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The Epidemiology and The Outcome of Bacteremia in Adult COVID-19 Patients: A Single-Center Study in Oman

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ABSTRACT

Introduction: *The rate of bloodstream infection is higher among COVID-19 patients who require ICU admission and is associated with worse outcomes. This study aims to describe the epidemiology of bacteremia among hospitalized COVID-19 patients and to analyze the effect of infection prevention and control measures on bacteremia incidence.*

Method: *A retrospective cohort analysis was conducted on all confirmed COVID-19 patients with positive blood cultures from May to October 2020. Data analysis was performed using IBM SPSS Statistics 29.0 software (IBM Corp., 2021). Statistical significance was defined as a p-value less than 0.05.*

Result: *During the study period, 767 blood cultures were collected, of which 212 (27.6%) were positive in 165 patients. The mean age of patients was 57.5 ± 14.7 years, and 70.3% were male. ICU admission occurred in 92% of cases, and hospital-acquired bacteremia developed a median of 12 days (interquartile range [IQR] 8–17) after admission. The cohort mortality rate was 45.5% (75/165). Univariate analysis identified age (p-value <0.001), diabetes mellitus (p-value 0.033), hypertension (p-value 0.035), chronic heart disease (p-value 0.001), femoral venous catheter (FVC) use (p-value 0.025), and internal jugular vein catheter (IJV) use (p-value 0.016) as significant risk factors for mortality. In multivariate analysis, age remained a significant independent risk factor for mortality (p-value < 0.001; CI: 1.056-1.129). True bacteremia accounted for 125 cases (59.0%), while contamination was identified in 87 cases (41.0%). Central line-associated bloodstream infection (CLABSI) was the most frequent source of bacteremia (72 cases, 57.6%), followed by ventilator-associated pneumonia (VAP) (14 cases, 11.2%) and catheter-associated urinary tract infections (CAUTI) (14 cases, 11.2%).*

Conclusion: *Bacteremia in critically ill COVID-19 patients is associated with an increased risk of mortality. Ongoing surveillance of healthcare-associated infections (HAIs) and strict adherence to infection prevention practices are essential to mitigate adverse patient outcomes during the pandemic.*

Keywords

COVID-19, Bacteremia, HAIs, Infection Prevention & Control.

Introduction

The emergence of severe acute respiratory syndrome coronary virus 2 (SARS-CoV-2) has presented a formidable medical challenge to health systems and clinicians. Many decisions have been made with limited clinical experience and scientific evidence, especially concerning treating patients hospitalized with coronavirus disease 2019 (COVID-19) and antibiotics use [1]. 15% of patients develop severe disease and require admission to the intensive care unit (ICU) and ventilatory support due to respiratory failure. Several studies showed a marked increase in bacterial and fungal super-infections, reported in up to 24% of hospitalized COVID-19

patients. The rate of bloodstream infections (BSIs) was higher in COVID-19 patients compared to patients not infected, and BSI development was associated with worse outcomes [2].

In a review article, Nag/Kaur found that the most common infections among COVID-19 patients were Ventilator Associated Pneumonia (VAP), followed by bacteremia and Urinary Tract Infections (UTIs) [3]. Among patients with positive blood cultures, COVID-19 patients had a significantly higher proportion of nosocomial bacteremia (95.5%) than non-COVID-19 patients (30.5%) ($p < 0.001$) being catheter-related bacteremia the primary origin [4].

The primary objective of this study is to describe the epidemiology of bacteremia among adult hospitalized COVID-19 patients from April to October 2020, including describing risk factors for mortality among them. The secondary objective is to analyze the effect of infection prevention and control measures to reduce the incidence of bacteremia among these patients.

Methods

study design and patients

A retrospective cohort analysis was conducted at the Royal Hospital, which is a tertiary care hospital with 760 beds. The confirmed COVID-19-positive patients were admitted to separate wards from the other admitted patients, including wards for critically ill and non-critical patients. All confirmed COVID-19 patients who had a positive blood culture from May to October 2020 were included. All episodes of bacteremia for the patients were included in the analysis. Isolates of the same organism grew in blood culture, and within 14 days, they were considered the same episode.

Data were collected from the hospital's electronic system. The study was approved by the hospital ethics and research committee (SRC#88/2020).

