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Original Article

Clinical characteristics analysis of COVID-19 patients from the first significant community outbreak by SARS-CoV-2 variant B.1.1.7 in Taiwan as experienced from a single northern medical center

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COVID-19;
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Taiwan;
Characteristics

Abstract *Background/Purpose:* Clinical characteristics of patients in the first community outbreak of coronavirus disease 2019 (COVID-19) by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant B.1.1.7 in Taiwan have not been characterized.
Methods: SARS-CoV-2 positive specimens from inpatients between May 7 and June 15 in 2021were screen for SARS-CoV-2 B.1.1.7 lineage by VirSNiP assay. Clinical characteristics were reviewed and compared with those from Feb 1 to April 30, 2020 and from Jan 1 to March 31, 2022.
Results: One hundred forty-one inpatients from May 7 to June 15, 2021 infected with SARS-CoV-2 B.1.1.7 lineage were included. The major presenting symptoms were fever (88.7%) and cough (59.6%). Incidence of relevant complications including pulmonary embolism, simultaneous infections with bacteria, virus, and fungi were 0.7%, 12.8%, 13.5%, and 2.1%, respectively. Old age, high Charlson comorbidity index, short of breath, and initial critical illness were independently associated with 28-day mortality (all $p < 0.05$). In comparison to COVID-19 inpatients from Feb 1 to April 30, 2020, patients from the outbreak by SARS-CoV-2 B.1.1.7 lineage were older, more severe in disease condition, higher mortality but less obvious initial presenting symptoms. After implementation of nationwide vaccination campaign in the next half year of 2021, COVID-19

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inpatients from Jan 1 to March 31 in 2022 indicated less severe diseases than those infected with SARS-CoV-2 B.1.1.7 lineage.
Conclusion: COVID-19 inpatients by SARS-CoV-2 variant B.1.1.7 with old age, multiple comorbidities, and more severe disease conditions were associated with increased mortality. Vaccination for this vulnerable populations may be helpful.

Introduction

The coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that first emerged in Wuhan, China, has become an ongoing global pandemic.[1,2] Because of June 2022, approximately 540 million confirmed cases and over 6 million COVID-related deaths have been reported.[3]

Following the first imported case from China in January 2020, there are several waves of COVID-19 in Taiwan. The first wave of COVID-19 in Taiwan broke out in February 2020, and until April 2020. The second wave began in early January the following year and ended on February 9 (https://sites.google.com/cdc.gov.tw/2019ncov/taiwan accessed on 24 July 2021). The third wave causing significant community outbreak initially occurred among "hostess bars" in a densely populated quarter of Taipei in May 2021. Different from previous waves in Taiwan, many patients linked to this outbreak were found to have contracted the B.1.1.7 variant, which was first identified in the United Kingdom (UK) in September 2020 and has been classified as one of "Variants of concern (VOCs)" because of its replicative advantage and enhanced transmissibility.[5—7] From May to June 24, the outbreak led to 14,353 newly confirmed cases in Taiwan, which were mainly be from Taipei and New Taipei city according to Taiwan Centers for Disease Control (https://sites.google.com/cdc.gov.tw/2019ncov/taiwan accessed on 24 July 2021). For the first time, the Taiwan Central Epidemic Command Center (CECC) announced a level 3 nationwide surveillance on May 19, 2021. To combat this significant outbreak in Taiwan, the CECC issued several strict infection control measures and launched mass COVID-19 vaccination programme. The third wave of COVID-19 therefore had been controlled. Nevertheless, the forth wave of COVID-19 in Taiwan occurred in the beginning of 2022. The wave mainly be caused by the Omicron variant (B.1.1.529) which could be escaped antibody responses among both people who had previous Covid-19 infection and those who have been fully vaccinated.[8] At the end of March 2022, a total of 7411 COVID-19 confirmed cases were reported (https://sites.google.com/cdc.gov.tw/2019ncov/taiwan accessed on 29 June 2022).

