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BLOODSTREAM INFECTIONS IN COVID-19 PATIENTS IN A TERTIARY CARE HOSPITAL IN NORTH INDIA

VARUN GOEL[1], SAVITA GUPTA[2], MANISH KUMAR SINGH[3] AND HARMESH MANOCHA[4]

[1,3,4] Department of Microbiology, GIMS, Greater Noida
[2]Department of Anaesthesia, GIMS, Greater Noida

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Abstract– Many COVID-19 studies are about epidemiological and clinical features but information about secondary bacterial infections is limited. The present study was conducted to determine the prevalence and characteristics of bloodstream infections in COVID-19 patients admitted to a tertiary care academic health care organization. All blood samples were obtained from patients with COVID-19 admitted were included in the study. Blood cultures were performed using BD BACTEC ™ FX40, and the diagnosis and bacterial identification and antimicrobial sensitivity was performed by manual method. 2200 patients with COVID-19 were hospitalized during a 6-month study period in which 315 blood cultures were performed. Of these, 24 (7.61%) were positive. The median age of patients with positive blood culture was 38 years and included 13 males and 11 females. Seventeen patients (70.83%) needed intensive care in the ICU. Significant correlations with blood culture positivity have been noted with parameters such as admission to the ICU, availability of accommodation, basic illness and adverse clinical outcomes. Bloodstream infections prevalence in COVID-19 patients is low. However, antibiotic prophylaxis needs to be used with caution, and immediate discontinuation should be made based on clinical judgment.

INTRODUCTION

COVID-19 is an infectious disease caused by the SARS-CoV-2 virus. The widespread and continuous distribution of SARS-CoV-2 during COVID-19 has led to high hospitalization rates and a rapid increase in general hospital capacity to manage the sudden and unexpected influx of admitted patients (Baccolini *et al.,* 2021). To manage this unexpected stress and provide appropriate care during emergencies, hospital strength and beds were increased (Nazir and Gupta, 2021; McCabe *et al.,* 2020). Increased beds both in ICU and wards, redistribution of resources, and shortage of medical personnel may have a negative impact on the management of common hospital infections (Iordanou *et al.,* 2017). Therefore, the prevention of hospital-acquired infections in COVID-19 patients is even more important than before because secondary nosocomial infections can cause increase in morbidity and mortality in patients.

Viral infections are often associated with secondary bacterial infections, thus complicating clinical outcome and prognosis.[5] Most studies during the existing coronavirus pandemic have focused on the epidemiological and clinical features. Information about secondary bacterial infections is limited. The present study was done to know prevalence, features, etiological agents involved, antimicrobial sensitivity pattern, and clinical outcomes in COVID-19 patients with bloodstream infections.

MATERIALS AND METHODS

This prospective study was conducted on patients in a 30-bed intensive care unit in a 430-bed hospital in North India, for a period of 6 months from January 2021 to June 2021. Since the beginning of the epidemic, this hospital was designated as a COVID facility. Approval was obtained from the Institutional Ethics Committee prior to conducting the study. The COVID-19 diagnosis was confirmed by positive result of inhouse real-time reverse-transcription polymerase chain reaction (RT-PCR) for respiratory specimens.

All blood samples obtained from COVID patients

admitted to COVID-designated ICUs and wards were included in the study. Blood cultures were performed using BD BACTEC ™ FX40, and tests for antimicrobial susceptibility tests of the isolate were performed either by manual methods. The interval from the period of blood culture collection to the gram stain was used to calculate the duration of blood culture positivity during the study period.

All data was entered in Microsoft Office Excel and analysed using Microsoft Excel version 15, and the statistical analysis was done using GraphPad Prism V.6.0 software (GraphPad Software, La Jolla, CA). *p* value <0.05 was considered statistically significant.

RESULTS

2200 patients with COVID-19 were admitted during the 6-month study period (January 6, 2021 to June 5, 2021). 315 blood cultures were received from these patients admitted to the Department of Microbiology. Of these, 24 (7.61%) showed a positive blood culture. Only one first isolate was included from each patient.