Definitions

Contaminant blood cultures were labeled as such if they were isolated once from the patient and belonged to a group generally defined as the skin commensal microbiota [5], and the patient remained clinically stable without receiving any antibiotic treatment.

True bacteremia was defined as a positive blood culture with clinical deterioration or symptoms of infection/sepsis and elevated inflammatory markers/white cell count. A positive blood culture with commensal flora was considered true if two sets of blood cultures were positive and the patient had a central line in place.

Community-acquired infection is defined as a positive blood culture collected within the first 48 hours of admission. Hospital-acquired infection is defined as a positive blood culture obtained after 48 hours of admission. If the patient had a positive blood culture within the first 48 hours after transfer from another hospital, the bacteremia was considered other hospital-acquired.

Ventilator-associated Pneumonia (VAP): A pneumonia where the patient is on mechanical ventilation for more than two consecutive calendar days on the date of the event, with day of ventilator placement being Day 1, and the ventilator was in place on the date of the event or the day before. The VAP is diagnosed if new or progressive persistent radiographic infiltrates on chest X-ray and clinical observation suggesting infection, such as new fever, virulent sputum, leukocytosis, increased ventilation arterial oxygenation, decline or need for increased pressure values, and positive microbiological culture from sputum [6].

Central Line-Associated Bloodstream Infection (CLABSI) was defined as A laboratory-confirmed Confirmed Bloodstream Infection (LCBI) that is not secondary to an infection at another body site, and a Central Venous Catheter is in place for more than two calendar days before a positive culture and is also in place the day of or the day prior to culture [7].

Catheter-associated urinary Tract Infection (CAUTI) was defined as a patient having an indwelling urinary catheter that had been in place for more than two consecutive days in an inpatient location on the date of the event and was either present for any portion of the calendar day on the date of the event, or removed the day before the date of the event. Patient has at least one of the following signs or symptoms: fever (>38.0°C), suprapubic tenderness, costovertebral angle pain or tenderness, urinary urgency, urinary frequency, dysuria. Patient has a urine culture with no more than two species identified, at least 1 of which is a bacterium with ≥ 10^5 CFU/ml [8].

The incidence density of the bacteremia was calculated as the total number of bacteremia in a week divided by the total number of patient days multiplied by 1000.

Statistical analysis

All the information was analyzed using IBM SPSS Statistics 29.0 software (IBM Corp., 2021). IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp. Descriptive statistics were performed and reported using mean and standard deviation for continuous variables and frequency and percentage for categorical variables. Relationships between categorical variables using chi-square tests. For continuous variables, independent t-tests were used. We performed a multivariate logistic regression analysis to identify factors independently associated with the outcome while accounting for other variables. Throughout the analysis, a p-value of less than 0.05 was considered statistically significant.

Infection prevention and control Interventions

The infection prevention and control department intensified measures to reduce infection following the initial peak of bacteremia. A multimodal approach was implemented, including regular weekly meetings with COVID-19 ward physicians, nursing administration, and frontline staff to provide updates on total blood

cultures and infection rates. Challenges related to the supply chain for patient care products, such as central lines, skin disinfectants, and environmental disinfection, were addressed. Training and education for physicians, nurses, and housekeeping staff were enhanced, with a second infection control practitioner assigned to supervise staff practices and identify educational opportunities. Ongoing education regarding care bundles for the prevention of healthcare-associated infections (HAIs) and proper blood culture collection was maintained. Additionally, stewardship activities were strengthened across all COVID-19 wards.

Results

Baseline characteristic

During the study period, 882 confirmed COVID-19 patients were admitted, and 767 blood cultures were collected from these individuals. Of these, 212 blood cultures were positive, resulting in a positivity rate of 27.6% among 165 patients. The mean patient age was 57.5 ± 14.7 years, and 70.3% were male. The median number of blood cultures obtained per patient during hospitalization was 5 (range 1–26). Intensive care unit (ICU) admission occurred in 92% of the cohort, and their bacteremia was associated with ICU care. When excluding bacteremia within the first 48 hours of admission, the initial bloodstream infection developed after a median of 12 days (interquartile range [IQR] 8–17) following hospital admission.

The baseline characteristics of patients are as in Table 1.

Table 1: Baseline characteristics of patients with bacteremia.

