BMC Infectious Diseases

RESEARCH

Open Access

Comparison of clinical characteristics and outcomes in candidaemia patients with and without COVID-19: a multicentre retrospective study

Sung Un Shin[1], Sohyun Bae[2], David Cho[1], Ahrang Lee[1], Hae Seong Jeong[1], Soyoon Hwang[2], Sarah Kim[1], Minji Kim[1], Seong Eun Kim[1], Uh Jin Kim[1], Seung-Ji Kang[1], Kyung-Hwa Park[1], Hyun-Ha Chang[2*] and Sook In Jung[1*]

Abstract

Background Invasive fungal infections have been reported as complications with significant mortality and morbidity in patients hospitalized with COVID-19. This study aimed to evaluate the clinical characteristics and outcomes of candidaemia patients with COVID-19 and to investigate the association between COVID-19 and mortality in candidaemia patients.

Methods This retrospective study included candidaemia patients aged 18 years or older admitted to four university-affiliated tertiary hospitals in South Korea between January 1, 2020, and December 31, 2022. The COVID-19 group comprised patients diagnosed with COVID-19 before the onset of candidaemia. Clinical features and outcomes were compared between the COVID-19 and non-COVID-19 groups. Multivariate logistic regression analyses were performed to identify risk factors related to 30-day mortality.

Results Of the 355 patients diagnosed with candidaemia, 39 (11.0%) had a prior diagnosis of COVID-19. The COVID-19 group exhibited greater rates of systemic corticosteroid use (20.5% vs. 8.9%, $p=0.042$), central venous catheter use (74.4% vs. 57.3%, $p=0.041$), and mechanical ventilation (53.8% vs. 31.6%, $p=0.006$) before the onset of candidaemia. The COVID-19 group had a greater rate of septic shock at the onset of candidaemia (61.5% vs. 32.0%, $p<0.0001$) and a greater 30-day mortality rate (69.2% vs. 50.9%, $p=0.031$). K–M survival analysis revealed that patients in the COVID-19 group had a lower 30-day survival rate than did those without COVID-19 ($p=0.003$ by log-rank test). However, in multivariate logistic regression analysis, COVID-19 did not significantly impact 30-day mortality.

Conclusions According to multivariate logistic regression analysis, COVID-19 was not an independent risk factor for mortality. However, candidaemia patients with a prior COVID-19 diagnosis were more likely to exhibit critical conditions such as mechanical ventilation and experience poor outcomes. Therefore, clinicians need to monitor and prevent candidaemia in critically ill patients with COVID-19.

*Correspondence:
Hyun-Ha Chang
changhha@knu.ac.kr
Sook In Jung
sijung@chonnam.ac.kr

Full list of author information is available at the end of the article

Keywords Candidaemia, COVID-19, Mortality, Mechanical ventilation

Background

During the global COVID-19 pandemic, hospitalisation for COVID-19 pneumonia and the demand for intensive care due to severe acute respiratory diseases have increased [1–4]. Candidaemia is a healthcare-associated infection that occurs in patients who need intensive care and is often linked to medical devices such as central venous catheters, immunosuppressant drugs, total parenteral nutrition, and antibiotics [5, 6]. Several studies have reported the incidence, risk factors, and clinical features of candidaemia in COVID-19 patients [7–9]. The incidence of candidaemia in patients with COVID-19 is significantly greater than that in patients without COVID-19 [10, 11]. COVID-19 is considered a risk factor for candidaemia during the COVID-19 pandemic [10, 12, 13]. Furthermore, since the risk factors for severe COVID-19 and candidaemia overlap significantly, receiving intensive care in medical facilities due to COVID-19 itself might be a risk factor for candidaemia [13–16].

A recent meta-analysis revealed that candidaemia patients with COVID-19 had high morbidity and mortality, as well as prolonged hospital stays [17]. Although candidaemia patients with COVID-19 were less likely to have the typical underlying conditions associated with candidaemia, all-cause in-hospital mortality was greater among those with COVID-19 than among those without [12]. However, most studies on coinfections of candidaemia and COVID-19 have small sample sizes and were conducted in single centres during the earlier stages of the COVID-19 pandemic [10, 18]. Further research is needed to better understand the outcomes of candidaemia patients with COVID-19 compared to those without, and to assess the impact of COVID-19 on the mortality of candidaemia.

Therefore, this study was conducted to evaluate the clinical characteristics and outcomes of candidaemia patients with COVID-19 compared to those without COVID-19 over a three-year period of the COVID-19 pandemic in multiple centres in Korea. Additionally, we analysed the risk factors associated with the mortality of candidaemia during the pandemic.

Methods

Patients

All patients older than 18 years with candidaemia at four university-affiliated tertiary hospitals in South Korea (Chonnam National University Hospital (CNUH), 1078 beds, Gwangju, Republic of Korea; Chonnam National University Hwasun Hospital (CNUHH), 684 beds, Hwansun, Republic of Korea; Kyungpook National University Hospital (KNUH), 912 beds, Daegu, Republic of Korea; and Kyungpook National University Chilgok Hospital (KNUCH), 1037 beds, Daegu, Republic of Korea) between January 1, 2020, and December 31, 2022, were investigated. The surveillance of candidaemia was conducted based on blood cultures for *Candida* species provided by the microbiology laboratories of four participating institutions. Patients with a recurrence of candidaemia during the study period were included only for the initial episode of candidaemia.

Definitions

Candidaemia was defined as a case in which *Candida* species were isolated from at least one blood culture in patients with signs and symptoms of infection [19, 20]. The COVID-19 group included patients who were diagnosed with COVID-19 within 30 days before the onset of candidaemia [12].

