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Original Research Article

Bloodstream infections (BSI) in COVID-19 patients admitted to a tertiary care hospital: A retrospective study

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ABSTRACT

Background: Bloodstream infections (BSIs) may cause significant adverse clinical outcomes among patients affected by Coronavirus disease 2019 (COVID-19). This study was conducted with the objective to characterize the bacterial isolates and their susceptibility pattern and to document the patient outcome as well as skin disinfection measures followed during the venepuncture for the blood collection procedure.

Materials and Methods: All blood cultures received from COVID-19 patients admitted in various COVID care wards and ICUs for a period of two years from June 2020 to May 2022 were included in the study. An automated BacT/ALERT system was used for blood culture. The microbial identification and antimicrobial susceptibility testing were done by standard methods. Patient demographic and treatment details and infection control and prevention practices followed during the blood specimen collection were documented.

Results: Out of 172 COVID-19-positive patients blood samples were sent for blood culture with clinical suspicion of sepsis. Out of these, 4.2% were positive. The median age of COVID-19 patients with positive blood cultures was 55 years and about 67% of patients had associated comorbidities. About 31% of patients were admitted to ICUs for their management. The blood culture positivity was documented more among patients with ICU admission, underlying comorbidities, and the presence of an indwelling device. Gram-positive bacterial isolation was more than gram-negative bacteria. About 54% showed clinical improvement at the time of discharge and death was recorded in 19% of patients. There was a lack of strict adherence to the aseptic techniques during the venepuncture for blood collection.

Conclusions: The incidence of bloodstream infections documented was low for COVID-19 patients. Hence, empirical antimicrobial agents should be used with care and prompt discontinuation should be done on clinical improvement and based on the microbiology culture report.

1. Introduction

The Coronavirus disease 2019 (COVID-19) is caused by Severe Acute Respiratory Syndrome Corona virus-2 (SARS-CoV-2) infection; which has affected globally, with more than 765 million confirmed cases and more than 6.9 million deaths, as of April 2023.[1] India is the second most affected country in terms of total COVID-19 cases, accounting for about 44 million confirmed cases of COVID-19 with 0.5 million deaths with 0.8% case fatality rate.[2]

The demographic details, the vast range of clinical presentations, and various treatment options available for the management of COVID-19 patients have been already

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extensively reported from different parts of the country.[3,4] The standard infection control and prevention measures to be followed and the overall survival rate of COVID-19 patients admitted to intensive care units have also been reported in many recently published data.[2,5] However, little is known about the development of secondary bloodstream infections among these hospitalized patients during the course of COVID-19 management.[6,7]

The development of complications such as bacterial or fungal bloodstream infections (BSI), due to central lines or usage of ventilators to stabilize these patients going for respiratory failure or may be due to compromise in infection control and preventive measures, which may in turn adversely influence the outcome of any ICU-admitted COVID-19 patient.[8,9] The use of empirical antimicrobials among patients with severe COVID-19 may be necessary, as it is difficult to predict secondary bacterial infections during the course of hospitalization.

Documenting bloodstream infections in COVID-19 patients admitted to tertiary care centers during the COVID-19 pandemic will help to associate the organisms involved and the disease severity or outcome of the disease, among these patients.[9,10] There is a scarcity of Indian data regarding the BSIs and their impact on the outcome of COVID-19 patients. The data on BSI and the organisms involved may help in prompt management and guide empirical antimicrobial therapy when clinically appropriate. Also, it is required in strategizing infection control practices and further management of patients in isolation. Hence, this study was undertaken to study bloodstream infections in patients among patients admitted to the tertiary care center with COVID-19 infection, to characterize the bacterial isolates and their susceptibility pattern, and to analyze the infection control measures followed for the management of these patients during their hospital stay.

2. Materials and Methods

A retrospective record-based observational study was carried out in a tertiary care center after obtaining a waiver of consent from the Institute Ethics Committee (IEC No. RC/2021/06). All patients with confirmed COVID-19 by a positive real-time reverse transcriptase polymerase chain reaction (RT-PCR) for SARS-CoV-2 on at least one respiratory specimen (nasopharyngeal swab, or oropharyngeal swab), who were admitted to a tertiary care center from June 2020 to May 2022 were included in the study.