Among several waves of COVID-19 in Taiwan, the wave caused by the B.1.1.7 variant were associated with the highest mortality rates and led to substantial influence on health care system in Taiwan. Characteristics of infected patients, however, has not been well described. Thus, the aim of the study was to characterize clinical features of COVID-19 inpatients from May 7 to June 15, 2021 which was corresponding to the wave of the B.1.1.7 variant. Furthermore, we compared the characteristics of these patients to those admitted from Feb 1 to April 30, 2020 corresponding to the first wave by the original Wuhan strain and those admitted between Jan 1 and March 31, 2022 corresponding to the early phase of the forth wave by the Omicron variant (B.1.1.529).

Methods

Study design and population

We conducted a retrospective cohort study at the Tri-Service General Hospital. COVID-19 confirmed patients based upon SARS-CoV-2 detection by real-time reverse transcription polymerase chain reaction (RT-PCR) admitted from Feb 1 to April 30, 2020, May 7 to June 15, 2021, and Jan 1 to March 31, 2022 were included in this study. First, clinical features of patients admitted between May 7 and June 15, 2021, which was the time the first significant community outbreak occurred, were analyzed, and divided into the survival and non-survival group (death within 28 days after diagnosed as COVID-19) for furthermore comparison to find out risk factors for mortality. Second, two comparisons of clinical characteristics between two infected patient cohorts based on different waves of COVID-19 in Taiwan were made. Namely, COVID-19 confirmed cases admitted from May 7 to June 15, 2021 versus those from February 1 to April 30, 2020 and versus those from January 1 to March 31, 2022, respectively.

SARS-CoV-2 detection by real-time RT-PCR and screen for SARS-CoV-2 lineage B.1.1.7

COVID-19 inpatients caused by SARS-CoV-2 was diagnosed by means of real-time RT-PCR method (LabTurbo AIO 48 system, Taipei City, Taiwan) from oropharyngeal or nasopharyngeal swab specimens of infected patients.[9] Cycle threshold (Ct) values from real-time RT-PCR were also recorded. To screen a SARS-CoV-2 B.1.1.7 lineage, we used VirSNiP SARS-CoV-2 Spike N501Y and Spike del H69/V70 (TIB Molbiol, Berlin, Germany) assay to detected the mutations N501Y and del 69—70 in SARS-CoV-2-positive specimens from infected patients admitted between May 7 and June 15, 2021 in which time the significant community outbreak in northern Taiwan occurred.[10]

Data collection

All clinical information of the included patients were retrieved by means of electronic patient records. Clinical symptoms were retrieved from medical records, which were

uploaded to the National Notifiable Disease Surveillance System. Disease severity was classified as either asymptomatic, mild, moderate, severe, or critical illness, which was based on a previous study.[11] A massive COVID 19 vaccination campaign has been launched because the next half year of 2021. Vaccination status of admitted COVID-19 patients were recorded. The Charlson comorbidity index (CCI) was used as an aggregate measure for underlying disease.[12] Medications, including tocilizumab, remdesivir, and steroids, which have been reported to be beneficial for COVID-19 patients, were prescribed according to the guidelines.[13–16] Empiric antibiotic use within 48 h after admission, anticoagulant prophylaxis for pulmonary embolism complications, and voriconazole for suspected invasive pulmonary aspergillosis were also documented. Particularly, pulmonary embolism has been reported as one of the serious complications among COVID-19 patients, and its diagnosis is based on chest CT findings, D-dimer levels, and clinical symptoms.[17] Furthermore, concurrent infections, including invasive pulmonary aspergillosis, bacterial, and other viral infections, were divided into co-infection and superinfection based on the time of onset. Specifically, we defined co-infection and superinfection as infection episodes secondary to other pathogens occurring within and after 48 h admission, respectively. Meanwhile, the diagnostic criteria for COVID-19-associated invasive pulmonary aspergillosis (CAPA) were based on the prescribed consensus.[18] Empiric antibiotics and anticoagulant prophylaxis were administered for patients who has possibility of bacterial infection and risk of pulmonary embolism, according to the clinician's judgment. Microbiological examination will be arranged if the clinicians found that signs and symptoms of the patients consistent with co-infection or superinfection by pathogens other than SARS-CoV-2. Bacterial infection at various sites, which were identified according to Centers for Disease Control and Prevention (CDC) surveillance definitions along with growth of bacteria in the respective appropriate culture specimens by means of computerized medical and microbiology systems.[19] Patients with atypical pathogen infection as mycoplasma and chlamydia pneumoniae were based on the results from FilmArray Respiratory Panel (BioFire Diagnostics, bioMe'rieux, Utah, USA). Patients with virus infection was diagnosed from FilmArray Respiratory Panel (BioFire Diagnostics, bioMe'rieux, Utah, USA), quantitative PCR on plasma, or virus documentation from the relevant organ by histopathology. Patients for whom no positive microbiologic results from specimens or no microbiology tests were requested were considered not to have infections. Clinical outcomes for this study were all causes of 28-day mortality and hospital stay after COVID-19 diagnosis.