Chronic kidney disease was defined as a glomerular filtration rate of less than 60 mL/min/1.73 m^2 over three months [21]. Neutropenia was defined as an absolute neutrophil count of less than 500/mm^3 [22]. Corticosteroid use was defined as a glucocorticoid dose equivalent to ≥20 mg of prednisone daily for four weeks within 30 days before the onset of candidaemia [23, 24]. Septic shock was defined as a state of sepsis with persistent hypotension requiring vasopressors to maintain a mean arterial pressure of 65 mm Hg or higher and a serum lactate level greater than 2 mmol/L (18 mg/dL) despite adequate volume resuscitation [25]. Central venous catheter (CVC)-related infection was defined as the isolation of a microorganism from the bloodstream of a patient who had concurrent clinical manifestations of sepsis and no other source of candidaemia other than the catheter [26–28]. Intra-abdominal infection was defined as gastrointestinal tract infection, which was considered the source of candidaemia if patients had signs or symptoms related to the gastrointestinal tract prior to the onset of candidaemia and did not have any other source, using a previously reported definition with minor modifications [29]. Urinary tract infection was defined based on the criteria proposed by Elbaz et al. [30]. When a source of candidaemia could not be identified, it was defined as "unknown".

Initial antifungal therapy was defined as the initiation of antifungal agent at the first clinical suspicion of fungal infection or initiation of any antifungal drug after a positive blood culture with yeast on a Gram stain, before species identification [31]; whereas modification of antifungal therapy was defined as adjustments made based on species identification, antifungal susceptibility, and the clinical condition.

Data collection and analyses

We retrospectively reviewed the patients' electronic medical records to collect their demographic and clinical data. The comorbidities included diabetes mellitus, congestive heart failure, chronic kidney disease, chronic liver disease, chronic lung disease, cerebrovascular accident, solid cancer, and hematologic disease. A history of neutropenia, steroid use, immunosuppressant use, antibiotic use, total parenteral nutrition (TPN), gastrointestinal surgery, central venous catheter use, indwelling urinary catheter use, renal replacement therapy, mechanical ventilation, and extracorporeal membrane oxygenation (ECMO) within 30 days were included as predisposing factors. The clinical data included the duration of candidaemia, the length of hospital stay before and after the onset of candidaemia, 30-day mortality rates, the suspected source of the candidaemia, the *Candida* species involved, and instances of septic shock. The clinical features and outcomes of candidaemia patients with and without COVID-19 within 30 days of the onset of candidaemia were compared.

Microbiological tests

Blood cultures were performed with the BACTEC 9240 system (Becton Dickinson, Sparks, MD, USA), VITEK system (bioMérieux, Hazelwood, MO, USA), and BacT/ALERT system (bioMérieux). *Candida* species were identified by a VITEK2 YST card (BioMérieux, Marcy L'Étoile, France). Additionally, two commercial matrix-assisted laser desorption/ionization-time of flight mass spectrometry (MALDI-TOF MS) systems, a VITEK MS (BioMérieux, Marcy L'Étoile, France), and a Biotyper (Bruker Daltonics, Billerica, MA, USA), were used together for species identification.

Statistical analyses

Continuous variables between the two groups were compared using the independent t test for variables for which the means and standard deviations (SDs) were reported. Categorical variables were compared using chi-square tests, with a significance level of $P<0.05$. K–M survival analysis and log-rank tests were conducted to compare survival rates (SRs). Multivariate logistic regression analyses were performed for variables related to 30-day mortality identified in the univariate analyses using the backwards likelihood ratio method. The odds ratio (OR) and 95% confidence interval (CI) were calculated. Statistical analyses were carried out using SPSS ver. 26.0 (SPSS, Chicago, IL, USA).

Results

During the 3-year study period from 2020 to 2022, a total of 384,407 hospitalized patients were recorded across the four institutions, of whom 11,125 were COVID-19 patients. A total of 355 candidaemia patients were identified: 96 at CNUH, 70 at CNUHH, 114 at KNUH, and 75 at KNUCH. Of these, 39 patients (11.0%) were diagnosed with COVID-19 within 30 days prior to the onset of candidaemia. The median time between COVID-19 diagnosis and the onset of candidaemia was 9 days (interquartile range [IQR]: 5.5–16 days). The mean ages were 71.9 ± 12.2 and 68.6 ± 12.9 years in the COVID-19 group and non-COVID-19 group, respectively, and there was no significant difference between the two groups ($p=0.133$). The Charlson comorbidity index was also similar between the groups (6.0±3.2 vs. 5.9±2.7, $p=0.912$). Predisposing factors, such immunosuppressant use (7.7% vs. 7.0%, $p=0.746$) and gastrointestinal surgery within the past 30 days (5.1% vs.15.5%, $p=0.081$), showed no significant differences between two groups. However, compared with the non-COVID-19 group, the COVID-19 group had greater rates of systemic corticosteroid use (20.5% vs. 8.9%, $p=0.042$), central venous catheter use (74.4% vs. 57.3%, $p=0.041$), urinary catheter use (87.2% vs. 60.8%, $p=0.001$), and mechanical ventilation use (53.8% vs. 31.6%, $p=0.006$) within 30 days before the onset of candidaemia. The occurrence of candidaemia during the stay in the intensive care unit was greater in the COVID-19 group (59.0% vs. 29.1%, $p<0.001$) (Table 1).