1. BSI after COVID-19 patient admission to the hospital is defined in the presence of at least one positive blood culture for bacteria or fungi, drawn at >48 hours after hospital admission.
2. Blood cultures were sent in patients with persisting fever (> 38.3 C), increased leukocyte counts, and clinical deterioration after initial improvement with signs of septic foci.
3. Data from case records of all consecutive COVID-19 patients admitted to ICU and wards with positive blood cultures (including those with coagulase-negative staphylococci), were included in the study.
4. For coagulase-negative staphylococci and other common skin contaminants, at least two consecutive blood cultures positive for the same pathogen were necessary to define as an episode of bloodstream infection.
5. Isolation of the same microorganisms from the bloodstream within the same length of hospital stay was excluded from the analysis.

2.1. *Blood culture and susceptibility testing*

Blood cultures were performed using BacT/ALERT automated blood culture system and microbial identification was done by colony morphology and standard biochemical tests.[11] Antimicrobial susceptibility testing of isolates was performed by Kirby Bauer disk diffusion testing.[12]

2.2. *Data collection*

The following data were extracted from the hospital information management system (HIMS): Patient demographic details (age, gender), risk factors for healthcare-associated BSIs like mechanical ventilation, indwelling catheters, use of immunosuppressants, associated comorbidities, the timing of blood culture drawn, duration of ICU/hospital stay, the outcome of the patient, treatment received by the patient, microorganism profile, antimicrobial susceptibility report, and infection control measures followed during the blood sample collection.

2.3. *Statistical analysis*

Collected data were entered in a Microsoft Excel sheet. Descriptive statistics such as frequencies, percentages, and standard deviation were used for analysis. Continuous variables were presented as mean ± standard deviation. Categorical variables are expressed as frequencies and percentages.

3. Results

During the study period of two years (June 2020 to May 2022), a total of 1,013 patients with real-time RT-PCR-confirmed COVID-19 were admitted to various wards/ICUs. Out of these 172 blood cultures were received from patients with clinical suspicion of bloodstream infection, after 48 hours of hospital admission. Overall, 4.2% of patients (42/1,1013) developed BSIs. The median age of all admitted COVID-19 patients with BSIs was 55 years (IQR 35–62).

The majority of patients 64% (27/42) were males.

Out of the 42 culture-proven COVID-19 patients with bloodstream infection thirteen patients (31%) were admitted to ICU during their hospital stay. Length of hospital stay ranged from 2 to 47 days with a median of 16 days. About 67% (28/42) were having underlying common underlying comorbidities. Among the comorbidities diabetes, hypertension, chronic kidney disease (CKD), ischemic heart disease (IHD), chronic liver disease (CLD), and COPD were common among these patients (Figure 1).

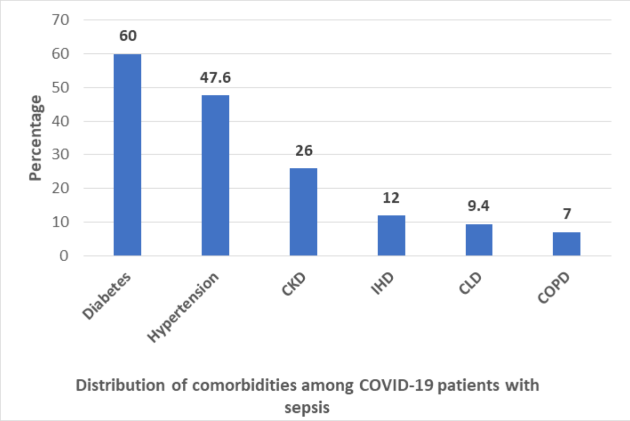

Fig. 1: Distribution of associated comorbidities in COVID-19 patients with sepsis

About 23.8% of the patients were on central lines during the course of their hospitalization.

Mechanical ventilation was used in 59.5% of patients with BSIs and about 52% of patients were on urinary catheters. About 57% (24/42) of patients received corticosteroids during the course of treatment in the hospital. Twelve patients received Remdesevir during their course of treatment. The majority of patients (81%) received one of the anticoagulants such as Rivaroxaban, heparin, or clexane as a preventive measure for the formation of blood clots.

In the present study, usage of antimicrobial agents for empiric treatment was as follows: more than one antibiotic was used in 22 patients (52%), penicillin group of antibiotics in 19%, cephalosporin group in 31%, fluoroquinolones in 9.5%, macrolides and aminoglycoside were used in 4.7% each.

Subsequently, antibiotics were changed based on the blood culture susceptibility report and clinical improvement. Thirteen patients (31%) were admitted to ICU with severe COVID with complications such as acute respiratory distress syndrome or COVID pneumonia. The remaining patients were admitted to wards with moderate COVID and 70% of them were on oxygen support to maintain the saturation.

