Pulmonary and Critical Care Medicine

Research Article ISSN: 2398-3108

Predictors of severity and mortality in hospitalized patients with COVID-19 in northeastern Taiwan

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Abstract

Background: The ongoing Coronavirus disease 2019 (COVID-19) pandemic has spread globally. In May 2021, community infections were increasingly reported in Northern Taiwan. Thus, an urgent need exists to identify predictors of severity and mortality in hospitalized patients with COVID-19.

Methods: Patients with laboratory-confirmed COVID-19 from May 1, 2021, to July 31, 2021, in a designated hospital in northeastern Taiwan were retrospectively enrolled in our study. Demographic and clinical data were collected, and predictors of severity and mortality in hospitalized patients with COVID-19 were analyzed through multivariable backward stepwise logistic regression models.

Results: Of the 91 patients included in the study, 66 (72.5%) were identified as having severe cases, and in-hospital mortality was 22.0%. Advanced age, a low pulse oximetric saturation/fraction of inspired oxygen (S/F) ratio, and low hemoglobin (Hb) levels on admission were independently associated with severity and mortality according to multivariable analyses. Older age and comorbid chronic kidney disease (CKD) were associated with mortality in patients with severe COVID-19.

Conclusion: On admission, advanced age, S/F ratio, and Hb level may be prognostic factors for patients with COVID-19. Underlying comorbidities, namely CKD may predict in-hospital mortality in patients with severe COVID-19.

Abbreviations: age, chronic kidney disease, COVID-19, hemoglobin, hypoxemia

Introduction

Since its first recorded case in the city of Wuhan (China) in December 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread rapidly, eventually leading to the global Coronavirus disease 2019 (COVID-19) pandemic [1]. This highly contagious virus has caused up to four waves of infection in many countries; as of July, 2021, more than 190 million people have been infected and 4 million have died worldwide [2]. Although the SARS-CoV-2 infection causes considerably more asymptomatic and mild illness than severe pneumonia, severe cases can develop into acute respiratory distress syndrome (ARDS) and result in death [3].

The Taiwanese government has imposed a 14-day quarantine requirement for all passengers entering Taiwan from abroad. By January 2020, no new cases of local transmission of COVID-19 were being reported in Taiwan, and all newly confirmed cases involved people having returned from abroad. However, in May 2021, community infections began to be reported in northern Taiwan. The sudden influx of patients in hospitals during the outbreak has overwhelmed the available personnel and facilities, particularly those designated for the care of critically ill patients, and has led to an urgent need for identification of potential risk factors to determine disease severity and mortality of COVID-19 and for the development of risk stratification measures [4].

In this paper, we present the details of all patients with laboratory-confirmed COVID-19 admitted to a designated hospital for patients with COVID-19 in northeastern Taiwan; moreover, we examine the predictors of severity and in-hospital death for patients during hospitalization.

Materials and methods

Study design and participants

This retrospective cohort study was conducted in Chang Gung Memorial Hospital in Keelung (Taiwan), which was a designated hospital for patients with COVID-19 at the time of this study. We evaluated all adult patients (aged ≥20 years) with laboratory-confirmed COVID-19 who were admitted between May 1, 2021, and July 31, 2021. COVID-19 diagnosis was based on World Health Organization guidelines and confirmed by positive results in polymerase chain reaction testing of a nasopharyngeal sample [5]. This study was approved by the Institutional Review Board of Chang Gung Memorial Hospital (IRB/CGMH No. 202101380B0) and informed consent to review medical records was not required. To maintain patient confidentiality, no patient identifiers were collected. All research processes were in accordance with the Declaration of Helsinki.