In the COVID-19 group, the suspected source of candidaemia was statistically significantly more likely to be a central venous catheter (71.8% vs. 32.9%, $p<0.001$). There were no differences in species distribution between the two groups ($p=0.432$), with *Candida albicans* being the most common species in both. No differences in initial antifungal use or type were observed between the two groups. The time from blood culture collection to antifungal initiation (3.1±2.2 days vs. 3.9±4.6 days, $p=0.425$) and the duration of antifungal therapy (12.1±9.7 days vs. 17.3±20.5 days, $p=0.233$) also showed no significant differences. Among patients receiving antifungal therapy, the proportion of those who underwent modification of antifungal treatment was not significantly different between the COVID-19 and non-COVID-19 groups (34.8% vs. 18.6%, $p=0.096$). Similarly, the duration of candidaemia (4.2±5.2 days vs. 4.7±7.6 days, $p=0.681$) and the length of hospital stay before and after candidaemia onset (14.6±13.6 days vs. 21.7±44.9 days, $p=0.330$; 18±31.2 days vs. 22.1±27.5 days, $p=0.384$) did not differ significantly. However, the COVID-19 group had a greater rate of septic shock at the onset of candidaemia (61.5% vs. 32.0%, $p<0.001$) and a greater 30-day mortality rate (69.2% vs. 50.9%, $p=0.031$) (Table 2). K–M survival analysis revealed that patients in the COVID-19 group had a lower 30-day survival rate than did those without COVID-19 ($p=0.003$ by log-rank test, Fig. 1).

Table 1 Clinical characteristics of candidaemia patients with and without COVID-19

	COVID-19 group (*N* = 39)	Non-COVID-19 group (N = 316)	*p*-value
Age, years, mean (SD)	71.9 (12.2)	68.6 (12.9)	0.133
Male	26 (66.7)	188 (59.5)	0.388
Comorbidities			
Diabetes mellitus	21 (53.8)	126 (39.9)	0.095
Congestive heart failure	5 (12.8)	30 (9.5)	0.566
Chronic kidney disease	8 (20.5)	43 (13.6)	0.246
Chronic liver disease	5 (12.8)	27 (8.5)	0.374
Chronic lung disease	7 (17.9)	46 (14.6)	0.575
Cerebrovascular accident	7 (17.9)	44 (13.9)	0.499
Solid cancer	11 (28.2)	139 (44.0)	0.060
Hematologic disease	2 (5.1)	36 (11.4)	0.406
Charlson comorbidity index, mean (SD)	6.0 (3.2)	5.9 (2.7)	0.912
Predisposing factors			
Neutropenia	1 (2.6)	27 (8.5)	0.340
Corticosteroid within past 30 d	8 (20.5)	28 (8.9)	0.042
Immunosuppressant within past 30 d	3 (7.7)	22 (7.0)	0.746
Exposure to antibiotics within past 30 d	37 (94.9)	269 (85.1)	0.096
Total parenteral nutrition	32 (82.1)	227 (71.8)	0.175
Gastrointestinal surgery within past 30 d	2 (5.1)	49 (15.5)	0.081
Central venous catheter	29 (74.4)	181 (57.3)	0.041
Indwelling urinary catheter	34 (87.2)	192 (60.8)	0.001
Renal replacement therapy within past 30 d	1 (2.6)	23 (7.2)	0.495
Mechanical ventilation within past 30 d	21 (53.8)	100 (31.6)	0.006
ECMO within past 30 d	2 (5.1)	9 (2.8)	0.345
Bacteremia within 30 d	14 (35.9)	117 (37.0)	0.890
LOS before candidaemia diagnosis, d, mean (SD)	14.6 (13.6)	21.7 (44.9)	0.330
Diagnosis of candidaemia in the ICU	23 (59.0)	92 (29.1)	< 0.001

Data are shown as n (%) unless otherwise stated

COVID: coronavirus disease; SD: standard deviation; d: day; ECMO: extracorporeal membrane oxygenation; LOS: length of hospital stay; ICU: intensive care unit

In addition, we compared the clinical characteristics of deceased patients between the two groups. Deceased patients in the COVID-19 group were significantly older than those in the non-COVID-19 group (75.7±9.2 years vs. 67.2±13.9 years, $p<0.001$). Compared to the non-COVID-19 group, deceased patients in the COVID-19 group had higher rates of mechanical ventilation use within 30 days before the onset of candidemia (63.0% vs. 40.4%, $p=0.028$) and a higher occurrence of candidemia during their stay in the intensive care unit (63.0% vs. 41.6%, $p=0.039$) (Supplementary Table 1). The time from the onset of candidemia to death was shorter in the COVID-19 group compared to the non-COVID-19 group (6.2±5.6 days vs. 9.6±7.9 days, $p=0.033$) (Supplementary Table 2).

We performed multivariate logistic regression analyses of variables related to 30-day mortality via univariate analyses. According to our multivariate logistic regression analysis, several factors significantly increased the risk of 30-day mortality. These included hematologic disease (OR 3.26, 95% CI 1.32–8.05, $p=0.010$), the use of immunosuppressants (OR 2.98, 95% CI 1.00–8.88, $p=0.049$), total parenteral nutrition (OR 2.70, 95% CI 1.54–4.74, $p=0.001$), mechanical ventilation (OR 1.86, 95% CI 1.06–3.26, $p=0.031$) and septic shock (OR 3.90, 95% CI 2.18–6.97, $p<0.001$). Conversely, the risk of 30-day mortality was significantly reduced by gastrointestinal surgery (OR 0.31, 95% CI 0.15–0.65, $p=0.002$) and antifungal therapy (OR 0.34, 95% CI 0.20–0.59, $p<0.001$) (Table 3). Notably, COVID-19 did not significantly affect 30-day mortality according to multivariate logistic regression analysis.