In the present study, 23 (54.8%) showed clinical improvement at the time of discharge, death was recorded in 8 (19%) patients, and 11 (26.2%) patients were discharged against medical advice. Among 42 COVID-19 patients with sepsis, gram-positive bacteria were isolated from 27 (64.2%) cases, gram-negative bacteria from 13 cases (31%), and Candida species were isolated from two (4.8%) cases. No polymicrobial BSI was documented in the study period. The distribution of the microbial profile among COVID-19 patients with blood culture-positive sepsis is shown in Figure 2.

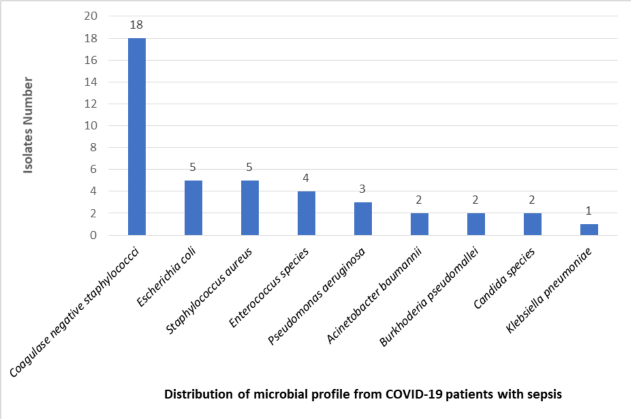

Fig. 2: Distribution of microbial profile from COVID-19 patients with sepsis (n=42)

The overall antimicrobial resistance rate observed among 12 gram-negative bacterial isolates in the decreasing order was as follows: ciprofloxacin (58.3%), ceftriaxone (50%), amoxicillin + clavulanate (50%), ceftazidime (41.6%), cefoperazone + sulbactam (33.3%), piperacillin + tazobactam (33.3%), gentamicin (33.3%), meropenem (25%), amikacin (25%), imipenem (16.7%). Among these, two isolates were Burkholderia pseudomallei and they are intrinsically resistant to amikacin, gentamicin and hence considered resistant for analysis.

Among 28 gram-positive bacterial isolates, the predominant isolate was coagulase-negative Staphylococcus 18 (66.7%), followed by Staphylococcus aureus five isolates (18.5%), and four (14.8%) were Enterococcus species. Among staphylococci isolates high level of methicillin resistance was observed (48%). A high level of resistance (60 to 90%) was also noted for commonly used antimicrobial agents like erythromycin, clindamycin, co-trimoxazole, and ciprofloxacin. However, they were, uniformly susceptible to vancomycin, and linezolid.

3.1. Two Candida isolates were susceptible to fluconazole

Among the 42 positive blood cultures, the time to positivity (TTP) for gram-negative bacterial isolates ranged from 8 hours to 21 hours, with a median TTP of 17 hours to 30 minutes, and for gram-positive bacterial BSIs, TTP ranged from 12 hours to 42 hours, with a median of 28hours. Both yeast isolates had TTP of more than 48 hours.

Out of 42 patients with COVID-19 sepsis, in the majority of the patients (71%) blood collection for culture was performed by median cubital vein venipuncture, followed by femoral in about (17%) and in the remaining 12% of cases venipuncture site was not documented in the case records. Betadine was the commonest disinfectant used for skin preparation (66%), compared to surgical spirit (26%) and in the remaining cases, it was not documented. Use of personnel protective equipment including face shield, surgical face mask or N95 respirators, and hand hygiene practice was followed for all patients.

4. Discussion

The data regarding secondary bacterial infections in COVID-19 patients are limited and even more so with bloodstream infections (BSI). Secondary bacteremia has been described as a complication of COVID-19 infection. COVID-19 and BSI have many clinical and laboratory parameters overlapping. In this study, the documented prevalence of BSIs among COVID-19 inpatients was 4.2%. A study from India has reported the prevalence of BSI in COVID-19 patients to be 3.6%.[13] However, He Y et al. reported 24.6% of bacteremia among COVID-19 patients and Li et al. reported 7.7% of bacteremia to be a complication in COVID-19 patients from Wuhan.[14,15] About 31% of patients who developed bacteremia were critically ill and were admitted to ICU. This indicates there is a high chance of blood culture positivity and ICU admission.