Statistical analysis

Clinical data were analyzed using a commercially available software package (SPSS, version 21.0; SPSS Inc., Chicago, IL, USA). Categorical and continuous variables were presented as n (%) and median (IQR), respectively. Bivariate analysis for the comparison of categorical variables was analyzed using the chi-squared or Fisher's exact-test, whereas the Mann–Whitney U test was used for continuous variables. Variables as comorbidity, age, sex, initial symptoms, disease severity, concomitant infections during the hospitalization with p-value < 0.05 on bivariate analysis in Table 1 and Table 2 were included in a Cox regression model for analysis of risk factors associated with 28-day mortality. Treatment medicine prescribed by clinicians were according to updated guidelines which may bias our analysis and therefore were not included in the logistic regression model. For all analyses, p-values were two-tailed, and a p-value < 0.05 was considered to be statistically significant.

Results

Clinical characteristics of COVID-19 patients in the outbreak from May 7 to June 15, 2021

During the outbreak from May 7 to June 15, 2021, a total of 141 confirmed COVID-19 patients were admitted in our hospital. The timeline of included cases was shown in Fig. 1.

Of 141 patients who were PCR positive for SARS-CoV-2 on a sample taken from May 7 to June 15 in 2021, they all infected with SARS-CoV-2 B.1.1.7 lineage according to VirSNiP results.

All inpatients during this outbreak were locally acquired and were divided into the survivor (n = 120) and non-survivor (n = 21) group as shown in Table 1. Among survivor group, 20 patients with critical illness, 46 patients with severe illness, 30 patients with moderate illness, and 24 patient with mild illness on admission. For non-survivor group (n = 21), 14 patients with critical illness, 6 patients with severe illness, and 1 patient with mild illness on admission. The median age of all patients was 62 years. On comparison between the two groups, the median age of patients in the non-survivor group was 73 years, which was significantly older than the survivor group with a median age of 61 years ($p < 0.01$).

Underlying disease analysis indicated that the non-survivor group had a significantly higher CCI than the survivor group (3 *vs.* 0.5, $p < 0.01$). The most common symptoms among inpatients were fever and cough (88.7% and 59.6%); however, no between-group differences on the reported symptoms were found, except for shortness of breath. Specifically, the non-survival group patients were more likely to present with shortness of breath than the survival group patients (57.1% *vs.* 24.2%, $p < 0.01$). We also observed that only 35 of the 86 (40.7%) patients with oxygen requiring pneumonia (classified as severe to critical disease) on admission presented shortness of breath initially. Regarding to medication treatment, more patients in the non-survivor group received tocilizumab and voriconazole, as compared with those in the survivor group (52.4% *vs.* 16.7%, 38.1% *vs.* 8.3%; both $p < 0.01$). Overall, 44 of the 141 (31.2%) patients received enoxaparin prophylaxis after admission, with higher rates of patients in the non-survivor group receiving enoxaparin prophylaxis (71.4% *vs.* 24.2%, $p < 0.01$).

Regarding other complications, 81 of the 131 (61.8%) admitted COVID-19 tested patients had elevated D-dimer levels (>0.55 mg/L) and 12 of them with elevated D-dimer levels received furthermore investigation with chest CT.

