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Original Research Article

Analysis of bloodstream infections and their antimicrobial susceptibility pattern in a COVID-19 dedicated centre: Six months hospital-based study

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ABSTRACT

Introduction: COVID-19 pandemic, caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), has been impacting the life and economy across the globe since December 2019 and has caused major disruptions worldwide. The COVID-19 pandemic had resurfaced in India in the form of a hard-hitting second wave around April 2021**.** Blood stream infections (BSI) are one of the most significant causes of morbidity and mortality in tertiary care hospitals amongst COVID-19 patients.
Aim: This study was conducted to assess the bloodstream infections and their antimicrobial susceptibility pattern of in a COVID-19 dedicated tertiary care centre.
Materials and Methods: This retrospective observational study was carried out from April 2021 to September 2021 in a bacteriology laboratory, department of Microbiology, at a dedicated COVID-19 tertiary care centre. Blood Cultures of all COVID-19 confirmed cases were sought for and Bacterial Identification and Antimicrobial Susceptibility were performed as per the standard guidelines.
Results: A total of 4200 blood culture samples from COVID-19 positive patients were received during April 2021- September 2021 for analyses of microorganisms and antimicrobial susceptibility profile of blood stream infection. 16.9% samples were grew significant bacteria. Gram-positive isolates outnumbered than Gram-negative organisms (1.36:1). Amongst Gram-negative microorganisms, most commonly isolated bacteria were *Klebsiella spp*. (11.8%) and amongst gram-positive organisms, *Staphylococcus aureus* (n=348; 48.9%) was most commonly isolated.
Conclusion: The blood culture positivity along with their antimicrobial susceptibility is the need of the hour in order to aid hospitals to formulate and implement antimicrobial stewardship guidelines

1. Introduction

Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) caused COVID-19 disease globally. The pandemic has been impacting the life and economy across the globe since December 2019 and has caused major disruptions worldwide. The COVID-19 pandemic had resurfaced in India in the form of a hard-hitting second wave around April 2021.[1]

The second wave of COVID-19 in India has had severe consequences in the form of escalation of cases, condensed supplies of essential treatments, and a greater than before death rate, particularly in the young population.[2] Critical COVID-19 is reported in around 5% of the cases, which requires hospitalization.[3]The case-fatality rate of COVID-19 infections was inconsistent (1.39–14%), depending on the multiple factors like; etiology of infection, demographic profile, the clinical presentation of patients, and epidemic wave dynamics.[4]

Blood stream infections (BSI) are the most significant cause of morbidity and mortality in tertiary care hospitals.[5]

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Patients clinical signs and symptoms, though useful in identification and diagnosing, possible microorganism of bacteremia have only narrow specificity and sensitivity. A bacteriologic culture and antimicrobial susceptibility testing (AST) profile of the blood sample helps clinician to treat patient properly. The results are usually not available at the appointed time, so correct etiology and antibiogram profile of blood pathogens is life saving and precious for early treatment of vitally ill patients with bloodstream infections.[6,7]

It is difficult to predict the secondary bacterial co-infection, which warrants the use of empirical antimicrobials in patients with severe SARS-CoV-2 infection. The prevalence of secondary bacterial infections from previously published studies (ranges from 14.3 to 67.7%) was showed conflicting results in BSIs.[8–12]

The previous reports have shown prolonged hospital stays, inappropriate use of antibiotics. Morbidity and mortality (odds ratio = 3.31, 95% CI 1.82–5.99) in the secondary bacterial BSI.[13,14] There is a paucity of data from India regarding the BSIs and their effects inpatient health in COVID-19. Knowing the microorganism etiology and the impact of BSIs is paramount in order to apply prompt management and guide empirical antimicrobial therapy. This study was conducted with the aim to analyze the bloodstream infections and their antimicrobial susceptibility pattern of in a COVID-19 dedicated tertiary care centre.

2. Materials and Methods

This retrospective observational study was carried out in a bacteriology laboratory, department of Microbiology, at a dedicated COVID-19 tertiary care centre situated in the eastern most part of Delhi. We have analysed the patient records from WHONET software from April 2021 to September 2021. All the patients in whom the Reverse Transcriptase Polymerase Chain Reactions (RT-PCR) for COVID-19 was positive from nasopharyngeal or oropharyngeal swab were admitted to the hospital. Isolation of the same microorganisms from the bloodstream within 14 days was not considered a novel event and excluded from the analysis.

A minimum of 8-10 ml of blood in adults and 1-3ml of blood in paediatric age group was drawn under sterile conditions and was inoculated in the conventional brain heart infusion broth blood culture bottle. Once the sample was collected it was sent to the Microbiology Laboratory within 2 hours of collection. After the sample was received it was aerobically incubated at 37^0C for 24hours. Blind subcultures from the blood culture bottle were done at 24h, 48h and 7^{th} day. Organisms were identified by standard biochemical methods. For significant pathogenic isolated microorganism, Antibiotic susceptibility testing was performed as per latest standard Clinical Laboratory Standard Institution (CLSI) guidelines.[15]

The Antibiotic susceptibility testing to microorganism in BSIs was determined by Kirby Bauer method using the commercially available antibiotic discs (Hi-Media, Laboratories Pvt. Ltd, Mumbai). The gram -negative bacteria were tested with disks containing Amoxicillin (10μg), Gentamicin (10μg), Cefotaxime (10μg), Ceftriaxone (30μg) and Ciprofloxacin (10mg). *Salmonella typhi (S.typhi)* and S. *paratyphi* were also tested with Chloramphenicol (30μg). *Pseudomonas aeruginosa (P. aeruginosa)* isolates were further tested with Ceftazidime (10μg), Piperacillin (30μg) and Amikacin (30μg). The gram-positive cocci were tested with Penicillin (10 units), Erythromycin (5μg), Amikacin (30μg), Gentamicin (10μg), and Ciprofloxacin (10μg). *Streptococcus pneumonia (S. pneumoniae)* strains were tested with 0.25 IU of penicillin disc and all resistant strains were further confirmed by using 1 mg oxacillin disc.

