Healthcare-associated infections: a threat to the survival of patients with COVID-19 in intensive care units

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A R T I C L E   I N F O

S U M M A R Y

Background: Wide variation in mortality rates among critically ill patients with coronavirus disease 2019 (COVID-19) has been reported. This study evaluated whether healthcare-associated infections (HAI) are a risk factor for death among patients with severe COVID-19 in the intensive care unit (ICU).

Methods: This retrospective cohort study included patients with severe COVID-19 hospitalized in the ICU of four hospitals in the city of Curitiba, Brazil. Patients with COVID-19 who died during ICU hospitalization were compared with those who were discharged. A second analysis compared patients who developed HAI in the ICU with those who did not. Multiple logistic regression models were used to control for confounders.

Results: In total, 400 patients were included, and 123 (31%) patients developed HAI. The most common HAI was lower respiratory tract infection (67%). Independent risk factors for death were: age [odds ratio (OR) 1.75, 95% confidence interval (CI) 1.43—2.15; $P<0.0001$]; clinical severity score (OR 2.21, 95% CI 1.70—2.87; $P<0.0001$); renal replacement therapy (OR 12.8, 95% CI 5.78—28.6; $P<0.0001$); and HAI (OR 5.9, 95% CI 3.31—10.5; $P<0.0001$). A longer interval between symptom onset and hospital admission was protective against death (OR 0.93, 95% CI 0.88—0.98; $P=0.017$). The only independent factors associated with HAI were high C-reactive protein and low PaO_2/FiO_2 ratio.

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Conclusions: No factors that could point to a high-risk group for HAI acquisition were identified. However, age, dialysis and HAI increased the risk of death in ICU patients with severe COVID-19; of these, HAI is the only preventable risk factor.

Introduction

The link between viral outbreaks and secondary bacterial infections is well established, as observed during influenza and coronavirus pandemics [1,2]. However, healthcare-associated infections (HAI) have been described in patients with coronavirus disease 2019 (COVID-19) with highly variable incidence, ranging from 6.1% to 50.5% across studies, with most studies reporting incidence >15% [3—14].

Wide variation in mortality rates among critically ill patients with COVID-19 has been described, ranging from 15% to 75.9% [3,4,8,12—14], and reaching 97% among patients on invasive mechanical ventilation [15]. This variability has been explained by differences between cases and organizations, differences in ICU bed availability between countries, and different lengths of follow-up [12]. Few studies have assessed risk factors for mortality in critically ill patients with COVID-19. Independent risk factors include older age, male gender, low PaO_2/FiO_2 ratio at hospital admission, comorbidities and higher Sequential Organ Failure Assessment score [10,12,14]. Even fewer studies have explored how HAI influence the mortality rate of critically ill patients [3,4,9,13]. Studies merely present mortality data for patients with COVID-19 with HAI without assessing whether HAI is a prognostic factor and without analysing the predictive factors for HAI [5—7,9,11,12,14].

The objective of this study was to evaluate the risk factors for death and HAI for patients with COVID-19 in the critical care setting.

Methods

This retrospective cohort study included a cohort of adult patients (≥18 years) with severe COVID-19 hospitalized in the intensive care units (ICU) of four hospitals in Curitiba, capital of the state of Paraná, and largest city in Southern Brazil: Santa Casa with 249 beds (48 ICU beds); Trabalhador Hospital with 222 beds (40 ICU beds); Rehabilitation Hospital with 82 beds (62 ICU beds); and Institute of Medicine with 100 beds (60 ICU beds). The characteristics of the patients in each hospital are shown in Table S1 (see online supplementary material).

Consecutive patients with severe COVID-19, defined as those with oxygen saturation ≤94% on room air, or requiring supplemental oxygen, or requiring mechanical ventilation, or requiring extracorporeal membrane oxygenation [16], admitted to an ICU from 1st March to 31st December 2020 were included in the study. Recruitment was continued until there were 100 patients from each hospital.