Table 1 Clinical characteristics of COVID-19 inpatients between May 7 and June 15, 2021.

Variable	Total (n = 141)	Survivor (n = 120)	Non-Survivor (n = 21)	*p*-value
Demographic feature				
Age, median (IQR)	62 (17)	61 (17)	73 (14)	<0.01
Male gender, n (%)	83 (58.9)	69 (57.5)	14 (66.7)	0.48
Charlson comorbidity index, median (IQR)	1 (2)	0.5 (1)	3 (3)	<0.01
Initial symptoms, n (%)				
Fever	125 (88.7)	106 (88.3)	19 (90.5)	>0.99
Short of breath	41 (29.1)	29 (24.2)	12 (57.1)	<0.01
Chest pain	6 (4.3)	4 (3.3)	2 (9.5)	0.22
Cough	84 (59.6)	71 (59.2)	13 (61.9)	>0.99
Headache	6 (4.3)	5 (4.2)	1 (4.8)	>0.99
Runny nose	10 (7.1)	10 (8.3)	0 (0)	0.36
Sore throat	23 (16.3)	20 (16.7)	0 (0)	0.08
Diarrhea	22 (15.6)	20 (16.7)	2 (9.5)	0.53
Muscle soreness	17 (12.1)	17 (14.2)	0 (0)	0.08
Smell and taste impairment	6 (4.3)	5 (4.2)	1 (4.8)	>0.99
Initial Ct values (n = 133), median (IQR)	19 (6.6)	20 (6.35)	18 (4)	0.25
Critical illness on admission, n (%)	34 (24.1)	20 (16.7)	14 (66.7)	<0.01
Treatment medicine, n (%)				
Initial empiric antibiotic	109 (77.3)	90 (75.0)	19 (90.5)	0.16
Steroid	115 (81.6)	96 (80.0)	19 (90.5)	0.37
Tocilizumab	31 (22.0)	20 (16.7)	11 (52.4)	<0.01
Remdesivir	68 (48.2)	55 (45.8)	13 (61.9)	0.24
Enoxaparin	44 (31.2)	29 (24.2)	15 (71.4)	<0.01
Voriconazole	18 (12.8)	10 (8.3)	8 (38.1)	<0.01
Hospital stay, median (IQR)	18 (11)	19 (13.8)	11 (13.0)	<0.01

IQR, interquartile range; Ct, cycle threshold.

Table 2 Pulmonary embolism and concurrent infections by other organisms in COVID-19 patients.

Variable, n (%)	Total (n = 141)	Survivor (n = 120)	Non-Survivor (n = 21)	*p*-value
Pulmonary embolism	1 (0.7)	0 (0)	1 (4.8)	0.16
Bacterial infection	18 (12.8)	13 (10.8)	5 (23.8)	0.15
Co-infection	2	1	1	
Superinfection	16	12	4	
Virus infection	19 (13.5)	10 (8.3)	9 (42.9)	<0.01
Co-infection	5	2	3	
Superinfection	14	8	6	
Pulmonary aspergillosis	3 (2.1)	0 (0)	3 (14.3)	<0.01
Co-infection	1	0	1	
Superinfection	2	0	2	

From there, one case was confirmed to have pulmonary embolism. The other two cases were acute stroke and acute arterial occlusion of right lower limb after admission. The overall incidence of thromboembolic complication was 2.1%. The summary of concurrent infections with bacteria, viruses, and fungi were shown in Table 2. Specifically, 24 bacterial infection episodes occurred in 18 patients, 22 of which were classified as superinfections. Of 2 co-infection episodes, both are respiratory tract infections. Identified pathogen included *Klebsiella* spp (n = 3) and *Streptococcus*