Clinical data collection and definitions

The following information was collected from patients' medical

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Received: February 12, 2022; **Accepted:** February 21, 2022; **Published:** February 24, 2022

records: age; sex; body mass index (BMI); pulse oximetric saturation (SpO_2)/fraction of inspired oxygen (FiO_2) [S/F] ratio on the first day of admission; Glasgow Coma Scale (GCS) score on the first day of admission; quick Sequential Organ Failure Assessment (qSOFA) [6] on the first day of admission; comorbidities, including chronic kidney disease (CKD), diabetes, cardiovascular disease (CVD), chronic lung disease, and cancer; and treatments, including antiviral agents, corticosteroids, and interleukin (IL)-6 antagonists. We extracted laboratory data from within the first 48 hours of admission, including blood count, D-dimer concentration, renal function, liver function, creatine kinase levels, lactate dehydrogenase (LDH) levels, serum ferritin levels, albumin levels, C-reactive protein (CRP) levels, and procalcitonin (PCT) levels. COVID-19 severity during hospitalization was assessed according to World Health Organization interim guidance and divided into two groups: non-severe (mild disease and moderate disease) and severe (severe disease and critical disease) [5]. Survivors were defined as patients who were alive for the entire period of hospitalization.

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) for Windows (version 19.0; SPSS Inc., Chicago, IL, USA). Patient characteristics are presented as mean ± standard deviation for continuous variables and number (%) for categorical variables. Differences in continuous variables were analyzed using the Mann-Whitney U test. Differences in categorical variables were analyzed using the chi-square test. Univariable logistic regression was performed to assess the associations between each variable and severity and mortality. In univariable analysis, variables were included that exhibited significant differences between the non-severe and severe groups and between non-survivors and survivors. The variables that were found to be significant in the univariable analysis and were considered clinically relevant were included in multivariable backward stepwise logistic regression models to identify predictors associated with severity and mortality. We excluded variables from the univariable analysis if the number of events was too small for an odds ratio (OR) to be calculated and if collinearity was observed. A p value of <0.05 was considered statistically significant.

Results

Patient characteristics

A total of 91 patients with COVID-19 were included in this study. The baseline demographics, clinical characteristics, and biochemical characteristics of the patients are listed in Table 1. The mean age of the participants was 65.1 years, with a mean BMI of 23.9 kg/m2, and 56.0% of the patients were male. The overall number of in-hospital deaths was 20 (22.0%). Nearly two-thirds of the patients (72.5%, 66 of 91) had severe cases and 27.5% (25 of 91) had non-severe cases of COVID-19 during hospitalization.

Comparison of non-survivors and survivors

Table 1 presents a comparison of the characteristics of the non-survivor and the survivor patients hospitalized with COVID-19. Age, D-dimer concentration, blood urea nitrogen (BUN) levels, and PCT levels were significantly higher in non-survivors than in survivors. Compared with the non-survivors, the survivors had significantly higher initial S/F ratios, initial GCS scores and hemoglobin (Hb), platelet (PLT), alanine aminotransferase (ALT), and albumin levels. The proportions of qSOFA ≥1, CKD, CVD, antiviral agents use, and corticosteroids use were significantly higher in the non-survivors than in the survivors. The results of the univariable logistic regression analysis of the predictors of in-hospital mortality are presented in Table 2. Age, initial S/F ratio, qSOFA ≥1, CVD, Hb levels, albumin levels, and antiviral agents use were selected for the multivariable backward stepwise logistic regression models for mortality. The initial GCS score was part of or associated with qSOFA and was, therefore, not included in the models. CKD was not included in the models because the number of events was insufficient. The results of the multivariable logistic regression models assessing the predictors of in-hospital mortality are displayed in Table 2. Age (OR: 1.126, 95% confidence interval [CI]: 1.054–1.203; p < 0.001), initial S/F ratio (OR: 0.993, 95% CI: 0.987–0.998; p = 0.011), and Hb levels (OR: 0.546, 95% CI: 0.363-0.820; p = 0.004) were independent predictors of mortality in hospitalized patients with COVID-19.

Table 1. Clinical characteristics of hospitalized patients with COVID-19 (non-survivors vs. survivors); Data are presented as mean ± standard deviation or number (%). Statistical comparison was performed with Mann–Whitney U test or chi-square test. BMI=body mass index, S/F=pulse oximetric saturation/fraction of inspired oxygen, GCS=Glasgow Coma Scale, qSOFA=quick Sequential Organ Failure Assessment, CKD=chronic kidney disease, CVD=cardiovascular disease, CLD=chronic lung disease, WBC=white blood cell count, Hb=hemoglobin, PLT=platelet, BUN=blood urea nitrogen, Cr = creatinine, ALT=alanine aminotransferase, T-bil=total bilirubin, CRP =C-reactive protein, PCT=procalcitonin, LDH=lactate dehydrogenase, CK=creatine kinase, IL=interleukin. * A p value of < 0.05 was considered statistically significant