COVID-19 was defined as an infection confirmed with a positive real-time reverse transcriptase polymerase chain reaction assay for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) from a nasopharyngeal swab. Patients with non-severe disease and those with COVID-19 defined by serological or antigen tests for SARS-COV-2 were excluded.

The following information was extracted from electronic medical records using a data collection form: demographic characteristics; clinical information (signs, symptoms, comorbidities); treatment and use of invasive devices in the ICU (orotracheal tube, central venous catheter, indwelling urinary catheter); laboratory tests at ICU admission and at HAI diagnosis [C-reactive protein (CRP), total leukocyte count, number of lymphocytes, creatinine, glucose, D-dimer, troponin, PaO_2/FiO_2 ratio]; and radiologic alterations based on chest X ray or computed tomography scan. The interval from symptom onset to hospitalization, length of hospital stay and length of ICU stay were also documented.

The World Health Organization (WHO) Clinical Progression Scale [17] was used to measure the severity of illness for each patient at ICU admission: 0, not infected; 1—3, ambulatory mild disease; 4—5, hospitalized with moderate disease; 6—9, hospitalized with severe disease; and 10, dead.

HAI were defined according to Brazilian national surveillance criteria [18] that are based on Centers for Disease Control and Prevention criteria [19] (Table S2, see online supplementary material). Only the first infection for each patient was considered. Although the study was retrospective, diagnoses of HAI were obtained from data produced by a designated surveillance team in each hospital. Thus, diagnoses of HAI were produced in real time using standardized criteria.

Meticillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), carbapenem-resistant (CR) Enterobacterales, CR *Acinetobacter* spp. and CR *Pseudomonas* spp. were defined as multi-drug-resistant (MDR) bacteria.

This study was approved by the research ethics committees of the study hospitals (Protocol No. 4.361.502, CAAE: 382398 20.8.0000.5225).

Data analysis

The sample size was calculated using OpenEpi Version 3.01 [20] with the following parameters: confidence interval (CI) of 95%; statistical power of 80%; ratio of exposed and unexposed in the sample equal to 1.0; proportion of positive unexposed 5%; and odds ratio (OR) of 3. The sample size was calculated to be 400. Continuous variables were described using means, and categorical variables were described using frequency.

Two outcomes in the ICU were studied (dependent variables): death and HAI. Both were followed until discharge from the ICU. Patients with COVID-19 who died during ICU hospitalization were compared with those who were discharged. A second analysis compared patients in the ICU who developed HAI with those who did not.

Possible associations of demographic and clinical variables with each dependent variable were initially tested in a bivariate analysis calculating OR and 95% CI for each variable. Variables potentially associated with the development of each dependent variable on bivariate analysis ($P<0.15$) were included in a multi-variate logistic regression model in order to

Table I

Evaluation of factors associated with death of patients with severe coronavirus disease 2019 in the intensive care units of four hospitals (Curitiba-PR, Brazil; March–December 2020)