The median age of COVID-19 patients showing a positive blood culture was 38 years (interquartile range: 21–70 years), and these included 13 males and 11 females. The 24 patients with a positive blood culture included 17 (70.83%) in ICU and7 (29.17%) in the ward.

The demographics, clinical features and outcome of the COVID-19 patients in positive blood culture patients are shown in Table 1. In the positive bloodstream culture samples, 17 (70.83%) had already received empirical antibiotics before the samples were sent for laboratory. The predominant isolate in the blood culture was *Staphylococcus aureus* 7 (29.17%) followed by *Klebsiella pneumoniae* (20.83%). Table 2 shows the bacterial distribution and the identified resistance pattern. Methicillin Resistant *Staphylococcus aureus* was found in 57% of isolates. Carbapenem resistance was found in many gram-negative bacilli. Commensal skin flora was found in four patients apart from the rest 24 positive bloodstream infections.

70% of the patients who developed bacteraemia in our study were critically ill and were admitted to the ICU. The association of blood culture and the need for intensive care in the ICU was found to be very high (p = 0.001). Oxygen therapy was required for 21/24 patients at some point during the hospital stay. Twelve of the 17 patients in the ICU had ventilatory support. All had an indwelling device such as endotracheal tube, urinary catheter, central line catheter and peripherally inserted central

Table 1. Shows demographics and clinical characteristics of COVID-19 patients in a positive blood culture, n (%)

Parameters	Number of patients (N = 24) n (%)
Median age	38 years (IQR: 21–70 years)
Gender	
Male	13 (54.16)
Female	11 (45.84)
Location	
ICUs	17 (70.83)
Wards	7 (29.17)
Severity score	
On oxygen therapy	20 out of 24 patients (83.33)
On ventilatory support	12 out of 17 ICU patients (70.58)
Presenting complaints	
Breathlessness	20 (83.33)
Fever	19 (79.16)
Cough	12 (50)
Underlying comorbid conditions	
Diabetes	9 (37.5)
Hypertension	12(50)
Lung disease	6 (25)
Cardiac disease	5(20.83)
Raised biochemical markers	
C-reactive protein	15 (62.5)
Final clinical outcome	
Discharged or referred	19 (79.16)
Deceased	5 (20.84)

catheter. Association of the presence of an indwelling device with blood culture positivity was also found to be significant (p = 0.0001).

Table 2. Distribution of pathogens and antibiotic resistance-associated in the bloodstream infections, n (%)

Organisms	Pathogens isolated	
	Total (24)	Resistance
Staphylococcus aureus	7(29.17)	
Methicillin resistant		4(57.14)
Klebsiella pneumoniae	5(20.83)	
Carbapenem resistant		3(60)
Pseudomonas aeruginosa	4(16.67)	
Multidrug resistant		2(50)
Acinetobacter baumannii	3(12.5)	
Carbapenem resistant		2(66.67)
Enterococcus sp.	3(12.5)	
Vancomycin-resistant Enterococcus		1(33.33)
Escherichia coli	2(8.33)	
Carbapenem resistant		1(50)

Shortness of breath (83.33%) and fever (79.16%) were the most common symptoms at presentation of patients. Symptoms begin 5 ± 3 days before admission. Most patients had some comorbid condition associated with high blood pressure (50%) followed by diabetes (37.5%). Each patient in our study had at least 14 days of follow-up. 83.33% of patients required oxygen therapy and ventilatory support in 70.58% during stay in hospital. Among the 24 patients with positive blood culture, 20.84% succumbed to infection. It was noted that the median time from onset to death is 7 days (interquartile range: 2-28 days).

DISCUSSION

Bacteraemia has been described as one of the complications of COVID-19 disease and blood culture is an important investigation into patient management. Bloodstream infections can cause serious illness, death, and increased health care costs including in COVID-19 patients. While many patients with COVID-19 are being treated empirically with antibiotics, early bloodstream pathogen and their antibiotic resistance is needed to improve the clinical outcome. This study shows a high incidence of bacterial bloodstream infection in ICU patients. Other studies also report a higher proportion of bacterial coinfections from ICU patients (Stevens *et al.,* 2020).