	All (n=91)	Non-survivors (n=20)	Survivors (n= 71)	p value
Age (years)	65.1 ± 16.5	78.3 ± 13.2	61.4 ± 15.5	< 0.001*
Male sex	51 (56.0)	13 (65.0)	38 (53.5)	0.361
BMI (kg/m²)	23.9 ± 4.0	22.4 ± 4.0	24.3 ± 4.0	0.082
Initial S/F ratio	368.3 ± 131.0	311.3 ± 144.9	384.4 ± 123.2	0.016*
Initial GCS score	13.7 ± 2.4	12.4 ± 3.2	14.1 ± 2.0	0.006*
qSOFA ≥ 1	37 (40.7)	14 (70.0)	23 (32.4)	0.002*
Comorbidities				
CKD	16 (17.6)	9 (45.0)	7 (9.9)	< 0.001*
Diabetes	21 (23.1)	6 (30.0)	15 (21.1)	0.405
CVD	50 (54.9)	15 (75.0)	35 (49.3)	0.041*
CLD	11 (12.1)	4 (20.0)	7 (9.9)	0.219
Cancer	8 (8.8)	1 (5.0)	7 (9.9)	0.498
Laboratory tests				
WBC (1000/μL)	7.2 ± 4.9	7.5 ± 7.0	7.1 ± 4.1	0.305
Hb (g/dL)	12.6 ± 2.1	11.3 ± 2.4	13.0 ± 1.9	0.007*
PLT (1000/μL)	201.5 ± 80.8	179.0 ± 91.7	207.9 ± 77.0	0.033*
Neutrophil (%)	74.5 ± 10.8	75.0 ± 11.1	74.4 ± 10.7	0.889
Lymphocyte (%)	17.9 ± 8.9	16.3 ± 9.1	18.4 ± 8.8	0.317
D-dimer (mg/L)	2.3 ± 8.6	2.4 ± 3.4	2.2 ± 9.6	0.005*
BUN (mg/dL)	23.7 ± 22.6	31.7 ± 20.9	21.4 ± 22.7	0.002*
Cr (mg/dL)	1.7 ± 2.6	2.6 ± 3.7	1.4 ± 2.2	0.072
ALT (U/L)	34.7 ± 36.6	24.4 ± 19.5	37.6 ± 40.0	0.034*
T-bil (mg/dL)	0.4 ± 0.2	0.4 ± 0.2	0.4 ± 0.2	0.791
CRP (mg/L)	42.7 ± 43.2	48.0 ± 35.5	41.3 ± 45.2	0.156
PCT (ng/dL)	1.0 ± 2.9	1.5 ± 2.5	0.9 ± 3.0	0.020*
LDH (U/L)	296.0 ± 236.4	272.1 ± 131.2	302.7 ± 258.8	0.893
CK (U/L)	163.9 ± 331.7	246.8 ± 661.8	140.5 ± 141.7	0.23
Ferritin (ng/dL)	1011.5 ± 1784.0	2021.9 ± 3403.3	726.9 ± 757.9	0.378
Albumin (g/dL)	3.8 ± 0.5	3.6 ± 0.4	3.9 ± 0.5	0.028*
Treatments				
Antiviral agents	44 (48.4)	14 (66.7)	30 (43.2)	0.028*
Corticosteroids	70 (76.9)	19 (94.4)	51 (71.6)	0.030*
IL-6 antagonists	18 (19.8)	5 (22.2)	13 (18.9)	0.507
Severe cases	66 (72.5)	20 (100)	46 (64.8)	0.002*

Table 2. Predictors of mortality in hospitalized patients with COVID-19 by multivariable backward stepwise logistic regression analysis; S/F = pulse oximetric saturation/fraction of inspired oxygen, GCS = Glasgow Coma Scale, qSOFA = quick Sequential Organ Failure Assessment, CKD = chronic kidney disease, CVD = cardiovascular disease, Hb = hemoglobin, PLT = platelet, BUN = blood urea nitrogen, ALT = alanine aminotransferase, PCT = procalcitonin. * A p value of < 0.05 was considered statistically significant