Variables	n (165), %
Age (Mean ± SD)	57.5 ±14.7
Gender - Male	149 (70.3)
Blood Culture sent per patient (Median, IQ)	5 (1, 26)
Co-morbidities	
Diabetes Mellitus	126 (59.4)
Hypertension	119 (56.1)
Chronic Kidney Disease	36 (17.0)
Chronic Heart Disease	22 (10.4)
Malignancy	6 (2.8)
Hemodialysis	23 (2.8)
Rheumatology	3 (1.4)
Obesity	27 (12.7)
Asthma	13 (6.1)
ICU admission	195 (92.0)
Femoral Venous Catheter (FVC)	43 (20.3)
IJV (Internal Jugular Vein)	81 (38.4
PICC (Peripherally Inserted Central Catheter) Line	53 (25.2)
CVC (Central Venous Catheter, brachial)	6 (2.8)
Permcath (Dialysis Catheter)	4 (22.2)
Urinary catheter	135 (64.0)
Ventilation	171 (81.0)
Tracheostomy	38 (18.0)
Nasogastric Tube (NGT)	138 (65.4)

Table 2: Association between characteristics and patient outcome.

Variables	Patient outcome		p-Value
	Discharged (n=118)	Died (n=92)	
Age (Mean ± SD)	64.70±11.54	51.29±13.78	<0.001
Gender - Male	86 (72.9)	61 (66.3)	0.363
Co-morbidities			
Diabetes mellitus	63 (53.4)	63 (68.5)	0.033
Hypertension	59 (50.0)	60 (65.2)	0.035
Chronic Kidney Disease	17 (14.4)	19 (20.7)	0.270
Chronic Heart Disease	5 (4.2)	17 (18.5)	0.001
Malignancy	4 (3.4)	2 (2.2)	0.698
Hemodialysis	13 (11.0)	10 (10.9)	1.000
Rheumatology	3 (2.5)	-	0.258
Obesity	19 (16.1)	8 (8.7)	0.146
Asthma	4 (3.4)	9 (9.8)	0.082
ICU admission	106 (89.8)	87 (94.6)	0.308
Past colonization with resistant organism	2 (1.7)	4 (4.3)	0.408
FVC	17 (14.4)	25 (27.2)	0.025
IJV	37 (31.4)	44 (47.8)	0.016
PICC Line	33 (28.2)	20 (21.7)	0.338
CVC	3 (2.5)	3 (3.3)	1.000
Permcath	2 (25.0)	2 (20.0)	1.000
Urinary catheter	70 (59.3)	64 (69.6)	0.148
Ventilation	96 (81.4)	74 (80.4)	0.862
Tracheostomy	22 (18.6)	16 (17.4)	0.858
NGT	70 (59.3)	67 (72.8)	0.057
Peripheral line	66 (55.9)	45 (49.5)	0.402
Arterial line	63 (53.4)	40 (43.5)	0.166
Pronning	44 (37.3)	35 (38.0)	1.000

Significance of culture Infection Contamination	63 (53.8) 54 (46.2)		60 (65.2) 32 (34.8)	0.119		
Infection Onset Royal Hospital Acquired Other Hospital Acquired Community Acquired	59 (92.2) 3 (4.7) 2 (3.1)		57 (95.0) 2 (3.3) 1 (1.7)	0.800		
Binary Logistic Regression						
Variables	**B**	**S.E.**	**Sig.**	**Exp(B)**	**95% CI for EXP(B)**	
					Lower	**Lower**
Age	0.088	0.017	<0.001	1.092	1.056	1.129
Diabetes mellitus	0.004	0.431	0.993	1.004	0.431	2.338
Hypertension	-0.365	0.422	0.388	0.694	0.304	1.588
Chronic Heart Disease	0.974	0.580	0.093	2.647	0.849	8.251
Obesity	-0.401	0.589	0.497	0.670	0.211	2.126
Asthma	1.413	0.845	0.095	4.106	0.784	21.517
Femoral Venous Catheter	0.175	0.428	0.682	1.192	0.515	2.757
Internal Jugular Vein	0.299	0.355	0.400	1.349	0.672	2.706
Urinary Catheter	-0.140	0.508	0.783	0.869	0.321	2.355
Nasogastric Tube	0.885	0.576	0.125	2.423	0.783	7.496
Arterial Line	-0.401	0.385	0.297	0.670	0.315	1.424
Significance of culture True bacteremia vs contaminant	-0.315	0.364	0.387	0.730	0.358	1.490

Mortality and risk factors

The mortality rate among the cohort was 45.5% (75/165). In univariate analysis, age was a significant risk factor for mortality (p-value <0.001), Diabetes mellitus (p-value 0.033), hypertension (p-value 0.035), and chronic heart disease (p-value 0.001). Having a femoral venous catheter (FVC) (p-value 0.025) and an internal jugular vein catheter (IJV) (p-value 0.016) were also significant risk factors. In multivariate analysis, age was the only significant independent risk factor for mortality (P value < 0.001; CI: 1.056-1.129). Details of uni and multivariate analysis are in Table 2.