Characteristics	Death $N=189$	Survival $N=211$	Bivariate analysis OR (95% CI)	P-value	Multi-variate analysis OR (95% CI)	P-value
Age, years, mean (SD)	67.4 (13.5)	58.1 (15.6)		0.02	1.75 (1.43–2.15)	0.0001
Gender, N (%)						
Male	99 (52)	125 (59)	0.75 (0.50–1.12)	0.16		
Female	90 (48)	86 (41)				
Comorbidities, N (%)						
Hypertension	126 (67)	108 (51)	1.9 (1.2–2.8)	0.0018		
Coronary heart disease	58 (31)	33 (16)	2.38 (1.4–3.8)	0.0004		
Diabetes	67 (35)	62 (29)	1.31 (0.86–2.0)	0.19		
Chronic kidney disease	12 (6)	13 (6)	1.03 (0.45–2.3)	0.93		
Chronic obstructive lung disease	22 (12)	17 (8)	1.50 (0.77–2.9)	0.23		
Cerebrovascular disease	23 (12)	14 (7)	1.94 (0.97–3.9)	0.06		
Cancer	5 (3)	2 (0.9)	2.83 (0.54–14)	0.21		
Body mass index, kg/m^2, N (%)						
18–24.9	16 (20)	17 (14)				
25–29.9	27 (33)	52 (41)	0.55 (0.24–1.2)	0.15		
$\geq$30	38 (47)	57 (45)	0.70 (0.31–1.5)	0.39		
Signs and symptoms at hospital admission, N (%)						
Cough	111 (59)	156 (74)	0.50 (0.32–0.76)	0.0014		
Fever $\geq$37.8 °C	83 (44)	124 (59)	0.54 (0.36–0.81)	0.0031		
Dyspnoea	154 (81)	177 (84)	0.84 (0.50–1.4)	0.52		
Desaturation (SpO$_2$<92%)	109 (51)	124 (59)	0.95 (0.64–1.4)	0.82		
Fatigue	43 (23)	70 (33)	0.59 (0.38–0.92)	0.02		
Diarrhoea	12 (6)	12 (6)	1.12 (0.49–2.56)	0.78		
Nausea or vomiting	12 (6)	24 (11)	0.52 (0.25–1.08)	0.08		
Headache	11 (6)	35 (17)	0.31 (0.15–0.63)	0.0012		
Anosmia	20 (11)	30 (14)	0.71 (0.39.1.3)	0.27		
Dysgeusia	15 (8)	25 (12)	0.64 (0.32–1.2)	0.19		
Sore throat	5 (3)	12 (6)	0.45 (0.15–1.3)	0.14		
Treatment and device use in the ICU						
Pronation, N (%)	117 (62)	75 (35)	2.94 (1.9–4.4)	<0.0001		
Renal replacement therapy, N (%)	66 (35)	11 (5)	9.7 (4.9–19)	<0.0001	12.8 (5.78–28.6)	<0.0001
MV, N (%)	181 (96)	70 (33)	45.5 (21–97)	<0.0001		
Mean days of MV (SD)	9 (6)	10 (6)		0.09		
CVC, N (%)	177 (94)	67 (32)	31.7 (16.5–60)	<0.0001		
Mean days of CVC (SD)	8 (6)	9 (4)		0.04		
IUC, N (%)	183 (97)	87 (41)	43.3 (18–102)	<0.0001		
Mean days of IUC	8 (6)	8 (5)		1.00		
Use of steroids, N (%)	146 (77)	134 (63)	1.95 (1.2–3.0)	0.003		
Use of anticoagulants, N (%)	185 (98)	208 (99)	0.66 (0.14–3.0)	0.59		
Therapeutic dose	19 (10)	14 (7)	1.57 (0.76–3.23)	0.21		
Prophylactic dose	166 (90)	194 (93)	0.63 (0.32–1.2)	0.17		
Use of antimicrobials, N (%)	182 (96)	194 (9)	2.27 (0.92–5.6)	0.07		
WHO scale score at ICU admission, mean (SD)	5.9 (1.14)	5.1 (0.82)		<0.0001	2.21 (1.70–2.87)	<0.0001
Interval from symptom onset to ICU admission, days, mean (SD)	6 (5)	8 (4)		<0.0001	0.93 (0.88–0.98)	0.017
HAI in ICU, N (%)	91 (48)	33 (16)	5.0 (3.1–8.0)	<0.0001	5.9 (3.31–10.5)	<0.0001

CI, confidence interval; CVC, central venous catheter; HAI, healthcare-associated infections; ICU, intensive care unit; IUC, indwelling urinary catheter; MV, mechanical ventilation; OR, odds ratio; SD, standard deviation; SpO$_2$, oxygen saturation; WHO, World Health Organization.