About 23.8% of the patients were on central lines during the course of their hospitalization. Mechanical ventilation was used in 59.5% of patients with BSIs and about 52% of patients were on urinary catheters. Similar observations were also documented by many other researchers. The association of the presence of an indwelling device with positive blood culture was also found to be significant.[13,14,16] About 57% of patients received corticosteroids and 28.5% received Remdesevir and 81% received one of the anticoagulants such as Rivaroxaban, heparin, or clexane as a preventive measure for the formation of blood clots. The longer hospitalization time with a higher rate of ICU admission, and immunosuppressive treatments like corticosteroids and anti-IL-6 drugs increase the risk of contracting healthcare-associated infections, including secondary BSI.[10,16,17]

In the present study, usage of antimicrobial agents for empiric treatment was as follows: more than one antibiotic was used in 52% of patients, penicillin group of antibiotics in 19%, cephalosporins in 31%, fluoroquinolones in 9.5%, macrolides and aminoglycoside were used in 4.7% each. Studies reported by many other researchers also documented that most patients with COVID-19 were treated with empirical antibiotics for potential bacterial coinfections.[13,16,17] Subsequently, antibiotics were escalated or de-escalated based on the blood culture susceptibility report and clinical improvement.

In the present study, about 54% of patients showed clinical improvement at the time of discharge, death in 19%, and 26% were discharged against medical advice even before the clinical improvement. Hence, their clinical outcome could not be documented. A study by Palanisamy N et al. documented a 100% mortality rate in severe COVID-19 pneumonia patients with BSIs admitted to ICU.[18] However, many other studies have reported 20–70% mortality in this group of patients.[13,17] The disparity in mortality rate could be due to various factors, such as ICU admission, invasive interventions, and the use of immunosuppressants for treatment. Associated comorbidity also played an important role in mortality, with nearly half of the patients in our study group having diabetes and hypertension.

In this study group, gram-positive bacteria were isolated from about 64% followed by 31% gram-negative bacteria and Candida from only 4.8% of cases. This observation is probably due to the high rate of skin commensal flora isolation from blood cultures. Probably due to the use of PPE while blood collection in COVID wards would have hindered the visibility of the person collecting blood due to the use of face shields or goggles. However, we have also documented that about 17% of patients blood collection was performed from the femoral site rather than a median cubital vein and also recommended 2-step disinfection of the venepuncture site before blood collection was not followed in the majority of patients. These reasons probably would have led to reporting of the increased rate of coagulase-negative staphylococci (CoNS) from blood cultures. However, as per the standard recommendation, we have included for analysis only the cases from where we have reported CoNS from two or more blood samples collected from different venepuncture sites. A similar observation also was documented in a study by Rajni E et al.[16] Reasons for this finding may be related to fear and uncertainty among healthcare providers when dealing with COVID-19-positive patients. The rapid increase in the number of patients has put great pressure on the existing healthcare system, especially critical care. This probably has resulted in suboptimal skin preparation before blood sample collection. It is difficult to determine whether these isolates were pathogens or skin contaminants.[16,19,20] Median TTP documented for positive blood cultures with gram-positive bacteria isolation was 28 hours which was more as compared to 17 hours. Probably BSI due to CoNS having TTP for more than 24 hours. This may be due to less bacterial load as the source was from the skin microflora.

In this study gram-negative bacteria were reported from 31% and Candida species were isolated from two (4.8%) cases. In contrast to this, few other researchers have reported predominant gram-negative bacterial sepsis in their studies.[13,18] This varied prevalence and distribution of microorganisms may attribute to different patient settings such as duration of hospital stays, the number of patients on mechanical ventilation, and other invasive interventions. Candida species were isolated from only the blood culture of two patients and both isolates were fluconazole sensitive. However, a study by Chaudhary et al. have reported BSIs caused by multidrug-resistant Candida auris.[19]

The matter of concern is regarding the massive antibiotic use while managing COVID-19 patients in healthcare would have created an enormous impact on the already existing issue of antimicrobial resistance (AMR). There was a definite increase in exposure to healthcare settings and invasive procedures due to the COVID-19 pandemic, which may compromise following infection control and hand hygiene practices because of this massive influx of patients. All these reasons may facilitate the rapid emergence of multidrug-resistant microorganisms in a great way. The usage of multiple prophylactic antibiotics in COVID-positive patients to keep secondary bacterial infections may also contribute to complicating the scenario of AMR.

5. Conclusion

The incidence of bloodstream infections seems to be low for COVID-19 patients. Hence, empiric antibiotics for patient management may be used with caution, and prompt discontinuation should be done based on clinical judgment and Microbiology culture report. Larger scale studies need to be carried out to get clear evidence on the outcome of COVID-19 patients with sepsis. Also, practice of infection control and prevention practices while patient management as well as disinfection of hospital equipment used for patient care and healthcare environment is mandatory to reduce the rate of healthcare-associated infections and also to improve the patient outcome.

6. Source of Funding

None.

7. Conflict of Interest

None.

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