Variables	Univariable analysis		Multivariable analysis	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Age (years)	1.091 (1.041-1.144)	< 0.001*	1.126 (1.054-1.203)	< 0.001*
Initial S/F ratio	0.996 (0.992-1.000)	0.026*	0.993 (0.987-0.998)	0.011*
Initial GCS score	0.771 (0.636-0.936)	0.008*		
qSOFA ≥ 1	4.870 (1.657-14.308)	0.004*		
CKD	7.481 (2.306-24.267)	0.001*		
CVD	3.086 (1.013-9.400)	0.047*		
Hb (g/dL)	0.684 (0.529-0.885)	0.004*	0.546 (0.363-0.820)	0.004*
PLT (1000/μL)	0.995 (0.988-1.002)	0.162		
D-dimer (mg/L)	1.002 (0.948-1.060)	0.936		
BUN (mg/dL)	1.017 (0.997-1.037)	0.097		
ALT (U/L)	0.979 (0.952-1.007)	0.138		
PCT (ng/dL)	1.063 (0.916-1.233)	0.421		
Albumin (g/dL)	0.286 (0.095-0.861)	0.026*		
Antiviral agents	3.189 (1.098-9.260)	0.033*		
Corticosteroids	7.451 (0.934-59.421)	0.058		

Comparison of non-severe cases and severe cases

The characteristics of non-severe and severe cases of hospitalized patients with COVID-19 are listed in Table 3. Age, neutrophil levels, D-dimer concentration, BUN levels, creatinine (Cr) levels, CRP levels, PCT levels, and ferritin levels were significantly higher in severe cases than in non-severe cases. Compared with severe cases, non-severe cases exhibited significantly higher initial S/F ratio, initial GCS scores, Hb levels, PLT levels, lymphocyte levels, and albumin levels. Proportions of Qsofa≥1, CKD, diabetes, CVD, antiviral agents use, corticosteroids use, and interleukin-6 (IL-6) antagonists use were significantly higher in severe cases than in non-severe cases. The results of the univariable logistic regression analysis of the predictors of severe COVID-19 are displayed in Table 4. Age, initial S/F ratio, qSOFA ≥1, Hb levels, neutrophil levels, lymphocyte levels, BUN levels, and albumin levels were selected for the multivariable backward stepwise logistic regression models for severity. Initial GCS score was part of or associated with qSOFA and was, therefore, not included in the models. CKD, CVD, antiviral agents use, corticosteroids use, and IL-6 antagonists use were also not included in the models because the number of events was either zero or too small. The results of multivariable logistic regression models assessing the predictors of severe COVID-19 are presented in Table 4. In the multivariable analyses, age (OR: 1.085, 95% CI: 1.032–1.140; p=0.001), initial S/F ratio (OR: 0.978, 95% CI: 0.961-0.996; p=0.017), and Hb levels (OR: 0.442, 95% CI: 0.247-0.792; p=0.006) were independent predictors of severity in hospitalized patients with COVID-19.

Predictors of mortality of severe COVID-19

Table 5 presents a comparison of the patient characteristics of hospitalized non-survivors and survivors of severe COVID-19. Non-survivors of severe COVID-19 were significantly older than the survivors. Compared with the non-survivors, the survivors had significantly higher D-dimer concentrations and ALT levels. The qSOFA ≥1 and CKD proportions were significantly higher in non-survivors compared with survivors. The results of the univariable logistic regression analysis assessing the predictors of mortality in severe COVID-19 are presented in Table 6. Age, CKD, and ALT levels were selected for the multivariable backward stepwise logistic regression models for mortality. The results of the multivariable logistic regression models assessing the predictors of mortality of severe COVID-19 are displayed in Table 6. In the multivariable analyses, age (OR: 1.083, 95% CI: 1.024-1.146; p=0.006) and CKD (OR: 4.596, 95% CI: 1.200–17.612; p=0.026) were independent predictors of mortality in hospitalized patients with severe COVID-19.