determine the adjusted OR. Age, CRP and PaO$_2$/FiO$_2$ ratio were transformed from continuous variables to categorical variables. For age, seven categories were used, according to Centers for Disease Control and Prevention criteria [21], to assess the risk of mortality for patients with COVID-19: 18–29 years, 30–39 years, 40–49 years, 50–64 years, 65–74 years, 75–84 years and $\geq$85 years. For CRP, the cut-off point was 108 mg/L, based on a study [22] which observed an increase in mortality

Table II
Bivariate analysis of factors potentially associated with acquiring healthcare-associated infections in patients admitted to intensive care units of four hospitals with severe coronavirus disease 2019 (Curitiba, Brazil; March–December 2020)

Characteristics	HAI $N=123$	Without HAI $N=277$	OR (95% CI)	P-value
Age, years, mean (SD)	62.6 (13.7)	62.4 (16)		0.90
Gender, N (%)				
Male	78 (63)	146 (53)	1.56 (1.01–2.41)	0.047
Female	45 (37)	131 (47)		
Comorbidities, N (%)	115 (94)	259 (94)	0.99 (0.42–2.36)	0.99
Hypertension	76 (61)	158 (57)	1.2 (0.78–1.88)	0.37
Coronary heart disease	26 (21)	64 (23)	0.89 (0.53–1.49)	0.66
Diabetes	39 (32)	89 (32)	0.98 (0.62–1.55)	0.93
Chronic kidney disease	7 (6)	18 (6)	0.87 (0.35–2.14)	0.75
Chronic obstructive lung disease	10 (8)	29 (10)	0.76 (0.36–1.61)	0.46
Cancer	2 (2)	5 (2)	0.89 (0.17–4.69)	0.89
Body mass index, kg/m^2, N (%)				
18–24.9	7 (6)	26 (9)		
25–29.9	31 (25)	50 (18)	2.3 (0.89–5.94)	0.08
$\geq$30	37 (30)	58 (21)	2.4 (0.93–6.0)	0.06
Signs and symptoms at hospital admission, N (%)				
Cough	78 (63)	189 (68)	0.80 (0.52–1.26)	0.34
Dyspnoea	108 (88)	222 (80)	1.78 (0.96–3.30)	0.06
Fever $\geq$37.8 °C	67 (54)	140 (50)	1.17 (0.76–1.79)	0.46
Desaturation (SpO$_2$ <92%)	77 (62)	156 (56)	1.30 (0.84–2.00)	0.24
Fatigue	43 (35)	70 (25)	1.59 (1.00–2.52)	0.047
Diarrhoea	4 (3)	19 (7)	0.45 (0.15–1.37)	0.16
Nausea or vomiting	11 (9)	25 (9)	0.99 (0.47–2.08)	0.97
Headache	15 (12)	31 (11)	1.10 (0.57–2.12)	0.77
Anosmia	18 (15)	31 (11)	1.36 (0.73.2.54)	0.33
Dysgeusia	11 (9)	29 (10)	0.84 (0.40–1.74)	0.63
Sore throat	4 (3)	13 (5)	0.68 (0.21–2.13)	0.51
Treatment and device use in the ICU				
Pronation, N (%)	87 (71)	106 (38)	3.89 (2.46–6.16)	<0.0001
Renal replacement therapy, N (%)	34 (28)	43 (16)	2.07 (1.24–3.46)	0.0051
MV, N (%)	122 (98)	129 (47)	140 (19.3–1015)	<0.0001
Mean days of MV (SD)	11 (7)	7 (5)		<0.0001
CVC, N (%)	119 (96)	124 (45)	36.7 (13.2–102)	<0.0001
Mean days of CVC (SD)	10 (6)	7 (5)		<0.0001
IUC, N (%)	121 (98)	147 (53)	53.5 (12.9–220)	<0.0001
Mean days of IUC (SD)	10 (6)	7 (5)		<0.0001
Use of steroids, N (%)	96 (78)	184 (66)	1.79 (1.0–2.9)	0.02
Use of anticoagulants, N (%)	96 (78)	177 (63)	2.0 (1.2–3.2)	0.0055
Therapeutic dose	11 (9)	15 (5)	1.71 (0.76–3.8)	0.19
Prophylactic dose	85 (69)	162 (58)	1.58 (1.01–2.49)	0.04
Use of antimicrobials, N (%)	121 (98)	260 (94)	2.6 (0.75–9.1)	0.12
Ceftriaxone	108 (89)	226 (87)	1.6 (0.87–3.0)	0.12
Azithromycin	107 (88)	223 (86)	1.6 (0.88–2.9)	0.11
Cefepime	26 (21)	31 (12)	2.1 (1.2–3.7)	0.0097
Piperacillin-tazobactam	13 (11)	16 (6)	1.9 (0.89–4.1)	0.09
Amikacin	12 (10)	15 (6)	1.8 (0.85–4.1)	0.11
Meropenem	3 (2)	4 (1)	1.7 (0.37–7.7)	0.48
Levofloxacin	7 (6)	1 (0.38)	16 (2.0–136)	0.0089
Vancomycin	11 (9)	9 (3.5)	2.9 (1.1–7.2)	0.02
WHO scale score at ICU admission, mean (SD)	5.8 (1)	5.5 (1)		0.0059
Interval between symptom onset and ICU admission, days, mean (SD)	6.6 (4.9)	7.1 (4.8)		0.34
Interval between hospital admission and ICU admission, days, mean (SD)	0.66 (1.2)	0.61 (1.3)		0.72