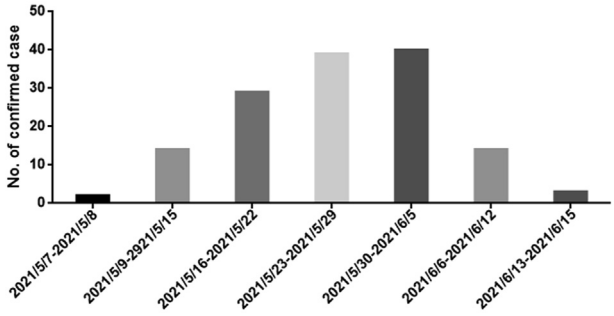

Fig. 1. Timeline of the confirmed COVID-19 cases during the outbreak by SARS-CoV-2 variant B.1.1.7 in weeks.

agalactiae (n = 1). Twenty two infection episodes were recorded as superinfections. Sixteen episodes were respiratory tract infections, five were bloodstream infections and one was a skin and soft tissue infection. Among the 53 identified bacteria from patients with superinfections, *Acinetobacter* spp. Constituted most of the cases, which was followed by *Stenotrophomonas maltophilia*. Distribution of identified pathogens and type of infections were shown in Fig. 2A, B and Fig. 3. Nineteen of the 141 (13.5%) patients had a viral infection other than COVID-19 based on PCR results from blood or FilmArray Respiratory Panel. Specifically, 17 patients were infected with Epstein–Barr virus (EBV), 5 with Cytomegalovirus (CMV), one with an adenovirus, and 3 patients were infected with both EBV and

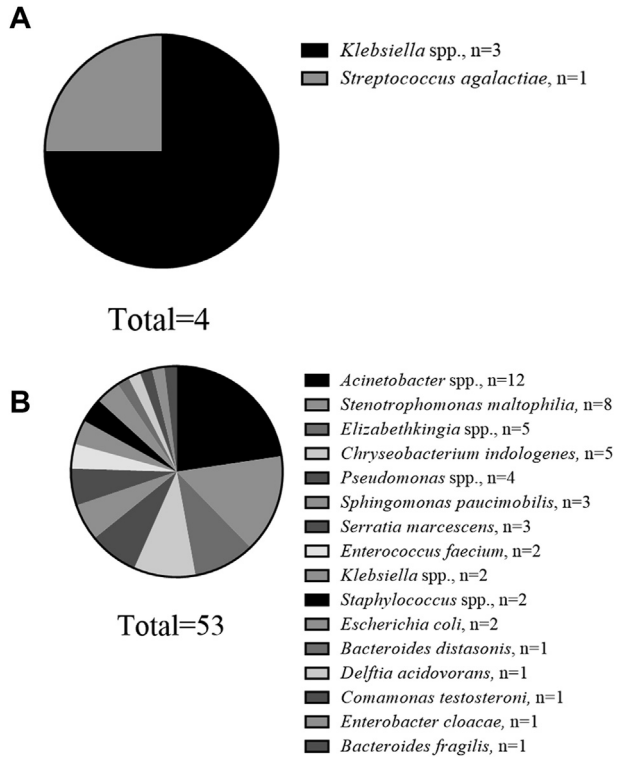

Fig. 2. Distributions of identified bacteria in COVID-19 patients with A. co-infections and B. superinfections.

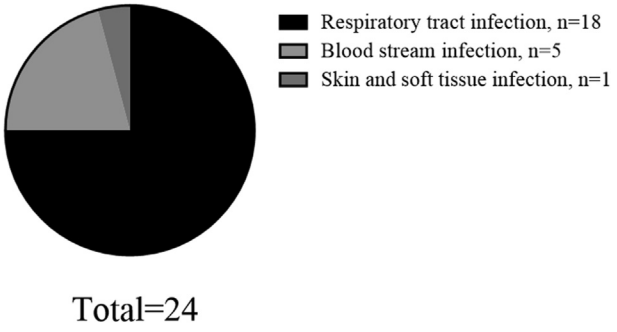

Fig. 3. Distributions of different types of infections in COVID-19 patients.

