rate, serum amyloid A, and C-reactive protein, were elevated in the COVID-19 patients, pointing to an increased likelihood of developing cytokine storm in these patients. Furthermore, the levels of these markers were significantly higher in patients with hypertension than in those without hypertension. Integrating these results with the chest CT results above, we can surmise that COVID-19 patients with hypertension were more likely to develop a more severe infection. Hence, patients in the hypertensive group had longer hospital stays than those in the non-hypertensive group. Moreover, there was no significant difference in clinical treatment between the two groups, except for the use of antihypertensive and lipid-lowering drugs.

Study Limitations

Our study had the following limitations. First, this study was retrospective and non-randomized. Thus, the clinical outcomes were not as accurate as those in prospective studies. Second, the severity of COVID-19 was not graded. As such, the proportion of patients with each grade could not be determined. Third, due to the outbreak isolation management and lack of equipment, the blood pressure was not measured daily. Fourth, systemic glucocorticoids have been widely used to treat COVID-19 patients, which may influence blood pressure. Therefore, multicenter and prospective studies are necessary to further explore the risk factors and severe events in COVID-19 patients with hypertension.

Conclusion

In conclusion, hypertension worsens the morbidity of COVID-19 patients. This study provided at least two essential lessons for the clinical management of COVID-19. First, controlling blood pressure in COVID-19 patients with hypertension is necessary. Second, increased clinical vigilance is warranted for COVID-19 patients with hypertension, given its chronicity and associated morbidity.

Ethics Statement

The study was performed in accordance with the Declaration of Helsinki and carried out in accordance with the recommendations of Chinese National Guidelines and Ethics Branch of the Biomedical Ethics Committee of Guangzhou University of Chinese Medicine (ZE2020-049-01).

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Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest in relation to this work.

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