Discussion

During the research period, we observed that a notable proportion (11.0%) of patients with candidaemia had received a diagnosis of COVID-19 before the onset of candidaemia. The median time from diagnosis of COVID-19 to the first *Candida* culture was 9 days. Patients in the COVID-19 group were more likely to use corticosteroids, have central venous catheters, and require mechanical ventilation than those in the

Table 2 Clinical courses and outcomes of candidaemia patients with and without COVID-19

	COVID-19 group (*N* = 39)	Non-COVID-19 group (N = 316)	*p*-value
Suspected source of candidaemia			< 0.001
Central line	28 (71.8)	104 (32.9)	< 0.001
Intra-abdominal	1 (2.6)	70 (22.2)	0.004
Urinary	3 (7.7)	33 (10.4)	0.781
Unknown	7 (17.9)	109 (34.5)	0.038
Candida species			0.432
C. albicans	19 (48.7)	139 (44.0)	
C. parasilosis	1 (2.6)	37 (11.7)	
C. tropicalis	10 (25.6)	53 (16.8)	
C. glabrata	7 (17.9)	63 (19.9)	
Others	2 (5.1)	20 (6.3)	
More than 2 species	0 (0)	4 (1.3)	
Septic shock	24 (61.5)	101 (32.0)	< 0.001
Antifungal therapy	23 (59.0)	210 (66.5)	0.353
Initial antifungal agents			0.571
Fluconazole	13 (33.3)	143 (45.3)	
Voriconazole	1 (2.6)	4 (1.3)	
Amphotericin B deoxycholate	0 (0)	3 (0.9)	
Liposomal Amphotericin B	0 (0)	6 (1.9)	
Caspofungin	0 (0)	2 (0.6)	
Micafungin	9 (23.1)	52 (16.5)	
Modification of antifungal therapy	8/23 (34.8)	39/210 (18.6)	0.096
Time from blood culture collection to antifungal initiation, d, mean (SD)	3.1 (2.2)	3.9 (4.6)	0.425
Duration of antifungal therapy, d, mean (SD)	12.1 (9.7)	17.3 (20.5)	0.233
Removal of central venous catheter	12/29 (41.4)	93/181 (51.4)	0.317
Duration of candidaemia, d, mean (SD)	4.2 (5.2)	4.7 (7.6)	0.681
LOS after candidaemia, d, mean (SD)	18.0 (31.2)	22.1 (27.5)	0.384
30-day mortality	27 (69.2)	161 (50.9)	0.031

Data are shown as n (%) unless otherwise stated

COVID: coronavirus disease; SD: standard deviation; d: day; LOS: length of hospital stay

non-COVID-19 group, which are associated with critical care conditions. Approximately 60% of patients in the COVID-19 group developed candidaemia while in the ICU and in more than two-thirds of the COVID-19 group, the suspected source of candidaemia was related to central venous catheters. Although COVID-19 itself was not an independent risk factor for mortality due to candidaemia, the COVID-19 group experienced a greater incidence of septic shock at the time of candidaemia and had a greater 30-day mortality rate. Therefore, clinicians must pay close attention to monitoring and preventing the occurrence of candidaemia in critically ill patients with COVID-19.

COVID-19 with viral sepsis or septic shock requiring critical care is expected to have a high mortality rate. A recent meta-analysis demonstrated that 78% of COVID-19 patients hospitalized in the ICU met the Sepsis 3.0 criteria for sepsis/septic shock with organ dysfunction, predominantly manifesting as acute respiratory distress syndrome [32]. In the study, ICU mortality and mortality among patients on invasive mechanical ventilation were reported to be approximately 33% and 42%, respectively. The mortality rate among candidaemia patients with COVID-19 ranged from 57.1 to 92.5% [11–13, 18, 33]. Although variations existed based on the study design and population, the overall prognosis was consistently poor. A recent systematic review with meta-analysis reported a mortality rate of approximately 63% [17]. In our study, the 30-day mortality rate for candidaemia patients with COVID-19 was 69.2%, while the 30-day mortality rate for candidaemia patients without COVID-19 was 50.9%. Notably, the mortality rate among candidaemia patients without COVID-19 was relatively higher than the generally recognized mortality rate for candidaemia (10 ~ 47%) [19, 34, 35]. One study reported that the mortality rate of critically ill patients without COVID-19 increased due to a lack of medical resources during the pandemic, which may explain our results [36].