Microbiology

The number of true bacteremia was 125 (59.0%), and the contamination was 87 (41.0%). The total number of organisms recovered from blood culture were 231 and 19/212 (9.0%) of the bacteremia episodes were polymicrobial. Excluding contaminant samples, Coagulase Negative Staphylococci (CONS) accounted for 27.2.4% (34) of the causative bacteria, 16% (20) were due to candida species, 15.2% (19) were due to Enterococci, 10.4%% were Carbapenemase Resistant Enterobacterales, and 8.8% (11) were *Staphylococcus aureus* and 7.2% (9) *Pseudomonades aeruginosa*. The total number of multi-drug-resistant organisms was 35 (28%) of the true bacteremia.

Central Line Bloodstream Infection (CLABSI) was the commonest source of bacteremia 72 (57.6.0%), followed by Ventilator Associated Pneumonia (VAP) 14 (11.2%), followed by Catheter associated urinary tract infections (CAUTI) 14 (11.2%) and wound the infections 10 (8.0%).

During the study period, the incidence of bacteremia was 34.3 per 1000 patient days. The rate peaked at 60.3 per 1000 patient days in week 26 of 2020, declined by week 28, and subsequently increased to 43.8 in week 33 and 87.5 in week 34 (Figure 1).

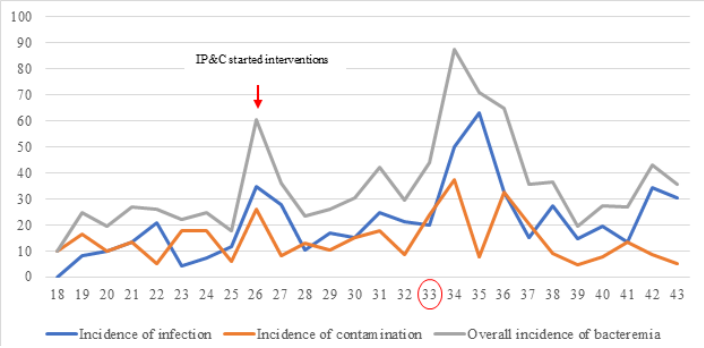

Figure 1: Weekly incidence of true bacteremia, contamination & overall bacteremia, Week 18-43, 2020.

The rate of contaminant bacteremia did not exhibit a discernible association with the total number of patient days (Figure 2).

The rate of true bacteremia generally increased in parallel with the number of patient days. Notably, between weeks 32 and 34, the rate increased even as the total patient days decreased (Figure 3).

The control chart evaluating the impact of infection prevention and control interventions indicated that overall bacteremia incidence fell below the mean after the initiation of multimodal interventions in week 26. However, this reduction was not sustained, as overall bacteremia increased again in week 32 before declining below the

Table 3: Microbiology of bacteremia.