Discussion

This retrospective cohort study identified prognostic factors for severity and in-hospital mortality in adults who were hospitalized with COVID-19 in northeastern Taiwan. Our findings may differ from those of previous studies because nearly two-thirds of the patients included in this study were identified as severe cases. Advanced age and low S/F ratios and Hb levels on admission were predictors of mortality and associated with higher risk of clinical severity. Additionally, comorbid CKD increased the risk of mortality in severe COVID-19 cases.

Table 3. Clinical characteristics of hospitalized patients with COVID-19 (non-severe vs. severe); Data are presented as mean ± standard deviation or number (%). Statistical comparison was performed with Mann–Whitney U test or chi-square test. BMI = body mass index, S/F = pulse oximetric saturation/fraction of inspired oxygen, GCS = Glasgow Coma Scale, qSOFA = quick Sequential Organ Failure Assessment, CKD = chronic kidney disease, CVD = cardiovascular disease, CLD = chronic lung disease, WBC = white blood cell count, Hb = hemoglobin, PLT = platelet, BUN = blood urea nitrogen, Cr = creatinine, ALT = alanine aminotransferase, T-bil = total bilirubin, CRP = C-reactive protein, PCT = procalcitonin, LDH = lactate dehydrogenase, CK = creatine kinase, IL = interleukin. * A p value of < 0.05 was considered statistically significant

	All (n=91)	Non-severe (n=25)	Severe (n = 66)	*p* value
Age (years)	65.1 ± 16.5	50.4 ± 16.0	70.7 ± 12.9	< 0.001*
Male sex	51 (56.0)	13 (52.0)	38 (57.6)	0.632
BMI (kg/m²)	23.9 ± 4.0	24.3 ± 3.6	23.7 ± 4.2	0.376
Initial S/F ratio	368.3 ± 131.0	460.7 ± 32.7	333.4 ± 137.3	< 0.001*
Initial GCS score	13.7 ± 2.4	14.9 ± 0.4	13.3 ± 2.6	0.002*
qSOFA ≥ 1	37 (40.7)	2 (8.0)	35 (97.2)	< 0.001*
Comorbidities				
CKD	16 (17.6)	0 (0)	16 (24.2)	0.007*
Diabetes	21 (23.1)	2 (8.0)	19 (28.8)	0.036*
CVD	50 (54.9)	3 (12.0)	47 (71.2)	< 0.001*
CLD	11 (12.1)	1 (4.0)	10 (15.2)	0.145
Cancer	8 (8.8)	2 (8.0)	6 (9.1)	0.87
Laboratory tests				
WBC (1000/μL)	7.2 ± 4.9	7.1 ± 6.0	7.2 ± 4.4	0.477
Hb (g/dL)	12.6 ± 2.1	14.0 ± 1.6	12.1 ± 2.1	< 0.001*
PLT (1000/μL)	201.5 ± 80.8	227.2 ± 74.8	191.8 ± 81.4	0.011*
Neutrophil (%)	74.5 ± 10.8	69.5 ± 8.6	76.5 ± 10.9	0.004*
Lymphocyte (%)	17.9 ± 8.9	22.4 ± 7.4	16.3 ± 8.8	0.002*
D-dimer (mg/L)	2.3 ± 8.6	0.5 ± 0.5	2.9 ± 10.1	0.001*
BUN (mg/dL)	23.7 ± 22.6	13.1 ± 6.7	27.7 ± 25.1	< 0.001*
Cr (mg/dL)	1.7 ± 2.6	0.8 ± 0.3	2.0 ± 3.0	0.021*
ALT (U/L)	34.7 ± 36.6	29.2 ± 34.7	36.8 ± 37.4	0.05
T-bil (mg/dL)	0.4 ± 0.2	0.4 ± 0.2	0.4 ± 0.2	0.543
CRP (mg/L)	42.7 ± 43.2	24.2 ± 47.5	49.8 ± 39.6	< 0.001*
PCT (ng/dL)	1.0 ± 2.9	1.0 ± 3.6	1.1 ± 2.7	0.001*
LDH (U/L)	296.0 ± 236.4	230.9 ± 86.9	320.6 ± 269.0	0.054
CK (U/L)	163.9 ± 331.7	92.3 ± 62.6	190.9 ± 385.0	0.079
Ferritin (ng/dL)	1011.5 ± 1784.0	478.1 ± 554.1	1213.6 ± 2035.3	0.004*
Albumin (g/dL)	3.8 ± 0.5	4.2 ± 0.5	3.7 ± 0.4	< 0.001*
Treatments				
Antiviral agents	44 (48.4)	0 (0)	44 (66.7)	< 0.001*
Corticosteroids	70 (76.9)	6 (24.0)	64 (97.0)	< 0.001*
IL-6 antagonists	18 (19.8)	0 (0)	18 (27.3)	0.004*
Mortality	20 (22.0)	0 (0)	20 (30.3)	0.002*