Table II (*continued*)

Characteristics	HAI $N=123$	Without HAI $N=277$	OR (95% CI)	*P*-value
Interval between ICU admission and death, days, mean (SD)	19 (11)	8 (6.9)		<0.0001
Death, N (%)	90 (73)	99 (36)	4.9 (3.0−7.8)	<0.0001
Laboratory test results at ICU admission, mean (SD)				
Leukocyte count (cells/mm^3)	10,307 (4891)	10,160 (6119)		0.81
Lymphocyte count (cells/mm^3)	1183 (975)	1137 (652)		0.57
C-reactive protein (mg/L)	168 (88)	136 (128)		0.0122
Creatinine (mg/dL)	1.4 (1.2)	1.5 (2)		0.60
Blood glucose (mg/dL)	190 (100)	181 (111)		0.60
PaO$_2$/FiO$_2$ ratio	166 (128)	228 (144)		<0.0001
D-dimer (ng/L)	1706 (2031)	2434 (3102)		0.08
Troponin (ng/mL)	0.10 (0.15)	0.55 (1.18)		0.067
Thoracic CT alterations at ICU admission, N (%)				
Ground glass opacities	81 (91)	221 (93)	0.76 (0.31−1.86)	0.55
Consolidation	21 (23)	46 (19)	1.21 (0.67−2.18)	0.51
Atelectasis	11 (12)	41 (18)	0.56 (0.28−1.14)	0.11
Interlobular thickening	18 (22)	43 (19)	0.93 (0.51−1.69)	0.81
Pleural effusion	11 (12)	35 (15)	0.67 (0.33−1.3)	0.08

CI, confidence interval; CT, computed tomography; CVC, central venous catheter; HAI, healthcare-associated infections; ICU, intensive care unit; IUC, indwelling urinary catheter; MV, mechanical ventilation; OR, odds ratio; SD, standard deviation; SpO$_2$, oxygen saturation; WHO, World Health Organization.

among patients with values above this cut-off. For PaO$_2$/FiO$_2$, four categories of severity for severe acute respiratory syndrome were used [23]: >300 mmHg, 200−299 mmHg, 100−199 mmHg and <100 mmHg.