Significance of blood culture		Infection (n, %)	Contamination (n, %)	Total
		125 (59.0%)	87 (41.0%)	212
Causative Organism		No. of organisms recovered		
	Coagulase Negative Staphylococci (CONS)	34	80	114
	Candida species includes 4 C. auris*	20		20
	Enterococcus species	19		19
	Carbapenem Resistant Enterobacterales*	13		13
	Methicillin Sensitive Staphylococcus aureus	11		11
	*Methicillin Resistant Staphylococcus aureus**	2		2
	Pseudomonas aeruginosa	9		9
	*Extended Spectrum Beta Lactamase- Enterobacterales**	7		7
	Escherichia coli	6		6
	Klebsiella pneumoniae	6		6
	Enterobacter. species	4		4
	Contaminant Gram positive Bacilli	0	7	7
	*Vancomycin Resistant Enterococci**	5		5
	Achromobacter species	2		2
	Burkholderia cepacia	1		1
	Multi-Drug-Resistant *Acinetobacter Baumannii**	3		3
	Multi-Drug-Resistant *Pseudomonas aeruginosa**	1		1
	Stenotrophomonas multophilia	1		1
Total organisms grew from blood cultures		144	87	231
Type of infection	Central Line Bloodstream Infection (CLABSI)	72 (57.6.0%)		
	Ventilator Associated Pneumonia.	14 (11.2%)		
	Catheter associated urinary tract infections	11 (8.8%)		
	Wound the infections.	10 (8.0%)		
	Abdominal infections.	7 (5.6%)		
	Undetermined source of bacteremia	5 (4.0%)		
	Chest infection	2 (1.6%)		
	Infective endocarditis (community associated)	1 0.8%)		
	Urinary Tract Infection	1 (0.8%)		
	peripheral line related infections.	1 (0.8%)		125
Total true bacteremia				125
Type of acquisition	⬧RH-acquired infections	116		
	⬧OH, acquired infections.	5		
	Community acquired infections	3		
*Multi-Drug-Resistant Organism (MDRO), ⬧ Royal Hospital (RH), ⬧Other Hospital (OH)				

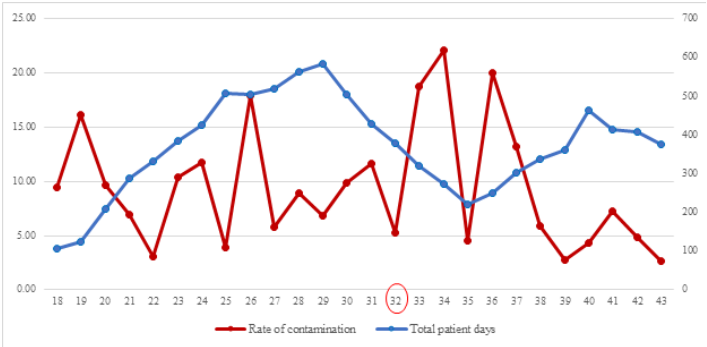

Figure 2: The weekly rate of blood culture contamination versus weekly Total Patient Days (Week 18-43, 2020).

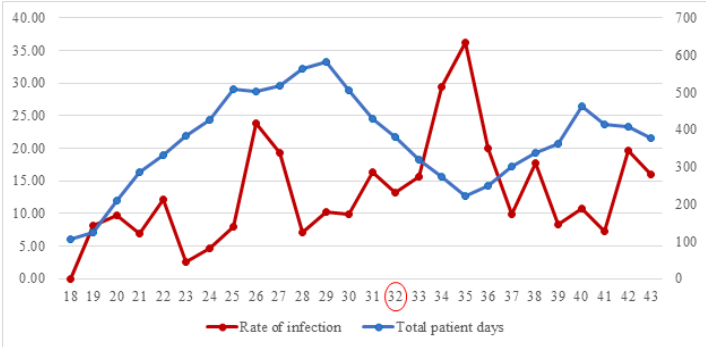

Figure 3: Weekly True Bacteremia incidence versus Total Patient Days (Week 18-43, 2020).

mean by week 37 (Figure 4).

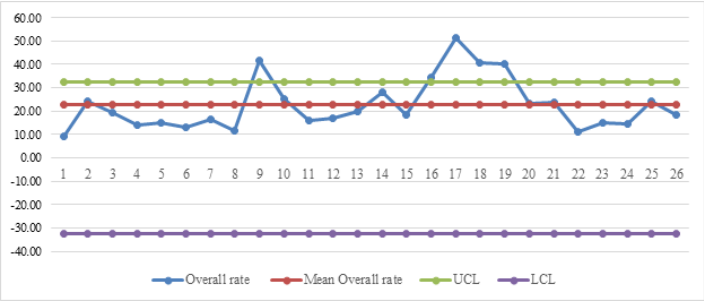

Figure 4: The Bacteremia Incidence Control Chart.

Discussion

The majority of cases in the study cohort were male, consistent with the existing literature. The observed blood culture positivity rate was similar to that reported by M. Cuntro and others [2,9,10,15] and remained high, potentially due to a high contamination rate. However, other studies have documented lower positivity rates [4,10-12]. A further explanation may be that patients experienced longer hospital stay, as reflected by patient days, and were more at risk of HAIs; hence, a more septic workup was mandated.