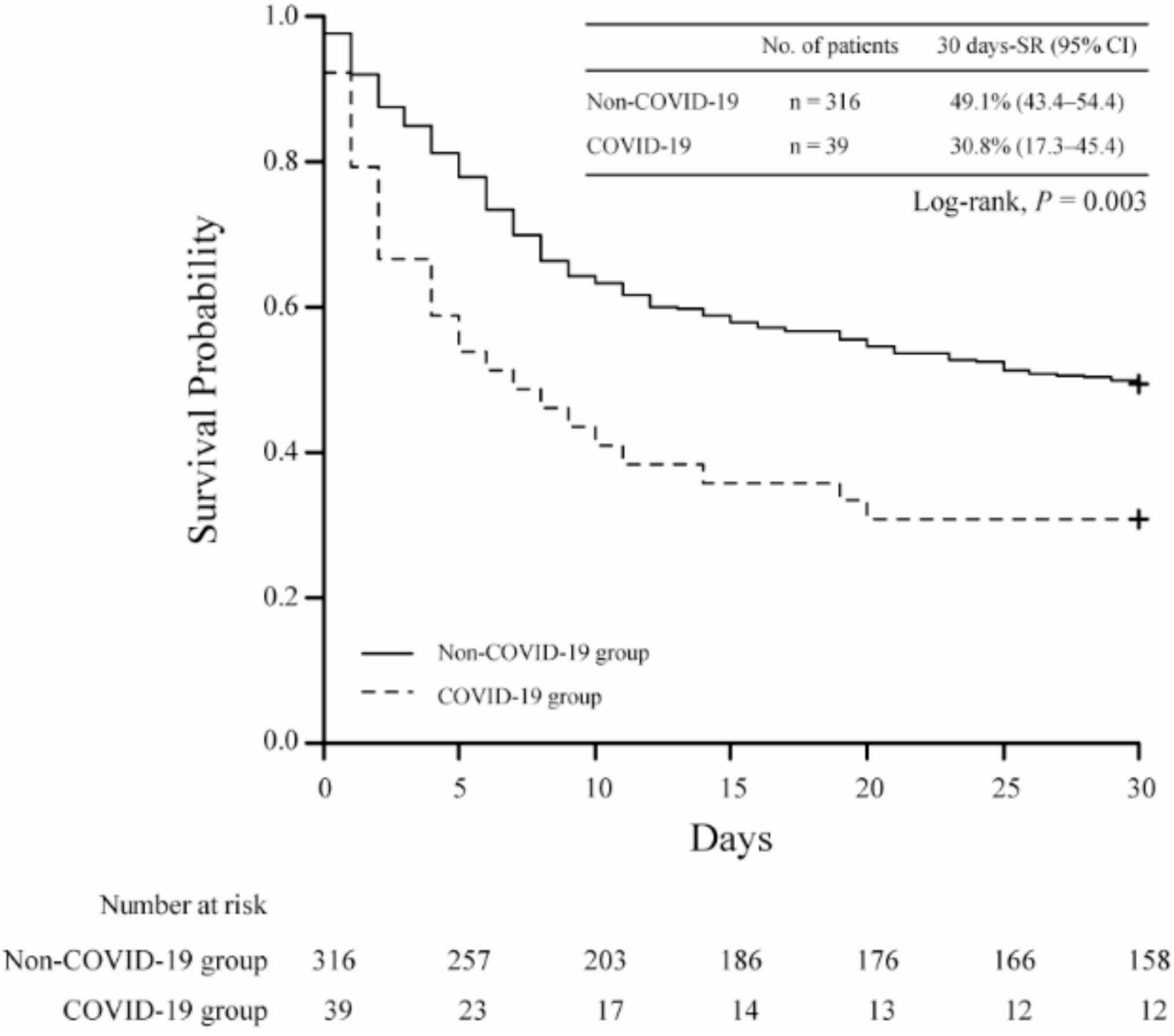

Fig. 1 K–M survival curves of candidaemia patients with and without COVID-19

However, multivariate logistic regression analysis indicated that COVID-19 did not independently contribute to mortality; mechanical ventilation, underlying comorbidities such as hematologic diseases, and severity at diagnosis of candidaemia played significant roles in the mortality of candidaemia patients. This suggests that factors such as critical care conditions related to COVID-19 and underlying diseases, rather than the virus itself, contributed to mortality. Multivariate logistic regression analysis by Kayaaslan et al. also revealed that COVID-19 was not an independent risk factor for mortality [13], which was consistent with the findings of the present study. However, further studies on the effect of respiratory viral infection requiring intensive care on the mortality of candidaemia are needed with larger sample sizes.

Candidaemia is a healthcare-associated infection that typically occurs in critically ill patients. A significant number of patients with severe COVID-19 require intensive care unit (ICU) care, nutritional support and mechanical ventilation, which, together with corticosteroid therapy, predispose them to candidaemia. Some studies have reported that patients with COVID-19 who develop candidaemia are less likely to have many of the typical underlying chronic conditions associated with candidaemia, such as chronic liver disease and solid-organ malignancies, and they often acquire candidaemia from healthcare exposures as a result of severe COVID-19 and related medical management [10, 12]. Although our study did not show significant differences in the typical underlying chronic conditions considered candidaemia risk factors between the two groups, the observation

Table 3 Multivariate logistic regression analysis of the risk factors for mortality

	Univariate logistic regression		Multivariate logistic regression	
	Odds ratio (95% CI)	***p*-value**	**Odds ratio (95% CI)**	***p*-value**
COVID-19 infection	2.17 (1.06–4.43)	0.034		
Hematologic disease	2.75 (1.29–5.85)	0.009	3.26 (1.32–8.05)	0.010
Corticosteroid within past 30 days	2.52 (1.18–5.40)	0.017		
Immunosuppressants within past 30 days	3.02 (1.18–7.75)	0.022	2.98 (1.00-8.88)	0.049
Exposure to antibiotics within past 30 days	2.15 (1.16–4.01)	0.016		
Total parenteral nutrition	2.68 (1.65–4.35)	< 0.001	2.70 (1.54–4.74)	0.001
Gastrointestinal surgery within past 30 days	0.32 (0.17–0.60)	< 0.001	0.31 (0.15–0.65)	0.002
Indwelling urinary catheter	1.74 (1.13–2.70)	0.013		
Central venous catheter	1.83 (1.19–2.80)	0.006		
Mechanical ventilation within past 30 days	2.54 (1.60–4.02)	< 0.001	1.86 (1.06–3.26)	0.031
Bacteremia	1.96 (1.26–3.05)	0.003		
Septic shock	5.29 (3.22–8.70)	< 0.001	3.90 (2.18–6.97)	< 0.001
Antifungal therapy	0.29 (0.18–0.47)	< 0.001	0.34 (0.20–0.59)	< 0.001

Data are shown as n (%) unless otherwise stated

COVID: coronavirus disease; CI: confidence interval

of numerous cases related to healthcare exposure in the COVID-19 group aligns with the results of previous studies.