CMV. On comparison between the two groups, patients in the non-survivor group had a significantly higher risk for concurrent viral infection than in the survival group patients (42.9% *vs.* 8.3%, $p < 0.01$). Furthermore, elevated galactomannan levels (>0.5 in blood) were observed in 19 of the 62 tested patients, wherein 11 of them received voriconazole accordingly, but only 3 patients met the criteria for probable COVID-19-associated pulmonary aspergillosis.

Bivariate analysis found that age, CCI, short of breath, critical illness on admission, concomitant virus and pulmonary aspergillosis were associated with mortality. However, only CCI, short of breath, critical illness on admission and age showed significant association with mortality based on the multivariate analysis, as shown in Table 3.

Table 3 Univariate and multivariate cox regression analyses of factors associated with 28-day mortality in COVID-19 patients.

Variable	Univariate		Multivariate	
	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
Age	1.09 (1.05–1.13)	<0.01	1.09 (1.04–1.14)	<0.01
Charlson comorbidity index	1.56 (1.29–1.89)	<0.01	1.51 (1.19–1.91)	<0.01
Short of breath	3.83 (1.61–9.61)	<0.01	2.71 (1.08–7.83)	0.04
Critical illness on admission	7.01 (2.83–17.38)	<0.01	5.43 (2.05–14.37)	<0.01
Virus infection	3.82 (1.59–9.18)	<0.01	1.11 (0.42–2.92)	0.83

HR, hazard ratio; CI, confidence interval.

Comparison of the clinical characteristics of COVID-19 patients in the outbreak from May 7 to June 15, 2021 versus those admitted from Feb 1 to April 30, 2020 and versus those from January 1 to March 31, 2022

Because shown in Table 4, patients in the outbreak from May 7 to June 15, 2021 were significantly older in age, and presented with a more severe disease, as compared with admitted COVID-19 patients from the first wave in Taiwan in 2020. Moreover, presenting symptoms, which included chest pain, cough, runny nose, diarrhea, nausea/vomitus, and smell/taste impairments, were significantly less reported (4.3% *vs.*17.9%, 59.6 *vs.*82.1, 7.1% *vs.* 42.9%, 15.6% *vs.* 35.7%, 0% *vs.* 10.7%, and 4.3% *vs.* 46.4%, respectively; $p = 0.01$, 0.02, <0.01, 0.01, <0.01 and <0.01, respectively). In contrast, fever was more frequently reported (88.7% *vs.* 60.7%, $p < 0.01$). Comparing to admitted COVID-19 patients from January 1 to March 31, 2022, rates of chest pain, headache, runny nose, sore throat and nausea/vomitus were similar (4.3% *vs.* 1.3%, 4.3% *vs.* 4.0%, 7.1% *vs.* 8.0%, 16.3% *vs.* 15.6%, and 0% *vs.* 1.3%, respectively; $p = 0.09$, 0.91, 0.74, 0.86 and 0.29, respectively) while other symptoms as fever, short of breath, cough, diarrhea, muscle soreness, smell/taste impairment were more often reported (all $p < 0.01$). Of note, 162 of 224 patients (72.3%) from January 1 to March 31, 2022 were asymptomatic. Among 3 waves of COVID-19 patients reported here, admitted patients from May 7 to June 15, 2021 corresponding to the wave of the B.1.1.7 variant had highest diseases severity and mortality rate.

Discussion

In present study, we included COVID-19 cases with SARS-CoV-2 B.1.1.7 lineage from the first community outbreak in northern Taiwan, provided extensive clinical information, including clinical presentations, other complications and

Table 4 Clinical characteristics comparison of admitted COVID-19 patients in different waves in Taiwan.