Table 4. Predictors of severity in hospitalized patients with COVID-19 by multivariable backward stepwise logistic regression analysis; S/F = pulse oximetric saturation/fraction of inspired oxygen, GCS = Glasgow Coma Scale, qSOFA = quick Sequential Organ Failure Assessment, CVD = cardiovascular disease, Hb = hemoglobin, PLT = platelet, BUN = blood urea nitrogen, Cr = creatinine, CRP = C-reactive protein, PCT = procalcitonin. * A p value of < 0.05 was considered statistically significant.

Variables	Univariable analysis		Multivariable analysis	
	OR (95% CI)	***p* value**	**OR (95% CI)**	***p* value**
Age (years)	1.107 (1.058-1.158)	< 0.001*	1.085 (1.032-1.140)	0.001*
Initial S/F ratio	0.979 (0.962-0.995)	0.011*	0.978 (0.961-0.996)	0.017*
Initial GCS score	0.420 (0.184-0.963)	0.040*		
qSOFA ≥ 1	12.984 (2.829-59.581)	0.001*		
Diabetes	4.649 (0.997-21.686)	0.051		
CVD	18.140 (4.852-67.820)	< 0.001*		
Hb (g/dL)	0.536 (0.376-0.763)	0.001*	0.442 (0.247-0.792)	0.006*
PLT (1000/μL)	0.995 (0.989-1.000)	0.067		
Neutrophil (%)	1.066 (1.017-1.117)	0.008*		
Lymphocyte (%)	0.921 (0.869-0.975)	0.005*		
D-dimer (mg/L)	3.027 (0.961-9.536)	0.059		
BUN (mg/dL)	1.130 (1.043-1.224)	0.003*		
Cr (mg/dL)	3.192 (0.877-11.609)	0.078		
CRP (mg/L)	1.020 (1.003-1.036)	0.017		
PCT (ng/dL)	1.016 (0.861-1.198)	0.85		
Ferritin (ng/dL)	1.001 (1.000-1.002)	0.061		
Albumin (g/dL)	0.059 (0.015-0.237)	< 0.001*		
Corticosteroids	101.333 (18.882-543.835)	< 0.001*		

Table 5. Clinical characteristics of hospitalized patients with severe COVID-19 (non-survivors vs. survivors); Data are presented as mean ± standard deviation or number (%). Statistical comparison was performed with Mann–Whitney U test or chi-square test. BMI = body mass index, S/F = pulse oximetric saturation/fraction of inspired oxygen, GCS = Glasgow Coma Scale, qSOFA = quick Sequential Organ Failure Assessment, CKD = chronic kidney disease, CVD = cardiovascular disease, CLD = chronic lung disease, WBC = white blood cell count, Hb = hemoglobin, PLT = platelet, BUN = blood urea nitrogen, Cr = creatinine, ALT = alanine aminotransferase, T-bil = total bilirubin, CRP = C-reactive protein, PCT = procalcitonin, LDH = lactate dehydrogenase, CK = creatine kinase, IL = interleukin. * A p value of < 0.05 was considered statistically significant