In this study, factors associated with critical care were observed more frequently in candidaemia patients with COVID-19 than in those without COVID-19. Notably, the rates of central venous catheter placement and mechanical ventilation were greater in the COVID-19 group. Additionally, patients with COVID-19 were significantly more likely to have their initial *Candida* culture collected within the ICU. These findings are consistent with those of previous studies [10, 12, 18]. Furthermore, our study revealed that a central venous catheter was significantly more likely to be the suspected source of candidaemia in the COVID-19 group. One study suggested that inadequate catheter care during the pandemic, due to underresourced public health systems and the increased workload of healthcare workers, might explain the increased incidence of candidaemia in COVID-19 patients [10]. Another study reported an increase in catheter-related bloodstream infections of all aetiologies during the pandemic [37]. Given the close association between critical care and healthcare-related infections such as candidaemia, these findings underscore the importance of heightened vigilance and enhanced infection prevention strategies, especially during a pandemic.

Corticosteroids suppress immune responses through various mechanisms, including inhibition of cytokine synthesis, inhibition of T-cell activation, and inhibition of monocyte/macrophage function [38]. They are recommended drugs for severe COVID-19 [39, 40] and are a well-known risk factor for candidaemia [6]. However, in the real world, the correlation between steroid use in patients with COVID-19 and candidaemia is controversial. Some studies have reported greater rates of corticosteroid use in candidaemia patients with COVID-19 than in those without COVID-19 [10, 11, 13]. Conversely, several other studies found no significant differences in steroid use rates between the two groups [33, 41]. Notably, many of these studies lacked a standardized definition for steroid dosage or usage, which might have obscured the impact of the intensity of corticosteroid therapy. In our study, we defined steroid use as the administration of more than 20 mg of prednisolone daily for four weeks or an equivalent dose, a regimen known to be associated with decreased immunity [23, 24]. Our findings revealed significant differences in steroid use between the two groups, suggesting that attention should be given to the occurrence of candidaemia following the use of a certain dose of steroids in patients with severe COVID-19.

This study had several limitations. First, the retrospective study design introduced potential limitations due to incomplete or inaccurate data from patients' electronic medical records (EMRs). Additionally, the source of candidaemia could not be identified in one-third patients. Second, the severity of COVID-19 according to coronavirus variants was not considered. As this study gathered data over a relatively extended period of approximately three years, various dominant coronavirus variants emerged during that timeframe. Because data on variants could not be verified, there is a risk that distinctions attributable to variants may have been overlooked. Lastly, the shortage of medical resources based on the number of cases and severity of COVID-19 during the pandemic has not been evaluated. Nevertheless, it is noteworthy that our study is a relatively larger series and multicentre study that demonstrates the clinical characteristics and outcomes of candidaemia in patients with COVID-19.

Conclusions

Candidaemia patients with a prior COVID-19 diagnosis were more likely to exhibit greater use of systemic corticosteroids and critical conditions such as central venous catheter use and mechanical ventilation. Although COVID-19 itself did not independently contribute to increased mortality, candidaemia patients with prior COVID-19 had poorer outcomes, including septic shock and 30-day mortality. Therefore, clinicians should be vigilant in monitoring and preventing candidaemia in critical care patients with COVID-19 to improve outcomes.

Abbreviations

CI	Confidence interval
COVID-19	Coronavirus disease 2019
CVC	Central venous catheter
ECMO	Extracorporeal membrane oxygenation
ICU	Intensive care unit
IQR	Interquartile range
K–M	Kaplan-Meier
LOS	Length of hospital stay
OR	Odds ratio
SD	Standard deviation
SR	Survival rate
TPN	Total parenteral nutrition

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12879-024-10373-5.

Supplementary Material 1

Acknowledgements

Not applicable.

Author contributions

Conceptualization: S.I.J.; Data curation: S.U.S., S.B., D.C., S.H.; Formal analysis: A.L., H.S.J.; Investigation: S.K., M.K.; Methodology: U.J.K., S.J.K.; Visualization: S.E.K., K.H.P.; Writing - original draft: S.U.S.; Writing - review & editing: H.H.C., S.I.J. All the authors have read and approved the final manuscript.

Funding

This work was supported by the Korea Health Industry Development Institute (KHIDI) funded by the Ministry of Health & Welfare, Republic of Korea (S.I.J.-HE20C0017050021).

Data availability

The datasets used and/or analysed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the institutional review board (IRB) of Chonnam National University Hospital (IRB number : CNUH-2023-260). The need for consent was waived given the retrospective nature of the study.

Consent for publication

Not applicable. The manuscript does not contain any identifiable personal data.

Competing interests

The authors declare no competing interests.