Variable	Patients admitted from May 7 to June 15, 2021 (n = 141)	Patients admitted from Feb 1 to April 30, 2020 (n = 28)	Patients admitted from Jan 1 to March 31, 2022 (n = 224)	*p*-value[a]	*p*-value[b]
Demographic feature					
Age, median (IQR)	62.0 (17)	35.5 (31)	34 (27.75)	<0.01	<0.01
Male gender, n (%)	83 (58.9)	15 (53.6)	110 (49.1)	0.60	0.07
Acquired from aboard, n (%)	0 (0)	24 (85.7)	191 (85.3)	<0.01	<0.01
Vaccination status on admission					
Unvaccinated	141 (100)	28 (100)	36 (16.1)	–	–
1 dose of any vaccine	0 (0)	0 (0)	8 (3.6)	–	–
2 doses of any vaccine	0 (0)	0 (0)	114 (50.9)	–	–
3 doses of any vaccine	0 (0)	0 (0)	66 (29.5)	–	–
Charlson comorbidity index, median (IQR)	1 (2)	0 (2)	0 (1)	0.12	<0.01
Initial symptoms, n (%)					
Fever	125 (88.7)	17 (60.7)	1 (0.4)	<0.01	<0.01
Short of breath	58 (41.1)	10 (35.7)	0 (0)	0.59	<0.01
Chest pain	6 (4.3)	5 (17.9)	3 (1.3)	0.01	0.09
Cough	84 (59.6)	23 (82.1)	2 (0.9)	0.02	<0.01
Headache	6 (4.3)	4 (14.3)	9 (4.0)	0.06	0.91
Runny nose	10 (7.1)	12 (42.9)	18 (8.0)	<0.01	0.74
Sore throat	23 (16.3)	8 (28.6)	35 (15.6)	0.05	0.86
Diarrhea	22 (15.6)	10 (35.7)	6 (2.7)	0.01	<0.01
Muscle soreness	17 (12.1)	5 (17.9)	4 (1.8)	0.54	<0.01
Nausea/vomitus	0 (0)	3 (10.7)	3 (1.3)	<0.01	0.29
Smell/taste impairment	6 (4.3)	13 (46.4)	0 (0)	<0.01	<0.01
Critical illness on admission, n (%)	34 (24.1)	1 (3.6)	0 (0)	0.01	<0.01
28-day mortality, n (%)	21 (14.9)	0 (0)	0 (0)	0.03	<0.01

[a] Comparison of admitted COVID-19 patients from May 7 to June 15, 2021 and from Feb 1 to April 30, 2020.
[b] Comparison of admitted COVID-19 patients from May 7 to June 15, 2021 and Jan 1 to March 31, 2022.
IQR, interquartile range.

outcomes related to COVID-19. We also identified risk factors associated with COVID-19-related deaths, including age, CCI score, short of breath and disease severity. Additionally, in comparison to admitted COVID-19 patients in our hospital from the first wave in 2020 and the forth wave in 2022, patients in the outbreak caused by SARS-CoV-2 B.1.1.7 lineage revealed the older age, increased disease severity, and higher mortality.

In this study, we found that most of the COVID-19 patients in the outbreak infected with SARS-CoV-2 B.1.1.7 lineage initially presented with non-specific flu-like symptoms. Interestingly, reports of abnormal smell and taste, which has been considered as a hallmark of COVID-19, were low.[20] Therefore, clinicians and patients may overlook the possibility of a COVID-19 infection, which may partly explain the extensive spread of this outbreak in the early phase. Notably, only 35 of the 86 (40.7%) patients with oxygen requiring pneumonia (classified as severe to critical disease) presented with dyspnea on admission. This so-called silent hypoxia in hypoxic COVID-19 patients may have led to delayed oxygen therapy, consequently increasing mortality.[21] Moreover, our prevalence data indicated the importance of constant arterial oxygenation monitoring in infected patents for immediate oxygen therapy.

Although COVID-19 patients are prone to develop pulmonary embolism, its exact incidence varies among countries. Based on the findings of one meta-analysis, the pooled in-hospital incidence was reported to be 14.7%.[22] In our study, only one was confirmed to have pulmonary embolism. However, the data presented here should be interpreted with caution, because only 12 of the 81 (14.8%) patients with elevated D-dimer levels received furthermore investigation with chest CT.