Shortness of breath (83.33%) and fever (79.16%) were the most common symptoms at presentation. 50% of patients had hypertension followed by diabetes. Other similar studies also report similar findings of conditions associated with positive blood culture ((Zhu *et al.,* 2020; Udomkarnjananun *et al.,* 2021).

In our study, we found a 7.61% increase (24/315) of bloodstream infections between COVID-19 positive patients. Various researchers from around the world have given variable data on nosocomial infection rates among COVID-19 patients. In a similar type of study from India, 12.1% of the 645 total blood samples were positive. Sepulveda et al[11] reported rate of bacteraemia was significantly lower among COVID-19 patients (3.8%). In a study by Bardi *et al.* (2021), bacterial and fungal nosocomial infection was a common complication in 25% cases of ICU admission in patients with COVID-19. It often appears as a serious form of infection, and is associated with high mortality and prolonged stay in the ICU. While a study from China[13] found nosocomial infection rate at 7.1% among 718 COVID-19 patients with bacterial infections in 24.6% cases. According to a meta-analysis of Rawson et al. (2020), 8% of patients reported exposure to bacterial or fungal coinfection during hospitalization.

The present study showed skin flora in four patients apart from rest 24 patients but a study by Sepulveda *et al.* (2020) reported a high proportion of organisms to be belonging to skin commensal flora. This may be due to COVID-19 patients carrying flora previously or suboptimal skin preparation before blood sample collection. In the present study S*taphylococcus aureus* were the most predominant bacterial isolate while studies report like *Acinetobacter baumannii*, *Enterococcus* sp., Coagulase Negative Staphylococci as common organisms as different hospitals can have different bacterial isolates.

There are always institutional antimicrobial recommendations regarding the use of different types of antibiotics in different settings, but during COVID times, due to the fear of BSI in COVID-19 patients, these recommendations are not being followed, and most of the COVID-19-positive patients are receiving empirical antibiotics. All patients with COVID-positive symptoms in our hospital were given empirical antibiotics in severe cases and the antibiotic azithromycin in mild cases of COVID-19 due to the fear of secondary

bloodstream infections in COVID-19 patients. However, in patients with suspected secondary bacterial infections, additional antibiotics were added to each case after the collection of a culture blood sample. Later, treatment was performed according to the antibiotic susceptibility reports. Patients in our study also received Injection methylprednisolone depending on the severity of the disease. A study from India on COVID-19 patients identified that only 17% demonstrated superimposed bacterial infections while 72% were given antibiotics.[10] All these necessitate the urgency of instituting and following antibiotic stewardship guidelines.

Each patient in this study had at least 14 days of follow-up. Among the 24 patients with positive blood culture, mortality was 20.84%. The cause of death was septicemia or multiorgan dysfunction. The average time from onset to death is 7 days (interquartile range: 2-29 days). Various studies link the presence of coinfections with the adverse clinical outcome. In a study by Bhatt and colleagues[16] found that 53.1% of patients with a secondary blood stream infections died during the hospitalization. Given the low prevalence of blood-borne pathogens, the default ordering of blood cultures as part of the initial workup for patients with suspected COVID-19 being admitted is probably not necessary, especially in a resource-limited setting.

There are limitations also in this study. Due to work overload, blood culture may have been missed. And during the epidemic, many new treatments such as hydroxychloroquine, macrolides, tetracyclines, and quinolone have been tried. Their potential role in low levels of bacterial infection among hospitalized patients needs to be explored. Long-term follow-up may provide better results for the patient condition.

The incidence of blood infections appears to be low in COVID-19 patients. Antibiotics should be used judiciously especially for empirical treatment based on the patient's clinical condition. More studies need to be done as the epidemic continues to emerge worldwide. Strong emphasis on infection control protocols and disinfection of hospital equipment and environment is needed for better patient outcomes.

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