Author details

[1]Department of Infectious Disease, Department of Internal Medicine, Chonnam National University Medical School, 42, Jebong Ro, Donggu, Gwangju 61469, South Korea
[2]Division of Infectious Disease, Department of Internal Medicine, School of Medicine, Kyungpook National University, Kyungpook National University Hospital, 130, Dongdeok-ro, Jung-gu, Daegu 41944, South Korea

Received: 17 July 2024 / Accepted: 18 December 2024
Published online: 28 December 2024

References

1. Grasselli G, Greco M, Zanella A, Albano G, Antonelli M, Bellani G, Bonanomi E, Cabrini L, Carlesso E, Castelli G, et al. Risk factors associated with mortality among patients with COVID-19 in intensive care units in Lombardy, Italy. JAMA Intern Med. 2020;180(10):1345–55.
2. Nasoufidou A, Kavelidou M, Griva T, Melikidou E, Maskalidis C, Machaira K, Nikolaidou B. Total severity score and age predict long-term hospitalization in COVID-19 pneumonia. Front Med (Lausanne). 2023;10:1103701.
3. Shah SA, Moore E, Robertson C, McMenamin J, Katikireddi SV, Simpson CR, Shi T, Agrawal U, McCowan C, Stock S, et al. Predicted COVID-19 positive cases, hospitalisations, and deaths associated with the Delta variant of concern, June-July, 2021. Lancet Digit Health. 2021;3(9):e539–41.
4. Basem JI, Roth AF, White RS, Tangel VE, Jiang SY, Choi JM, Hoffman KL, Schenck EJ, Turnbull ZA, Pryor KO, et al. Patient care in rapid-expansion intensive care units during the COVID-19 pandemic crisis. BMC Anesthesiol. 2022;22(1):209.
5. Yapar N. Epidemiology and risk factors for invasive candidiasis. Ther Clin Risk Manag. 2014;10:95–105.
6. Kullberg BJ, Arendrup MC. Invasive candidiasis. N Engl J Med. 2015;373(15):1445–56.
7. Oh KH, Lee SH. COVID-19 and fungal diseases. Antibiot (Basel). 2022;11(6).
8. Pemán J, Ruiz-Gaitán A, García-Vidal C, Salavert M, Ramírez P, Puchades F, García-Hita M, Alastruey-Izquierdo A, Quindós G. Fungal co-infection in COVID-19 patients: should we be concerned? Rev Iberoam Micol. 2020;37(2):41–6.
9. Seyedjavadi SS, Bagheri P, Nasiri MJ, Razzaghi-Abyaneh M, Goudarzi M. Fungal infection in co-infected patients with COVID-19: an overview of case reports/case series and systematic review. Front Microbiol. 2022;13.
10. Machado M, Estévez A, Sánchez-Carrillo C, Guinea J, Escribano P, Alonso R, Valerio M, Padilla B, Bouza E, Muñoz P. Incidence of candidemia is higher in COVID-19 versus non-COVID-19 patients, but not driven by intrahospital transmission. J Fungi. 2022;8(3):305.
11. Riche CVW, Cassol R, Pasqualotto AC. Is the frequency of Candidemia Increasing in COVID-19 patients receiving corticosteroids? J Fungi (Basel). 2020;6(4).
12. Seagle EE, Jackson BR, Lockhart SR, Georgacopoulos O, Nunnally NS, Roland J, Barter DM, Johnston HL, Czaja CA, Kayalioglu H, et al. The landscape of candidemia during the Coronavirus Disease 2019 (COVID-19) pandemic. Clin Infect Dis. 2022;74(5):802–11.
13. Kayaaslan B, Eser F, Kaya Kalem A, Bilgic Z, Asilturk D, Hasanoglu I, Ayhan M, Tezer Tekce Y, Erdem D, Turan S, et al. Characteristics of candidemia in COVID-19 patients; increased incidence, earlier occurrence and higher mortality rates compared to non-COVID-19 patients. Mycoses. 2021;64(9):1083–91.
14. Dixit D, Jen P, Maxwell TD, Smoke S, McCracken JA, Cardinale-King M, Haribhakti A, Patel P, Cani E, Choi SC, et al. Risk factors and clinical outcomes of candidemia associated with severe COVID-19. Crit Care Explor. 2022;4(9):e0762.
15. Bajwa S, Kulshrestha A. Fungal infections in intensive care unit: challenges in diagnosis and management. Ann Med Health Sci Res. 2013;3(2):238–44.
16. Paiva JA, Pereira JM, Tabah A, Mikstacki A, de Carvalho FB, Koulenti D, Ruckly S, Çakar N, Misset B, Dimopoulos G, et al. Characteristics and risk factors for 28-day mortality of hospital acquired fungemias in ICUs: data from the EUROBACT study. Crit Care. 2016;20:53.
17. Colaneri M, Giusti EM, Genovese C, Galli L, Lombardi A, Gori A. Mortality of patients with candidemia and COVID-19: a systematic review with meta-analysis. Open Forum Infect Dis. 2023;10(7):ofad358.
18. Nucci M, Barreiros G, Guimarães LF, Deriquehem VAS, Castiñeiras AC, Nouér SA. Increased incidence of candidemia in a tertiary care hospital with the COVID-19 pandemic. Mycoses. 2021;64(2):152–6.
19. Pappas PG, Kauffman CA, Andes DR, Clancy CJ, Marr KA, Ostrosky-Zeichner L, Reboli AC, Schuster MG, Vazquez JA, Walsh TJ, et al. Clinical practice guideline