The mortality rate among bacteremic COVID-19 patients was comparable to rates reported in previous studies [10-12]. This may be attributed to the fact that, in this cohort, most cases of bacteremia developed during intensive care unit (ICU) admission and were associated with a high prevalence of comorbidities. Univariate analysis identified comorbidities such as hypertension, diabetes, and chronic heart disease as significant factors for mortality, consistent with findings from Palanisamy et al., Baccolini et al. and Yan He et al. [11,14,16]. Additionally, the presence of invasive lines, including femoral venous catheters (FVC) and internal jugular vein (IJV) catheters, was a significant risk factor. However, multivariate analysis indicated that only age remained a statistically significant predictor of mortality, which may be attributable to the limited sample size.

The commonest organism caused bacteremia in this cohort were CONS followed candida species and enterococci. The dominance of CONS bacteremia among COVID-19 patients was addressed in other settings [9,12]. The onset of hospital-acquired bacteremia was similar to other reports [10,11,15]. The incidence of bacteremia among the study cohort was high which could be due infection prevention and control practices that were implemented during the pandemic.

The contamination rate in blood cultures was high compared with other studies, which might be due to overcollection of blood cultures, excessive use of PPE, or other factors addressed in the literature [4]. The bacteremia due to MDRO in this cohort was lower than in some studies [9,11], which may reflect an earlier stage of the pandemic and the COVID-19 wards did not experience outbreaks. Gram-positive bacteremia was more common than Gram-negative bacteremia, unlike Palanisamy's report, which may be due to differences in clinical settings [11,14]. The most common cause of bacteremia was CLABSI, followed by VAP, findings similar to those of N. Buetti and S. Mormeneo [4,13]. During the pandemic, the FVC was used for the first 7 days of ICU admission, then changed to either a PICC line or an IJV, depending on availability and patient factors. Our data confirm the previous findings of high risk of infection in FVC lines. Bacteremia in patients with IJV was also high in our setting, which might reflect the staffing aspects during the pandemic, where trained critical care staff shortage dominated, and utilization of other non-critical care staff from our hospital and other healthcare institutions might have affected the implementation of CLABSI prevention bundles, as discussed in other studies [14,15].

Multiple factors contributed to the second peak of bacteremia observed during weeks 32 to 37, despite ongoing infection control support for the COVID-19 wards and a reduction in the COVID-19 inpatient census. During the study period, the hospital integrated 300 expatriate staff who were new to the healthcare system. These staff members completed a one-week hospital orientation that included infection prevention and control principles before beginning work in both critical and noncritical COVID-19 wards. Unfamiliarity with institutional protocols may have contributed to non-compliance with established care bundles. The large influx of new staff to the same wards likely compounded this effect. In addition, personnel from other hospitals and from the RH hospital's noncritical wards were reassigned to the COVID-19 wards. Previous studies have demonstrated that staffing changes influence healthcare-associated infection (HAI) rates, particularly when combined with increased critical care capacity and modifications in personal protective equipment (PPE) use during the pandemic. After the implementation of sustained multimodal interventions, the control chart indicated that bacteremia rates again fell below the mean infection rate.

A key strength of this study is its focus on a significant healthcare-associated infection (HAI) and the identification of potential factors contributing to increased rates of bacteremia during a pandemic. These findings may help hospitals recognize the challenges faced by healthcare systems in such contexts and develop strategies to mitigate the impact of pandemics on infection prevention and patient care. However, the study has several limitations. The retrospective design and the lack of assessment of COVID-19 disease severity scores (e.g., SOFA score) may have influenced the observed mortality rates. Additionally, the relatively small sample size may have limited the analysis's statistical power. The absence of data on antibiotic exposure is another limitation, as this factor could have affected the incidence of multidrug-resistant organism (MDRO) bacteremia and mortality. Furthermore, during the pandemic, only bacteremia was monitored, as it was not feasible to continue targeted HAI surveillance in the intensive care unit (ICU). This limitation hindered direct comparison with pre-pandemic HAI data.

Conclusion

Bacteremia among COVID-19 patients who are critically ill is associated with increased risk of mortality. Monitoring HAIs alongside adherence to meticulous infection prevention practices are important elements during the pandemic to reduce the impact on patient outcomes.

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