Aside from pulmonary embolism, concurrent infections with other pathogens in COVID-19 patients is another important issue.[23] Similarly, the prevalence of concurrent infections in COVID-19 patients varied across different studies, including bacterial, mycoplasma, viral, and fungal infections. A meta-analysis on the overall incidence of bacterial infections among hospitalized COVID-19 patients was reported to be 7%, with *Mycoplasma pneumoniae* as the most identified organism.[24] In our study, a higher incidence was reported, and the major identified bacteria were *Acinetobacter* spp and *Stenotrophomas maltophilia*, which reflected regional discrepancies. Therefore, more clinical data from multicenters in Taiwan are warranted to guide proper empiric antibiotics use. Furthermore, the most identified viral were EBV and CMV. Due to limited identified cases in our study, furthermore analysis were not be performed. CMV and EBV are human herpesviruses belonging to the family Herpesviridae. Concomitant CMV and EBV infection has been reported in critical ill COVID 19 patients.[25–27] All identified

CMV and EBV infection in our study were diagnosed from positive plasma virus testing rather than from histopathologic evidence. Colonization rather than true infection could not be excluded. The clinical implication of simultaneous EBV or CMV infections in COVID-19 patients and benefit of targeted treatment remained uncertain and furthermore investigation are warranted.

Identified risk factors for mortality in our study were old age, increased CCI, short of breath and increased disease severity, which were consistent with other studies.[28,29] To address increased disease severity, vaccination is reported to be a viable solution, which has been associated with a significant reduction in symptoms and severe disease presentation based on real-world data.[30,31] Our study revealed similar results. More than 80% admitted COVID-19 patients from the forth wave by the Omicron variant (B.1.1.529) in our study received at least one dose of a COVID-19 vaccine. Most included cases presented with mild to moderate diseases severity and no critical severity or mortality cases were observed (Table 4). Therefore, vaccination in patients with old age and multiple comorbidities may be helpful in decreasing severe disease presentation and mortalities, subsequently relieving a substantial burden in health care systems.

In comparison to COVID-19 inpatients from the first wave in 2020 who were mostly imported cases, COVID-19 patients during the outbreak with SARS-CoV-2 B.1.1.7 lineage were older and presented with multiple comorbidities. More severe disease presentations and higher mortality rates were observed. Moreover, patients during the outbreak less frequently presented with clinical symptoms exception for fever. This may possibly be attributed to the old age and comorbidities in these patients, which may have masked symptomatic presentation, consequently resulting in delayed diagnosis and treatment and contributing to higher mortality. Besides, SARS-CoV-2 variant B.1.1.7 causing this outbreak in Taiwan has been reported increased pathogenicity in animal studies and mortality in infected patients comparing to pre-existing SARS-CoV-2 variants in the early phase of the pandemic.[32—34] This may also account for increased mortality of infected patients in this outbreak compared with other waves in Taiwan from our study. The emergence of new variants is inevitable as SARS-CoV-2 transmission continues at scale. The new variants may be accompanied with transmissibility and pathogenicity changes resulting in influence on clinical outcomes and presentations of infected patients as shown in our study. Relevant reports about clinical characteristics of infected patients by different variants of SARS-CoV-2 may therefore be important to provide insights for clinicians into proper medical interventions to improve survival outcome of COVID-19 patients.

There are also certain limitations. First, the study were retrospective and the symptoms recorded by means of National Notifiable Diseases Surveillance System were based on patients' recall and this may have some degree of recall-bias. Second, all the microbiologic examinations in the study were requested by clinicians rather than routinely performed in all of the inpatients, some infectious cases may be missed and may bias the analysis. Third, during the peak wave of COVID-19, many infected cases with mild disease severity were referred to centralized quarantine stations. Therefore, incidence data from the included patients could not totally represent the overall COVID-19 patient population. Lastly, clinical data were collected from a single center, which may not be generalizable to all COVID-19 patients.

In conclusion, our study summarized clinical characteristics of admitted COVID-19 patients during the first community outbreak by SARS-CoV-2 variant B.1.1.7 in Taiwan from a single medical center. Based on the results, clinicians should be more alert with newly confirmed cases with an old age and comorbidities because of their increased risk of mortality. Prioritized this vulnerable populations for COVID-19 vaccination is warranted.

Declaration of competing interest

None.

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None.

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