for the management of candidiasis: 2016 update by the Infectious Diseases Society of America. Clin Infect Dis. 2016;62(4):e1–50.
20. Weinstein MP. Blood culture contamination: persisting problems and partial progress. J Clin Microbiol. 2003;41(6):2275–8.
21. Levey AS, Coresh J. Chronic kidney disease. Lancet. 2012;379(9811):165–80.
22. Boxer LA. How to approach neutropenia. Hematol Am Soc Hematol Educ Program. 2012;2012:174–82.
23. Sepkowitz KA, Brown AE, Armstrong D. Pneumocystis carinii pneumonia without acquired immunodeficiency syndrome. More patients, same risk. Arch Intern Med. 1995;155(11):1125–8.
24. Sepkowitz KA. Opportunistic infections in patients with and patients without acquired Immunodeficiency Syndrome. Clin Infect Dis. 2002;34(8):1098–107.
25. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, Bellomo R, Bernard GR, Chiche JD, Coopersmith CM, et al. The Third International Consensus definitions for sepsis and septic shock (Sepsis-3). JAMA. 2016;315(8):801–10.
26. Kang SJ, Kim SE, Kim UJ, Jang HC, Park KH, Shin JH, Jung SI. Clinical characteristics and risk factors for mortality in adult patients with persistent candidemia. J Infect. 2017;75(3):246–53.
27. Chen CY, Huang SY, Tsay W, Yao M, Tang JL, Ko BS, Chou WC, Tien HF, Hsueh PR. Clinical characteristics of candidaemia in adults with haematological malignancy, and antimicrobial susceptibilities of the isolates at a medical centre in Taiwan, 2001–2010. Int J Antimicrob Agents. 2012;40(6):533–8.
28. Ruan SY, Chien JY, Hou YC, Hsueh PR. Catheter-related fungemia caused by Candida intermedia. Int J Infect Dis. 2010;14(2):e147–149.
29. Kim SH, Yoon YK, Kim MJ, Sohn JW. Clinical impact of time to positivity for Candida species on mortality in patients with candidaemia. J Antimicrob Chemother. 2013;68(12):2890–7.
30. Elbaz M, Chikly A, Meilik R, Ben-Ami R. Frequency and clinical features of Candida bloodstream infection originating in the urinary tract. J Fungi (Basel). 2022;8(2).
31. González-Lara MF, Torres-González P, Cornejo-Juárez P, Velázquez-Acosta C, Martinez-Gamboa A, Rangel-Cordero A, Bobadilla-Del-Valle M, Ostrosky-Zeichner L, Ponce-de-León A, Sifuentes-Osornio J. Impact of inappropriate antifungal therapy according to current susceptibility breakpoints on Candida bloodstream infection mortality, a retrospective analysis. BMC Infect Dis. 2017;17(1):753.
32. Karakike E, Giamarellos-Bourboulis EJ, Kyprianou M, Fleischmann-Struzek C, Pletz MW, Netea MG, Reinhart K, Kyriazopoulou E. Coronavirus disease 2019 as cause of viral sepsis: a systematic review and meta-analysis. Crit Care Med. 2021;49(12):2042–57.
33. Mastrangelo A, Germinario BN, Ferrante M, Frangi C, Li Voti R, Muccini C, Ripa M. Candidemia in Coronavirus Disease 2019 (COVID-19) patients: incidence and characteristics in a prospective cohort compared with historical non-COVID-19 controls. Clin Infect Dis. 2021;73(9):e2838–9.
34. Pfaller M, Neofytos D, Diekema D, Azie N, Meier-Kriesche HU, Quan SP, Horn D. Epidemiology and outcomes of candidemia in 3648 patients: data from the prospective antifungal therapy (PATH Alliance®) registry, 2004–2008. Diagn Microbiol Infect Dis. 2012;74(4):323–31.
35. Morgan J, Meltzer MI, Plikaytis BD, Sofair AN, Huie-White S, Wilcox S, Harrison LH, Seaberg EC, Hajjeh RA, Teutsch SM. Excess mortality, hospital stay, and cost due to candidemia: a case-control study using data from population-based candidemia surveillance. Infect Control Hosp Epidemiol. 2005;26(6):540–7.
36. Kim S, Choi H, Sim JK, Jung WJ, Lee YS, Kim JH. Comparison of clinical characteristics and hospital mortality in critically ill patients without COVID-19 before and during the COVID-19 pandemic: a multicenter, retrospective, propensity score-matched study. Ann Intensive Care. 2022;12(1):57.
37. Pérez-Granda MJ, Carrillo CS, Rabadán PM, Valerio M, Olmedo M, Muñoz P, Bouza E. Increase in the frequency of catheter-related bloodstream infections during the COVID-19 pandemic: a plea for control. J Hosp Infect. 2022;119:149–54.
38. Rhen T, Cidlowski JA. Antiinflammatory action of glucocorticoids–new mechanisms for old drugs. N Engl J Med. 2005;353(16):1711–23.
39. Horby P, Lim WS, Emberson JR, Mafham M, Bell JL, Linsell L, Staplin N, Brightling C, Ustianowski A, Elmahi E, et al. Dexamethasone in hospitalized patients with Covid-19. N Engl J Med. 2021;384(8):693–704.
40. Wang W, Snell LB, Ferrari D, Goodman AL, Price NM, Wolfe CD, Curcin V, Edgeworth JD, Wang Y. Real-world effectiveness of steroids in severe COVID-19: a retrospective cohort study. BMC Infect Dis. 2022;22(1):776.
41. Macauley P, Epelbaum O. Epidemiology and mycology of candidaemia in non-oncological medical intensive care unit patients in a tertiary center in the United States: overall analysis and comparison between non-COVID-19 and COVID-19 cases. Mycoses. 2021;64(6):634–40.

Publisher's note