	All (n = 66)	**Non-survivors (n = 20)**	**Survivors (n = 46)**	***p* value**
Age (years)	70.7 ± 12.9	78.3 ± 13.2	67.5 ± 11.4	0.001*
Male sex	38 (57.6)	13 (65.0)	25 (54.3)	0.421
BMI (kg/m²)	23.7 ± 4.2	22.4 ± 4.0	24.2 ± 4.2	0.125
Initial S/F ratio	333.4 ± 137.3	311.3 ± 144.9	343.0 ± 134.4	0.367
Initial GCS score	13.3 ± 2.6	12.4 ± 3.2	13.7 ± 2.3	0.078
qSOFA ≥ 1	35 (97.2)	14 (70.0)	21 (45.7)	< 0.001*
Comorbidities				
CKD	16 (24.2)	9 (45.0)	7 (15.2)	0.009*
Diabetes	19 (28.8)	6 (30.0)	13 (28.3)	0.886
CVD	47 (71.2)	15 (75.0)	32 (69.6)	0.654
CLD	10 (15.2)	4 (20.0)	6 (13.0)	0.469
Cancer	6 (9.1)	1 (5.0)	5 (10.9)	0.446
Laboratory tests				
WBC (1000/μL)	7.2 ± 4.4	7.5 ± 7.0	7.0 ± 2.7	0.187
Hb (g/dL)	12.1 ± 2.1	11.3 ± 2.4	12.4 ± 1.8	0.072
PLT (1000/μL)	191.8 ± 81.4	179.0 ± 91.7	197.3 ± 76.9	0.132
Neutrophil (%)	76.5 ± 10.9	75.0 ± 11.1	77.1 ± 10.9	0.399
Lymphocyte (%)	16.3 ± 8.8	16.3 ± 9.1	16.2 ± 8.8	0.961
D-dimer (mg/L)	2.9 ± 10.1	2.4 ± 3.4	3.2 ± 11.9	0.044*
BUN (mg/dL)	27.7 ± 25.1	31.7 ± 20.9	25.9 ± 26.8	0.052
Cr (mg/dL)	2.0 ± 3.0	2.6 ± 3.7	1.8 ± 2.7	0.27
ALT (U/L)	36.8 ± 37.4	24.4 ± 19.5	42.2 ± 42.0	0.003*
T-bil (mg/dL)	0.4 ± 0.2	0.4 ± 0.2	0.4 ± 0.2	0.59
CRP (mg/L)	49.8 ± 39.6	48.0 ± 35.5	50.5 ± 41.6	0.989
PCT (ng/dL)	1.1 ± 2.7	1.5 ± 2.5	0.9 ± 2.7	0.137
LDH (U/L)	320.6 ± 269.0	272.1 ± 131.2	341.7 ± 309.4	0.447
CK (U/L)	190.9 ± 385.0	246.8 ± 661.8	166.7 ± 164.8	0.052
Ferritin (ng/dL)	1213.6 ± 2035.3	2021.9 ± 3403.3	862.2 ± 822.6	0.989
Albumin (g/dL)	3.7 ± 0.4	3.6 ± 0.4	3.7 ± 0.4	0.418
Treatments				
Antiviral agents	44 (66.7)	14 (70.0)	30 (65.2)	0.705
Corticosteroids	64 (97.0)	19 (95.0)	45 (97.8)	0.021*
IL-6 antagonists	18 (27.3)	5 (25.0)	13 (28.3)	0.507

Table 6. Predictors of mortality in hospitalized patients with severe COVID-19 by multivariable backward stepwise logistic regression analysis; qSOFA = quick Sequential Organ Failure Assessment, CKD = chronic kidney disease, ALT = alanine aminotransferase. * A p value of < 0.05 was considered statistically significant

Variables	Univariable analysis		Multivariable analysis	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Age (years)	1.084 (1.027-1.144)	0.003*	1.083 (1.024-1.146)	0.006*
qSOFA ≥ 1	2.778 (0.908-8.501)	0.073		
CKD	4.558 (1.383-15.030)	0.013*	4.596 (1.200-17.612)	0.026*
D-dimer (mg/L)	0.992 (0.934-1.053)	0.782		
ALT (U/L)	0.966 (0.935-0.999)	0.044*		
Corticosteroids	0.422 (0.025-7.106)	0.549		

Older age has been reported to be a key independent predictor of mortality and severity in patients with COVID-19 [7-10]. A retrospective cohort study in Italy involving 1,591 patients with a median age of 63 years and who were critically ill with COVID-19 revealed that older patients (age ≥64 years) had higher mortality (36% vs. 15%) than younger patients (age ≤63 years) [7]. Another retrospective study of 548 patients hospitalized with COVID-19 in Wuhan (China) reported that nearly half of the patients (49.1%) were severe cases and advanced age was identified as a risk factor for severity [8,9]. Our findings are consistent with those of these two studies; they indicated that the mean age of the severe cases was 70.7 years and that of non-survivors was 78.3 years. Our study confirmed that older age is an independent predictor of severity and in-hospital mortality in patients with COVID-19. An animal study also demonstrated that aged macaques have a stronger host response to virus infection than do young adult macaques and exhibit an increase in differential expression of genes associated with inflammation. The study concluded that aged macaques infected with SARS-CoV-2 develop more severe pathology than young adult animals do [10,11].