Statistical analyses were performed using EPI-Info 7 Version 7.2.4 (Centers for Disease Control and Prevention, Atlanta, GA, USA). $P<0.05$ was considered to indicate statistical significance.

Results

Four hundred patients with severe COVID-19 hospitalized in ICUs were included in this study (100 patients from each hospital). Characteristics and outcomes of patients are shown in Tables I and II. Factors associated with increased risk of death on bivariate analysis were: older age; hypertension; coronary heart disease; presence of cough, fever, fatigue and headache at hospital admission; low leukocyte count, high CRP, low PaO$_2$/FiO$_2$ ratio, high troponin and high D-dimer on ICU admission; renal replacement therapy; and HAI. On multi-variate analysis, the variables that increased the risk of death significantly were: age; HAI; WHO Clinical Progression Scale score; and renal replacement therapy. A longer interval between symptom onset and hospital admission was protective against death. For each increase in age category, there was an increase in the risk of death by 75%. HAI increased the risk of death six-fold (OR 5.9, 95% CI 3.31−10.5; $P<0.0001$). Clinical severity according to the WHO scale increased the risk of death two-fold per point, and undergoing renal replacement therapy increased the risk of death 13-fold (Table I).

Among 400 patients studied, 123 had HAI (Table II); however, of these, 16 patients had two infections at the first diagnosis, so the total was 139 infections. The most common HAI were lower respiratory tract infections [68 (49%) ventilator-associated pneumonia (VAP), 17 (12%) tracheobronchitis, eight (6%) non-ventilator-associated pneumonia], followed by central-venous-

catheter-related bloodstream infections [CLABSI; 38 (27%)], catheter-associated urinary tract infections [CAUTI; 7 (5%)] and tracheostomy stoma infection [1 (0.7%)]. The VAP rate was 29.3 per 1000 ventilator-days, the CLABSI rate was 18.0 per 1000 catheter-days, and the CAUTI rate was 3.2 per 1000 catheter-days.

More than one-fifth of HAI were caused by MDR bacteria: CR *Acinetobacter baumannii*, CR Enterobacterales, MRSA, CR *Pseudomonas* spp. and VRE (Table III).

On bivariate analysis for factors associated with HAI, there was a significant difference in the mean number of days of use of invasive devices. WHO Clinical Progression Scale, CRP and PaO$_2$/FiO$_2$ values at ICU admission were higher in the HAI group. On multi-variate analysis, CRP >108 mg/L increased the risk of HAI 2-fold (OR 2.02, 95% CI 1.17−3.47; $P=0.010$). The PaO$_2$/FiO$_2$ ratio increased the chance of having HAI by 29% for each category (OR 1.29, 95% CI 1.01−1.66; $P=0.04$).

Discussion

This retrospective cohort study of 400 patients with COVID-19 admitted to the ICUs of four hospitals found that the independent factors associated with death were age, clinical severity score on ICU admission, dialysis and HAI. The interval between symptom onset and hospitalization was inversely associated with the risk of death. No factors that could point to a high-risk group for HAI acquisition were identified.

As HAI is the only modifiable factor associated with death, the authors attempted to identify independent factors associated with HAI. Is it possible to identify which patients are at higher risk of death, and therefore implement preventive measures directed at this population? Only CRP and PaO$_2$/FiO$_2$ ratio were found to be associated with HAI. Unfortunately, the changes in CRP and PaO$_2$/FiO$_2$ ratio may represent the consequence and not the cause or risk factors for HAI. Due to the severity of illness, these patients require mechanical

Table III

Micro-organisms that caused healthcare-associated infections in patients with severe coronavirus disease 2019 admitted to the intensive care units of four hospitals (Curitiba, Brazil; March−December 2020)

Type of infection	N (%)	MDR isolates	N (%)
Microbiologically confirmed LRI	82 (65)		31 (84)
Staphylococcus aureus	22 (27)	MRSA	7 (23)
Acinetobacter baumannii	17 (21)	CR *Acinetobacter baumannii*	17 (55)
Pseudomonas aeruginosa	15 (18)	CR *Pseudomonas aeruginosa*	3 (10)
Klebsiella pneumoniae	10 (12)	CR *Klebsiella pneumoniae*	3 (10)
Enterobacter cloacae	5 (6)	-	
Stenotrophomonas maltophilia	4 (5)	-	
Escherichia coli	2 (2)	CR *Escherichia coli*	1 (3)
Others	7 (9)	-	
Bloodstream infections	38 (30)		6 (16)
Coagulase-negative staphylococci	12 (32)	-	
Enterococcus faecalis	11 (29)	VRE	1 (2)
Staphylococcus aureus	6 (16)	MRSA	1 (2)
Klebsiella pneumonia	3 (8)	-	
Acinetobacter baumannii	2 (5)	CR *Acinetobacter baumannii*	2 (3)
Serratia marcescens	2 (5)	CR *Serratia marcescens*	2 (3)
Candida albicans	2 (5)	-	
Urinary tract infections	7 (6)		
Enterococcus faecalis	4 (57)	-	
Klebsiella pneumonia	2 (29)	-	
Enterobacter cloacae	1 (14)	-	

CR, carbapenem-resistant; LRI, lower respiratory infection; MDR, multi-drug-resistant bacteria; MRSA, meticillin-resistant *Staphylococcus aureus*; VRE, vancomycin-resistant enterococci.

ventilation and invasive devices for prolonged periods, and are therefore more susceptible to HAI, especially lower respiratory tract infections [6].

Length of ICU stay, use of invasive devices, age, comorbidities and symptoms were not found to be predictive of which patients would develop HAI. It does not seem possible to identify which patients are at increased risk for HAI, which in turn increases the risk of death 6-fold. This risk was close to that found by Shafran *et al.* [13], who reported that one infection increased the risk of death 2.48-fold, and having more than one infection increased the risk of death 7.64-fold in patients with COVID-19.

It is important to stress that a large proportion of HAI caused by MDR bacteria such as CR *Acinetobacter* spp. are preventable by implementing effective infection prevention control measures. In this study, 123 patients had 139 HAI, of which 29.1% (37/127 isolates) were caused by MDR bacteria. One of the possible explanations could be the extensive use of antimicrobials, especially at the beginning of the pandemic, when the clinical course of COVID-19 was not yet clear and there was a shortage of diagnostic tools [24]. In addition, in many countries, including Brazil, the heavy strain placed on the healthcare system by COVID-19 led to high demand for healthcare workers, and shortages of specialized and experienced personnel in hospitals with inadequate infrastructure, contributing to cross-transmission of pathogens between patients and MDR bacteria outbreaks.

Dialysis was associated with death in this study. The same mechanisms underlying the development of severe acute respiratory syndrome in COVID-19 appear to lead to acute kidney injury, including viral septicaemia, an enhanced inflammatory response and endothelial damage [25].

The strengths of this study include the large number of patients and the multi-centre design. However, the study is limited by its retrospective design, which reduces control over multiple confounders and data collection. Also, only the first episode of infection was included in this study, which may have led to underestimation of the true burden of HAI. Furthermore, although this was a multi-centre study, only hospitals in Curitiba (Southern Brazil) were included, which may not reflect the reality of other geographical regions of Brazil. Finally, these hospitals could have had some differences in patterns of care and resources, which could be associated with the two outcomes of interest.

In conclusion, this study found that age, dialysis and HAI increased the risk of death among patients with severe COVID-19 in ICUs. PaO_2/FiO_2 and CRP were associated with HAI, but seem to be a consequence of the infection. No important factors that could define a population at increased risk for HAI were identified. As a consequence, infection prevention and control measures should be prioritized in order to reduce the impact of COVID-19 in critically ill patients.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhin.2022.05.013.

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