Previous studies have reported a strong association between hypoxemia and poorer clinical outcomes in patients with COVID-19 [12,13]. In a retrospective observational study, researchers collected the data of patients with COVID-19 from two centers in Chongqing, China; partial pressure arterial oxygen (PaO_2) on admission was reported as having a high distinguishing power for predicting a patient's progression to severe illness [12]. A study of 140 patients with COVID-19–associated pneumonia in Wuhan, China revealed that SpO2 >90.5% on admission yielded 84.6% sensitivity and 97.2% specificity for prediction of survival [13]. The S/F ratio has been found to correlate with the PaO2/FiO2 ratio and may be a reliable tool for hypoxemia screening [14,15]. In our study, hypoxemia according to the S/F ratio on admission was independently associated with severity and in-hospital mortality for patients with COVID-19. Hypoxemia is caused by intrapulmonary shunting, dysregulated hypoxic pulmonary vasoconstriction, impaired lung diffusion, and formation of intravascular microthrombi and is a primary pathophysiological feature and the main cause of mortality in patients with severe COVID-19 [16,17].

Hb concentration is a major determinant of the oxygen-carrying capacity of the blood. A previous meta-analysis revealed that anemia is associated with a 41% increased risk of all-cause mortality in the general population [18]. In patients with COVID-19, low Hb levels may reduce the body's capacity to support the increased peripheral tissue demands for oxygen during infection. A systematic review and meta-analysis involving 57,563 patients with COVID-19 reported that patients with severe cases had lower Hb levels than those with moderate cases. However, no significant difference was observed in the Hb levels of survivors and non-survivors [19]. In our study, Hb levels appeared to play a central role in determining severity and mortality in patients with COVID-19.

Underlying health conditions predispose patients with COVID-19 to an unfavorable clinical course and an increased risk of severity and death [8, 20-22]. A study that retrieved data from large international databases and used prevalence data from the Global Burden of Diseases, Injuries, and Risk Factors study 2017 and the United Nations population estimates for 2020 projected the global population of at-high risk for severe COVID-19 individuals to be 1.7 billion people; this number comprises 22% of the global population, of whom 349 million individuals would require hospital admission if infected. The study suggested that CKD was the most prevalent risk factor for severe COVID-19 worldwide [23]. In a multicenter retrospective observational study involving 1,210 hospitalized adult patients with COVID-19 in Turkey, patients with CKD were revealed to have significantly higher mortality (28.4% vs. 4.0%) than patients without CKD [24]. In our study, 24.2% of patients with severe COVID-19 had CKD, and the mortality rate for those patients was 56.3%. Comorbid CKD may predict the prognosis of severe COVID-19 in patients.

Our study has several limitations. First, this was a small-scale, retrospective study; missing data on some variables may have led to bias in estimations. Second, patient data were collected from a single hospital. Selection bias resulting from differing protocols of care (including choice and timing of medication, intensive care unit admission, and end-of-life care) could not be eliminated. Accordingly, further prospective and large-scale studies are required.

Conclusions

Overall, this retrospective cohort study performed in northeastern Taiwan revealed that advanced age, low S/F ratio, and low Hb levels on admission were independent predictors of severity and mortality in hospitalized patients with COVID-19. Among patients with severe COVID-19, older age and comorbid CKD may lead to a high risk of mortality. Further research through additional cohorts and comparisons of the predictive ability of these variables is required to support our findings.

Acknowledgement

The authors thank all the staff at Chang Gung Memorial Hospital in Keelung, Taiwan for providing clinical assistance.

Conflict of interest

The authors have no conflict of interest relevant to this article to disclose

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