Reference strains of *Escherichia coli* ATCC 25922, *Staphylococcus aureus* ATCC 25923 and *Pseudomonas aeruginosa* ATCC 27853 used for quality control for antimicrobial susceptibility tests.

All samples were processed under Biosafety cabinet II (a) along with personal protective equipment were used for processing the specimens and cultures. 5% phenol was used for discard and 1% sodium hypochlorite was used for spills.[16]

This study protocol was approved by the Institutional ethic committee However; ethical approval for this retrospective study was not required.

2.1. Statistical analysis

All the data was recorded on a patient prescription slip and responses were coded for entry in the WHONET software. All the entries were doubly checked for any possible keyboard errors. We performed statistical analysis using SPSS 21. The statistical tests were used to find significant association. P value <0.05 was considered statistically significant.

3. Results

In this study, a total of 4200 blood culture samples from COVID-19 positive patients were received during April 2021- September 2021 for analyses of secondary bacterial co-infection and antimicrobial susceptibility profile of blood stream infection. 711 (16.9%) samples were grew significant bacteria.

The age of the patients ranged from 1 year to 85 years, with mean age of 35.26 years. The commonest age group was 33-55 years (33%) followed by 12-35 years (26%). The median range of age was 35 years. The Interquartile range at 25^{th} and 75^{th} percentile was 1, 2.5 respectively. Male has outnumbered than female (M: F= 1.3:1). Majority of the bacteremia cases were isolated from the Intensive care units

(NICU; 17%), which is statistically significant (p <0.001, chi-square test) (Table 1).

Amongst Gram-negative microorganisms, most commonly isolated bacteria were *Klebsiella species*. (11.8%) followed by *Acinetobacter baumanii* (10.8%) in COVID-19 positive bloodstream infection patients. Gram-positive organisms, *Staphylococcus aureus* (n=348; 48.9%) was most commonly isolated followed by Coagulase negative *staphylococcus* (n=43; 6.04%), *Enterococcus spp*. (n=14; 1.9%) and *Streptococcus pneumoniae* (n=5; 0.7%).

Majority of pathogens isolated were Gram-positive isolates (n=410; 58%) followed by Gram-negative organisms (N=301;42%) with a ratio of 1.36:1 (Figure 1)

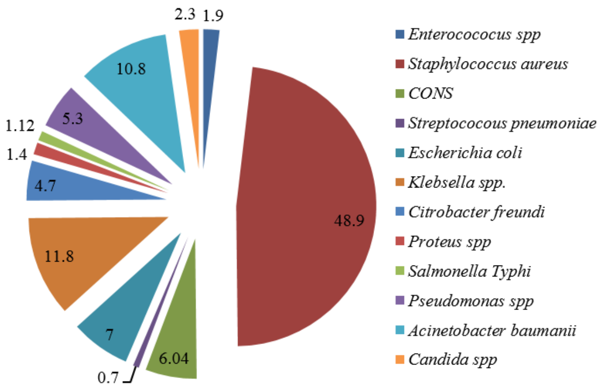

Fig. 1: Distribution of the bacteremia amongst the COVID-19 positive bloodstream infections in the study group (n=711) *CONS: Coagulase Negative *Staphylococcus*

In Gram positive bacteremia amongst COVID-19 positive patients were as follows: Ampicillin (100%), Amoxicillin (80%), Trimethoprim-sulfamethoxazole and Ciprofloxacin (60%) each and Erythromycin (50%) were resistant. (Figure 2)

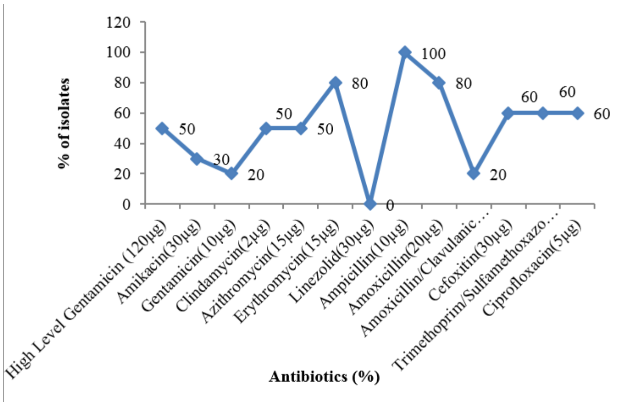

Fig. 2: Antimicrobial resistant pattern of Gram-positive microorganisms of Bloodstream infection amongst COVID-19 positive patients. (n=711)

Third generation cephalosporins (60-80%), macrolides (100%), aminoglycosides (50-60%) and ciprofloxacin (80%) were resistant amongst Gram-negative isolates in COVID-19 positive bloodstream infection.

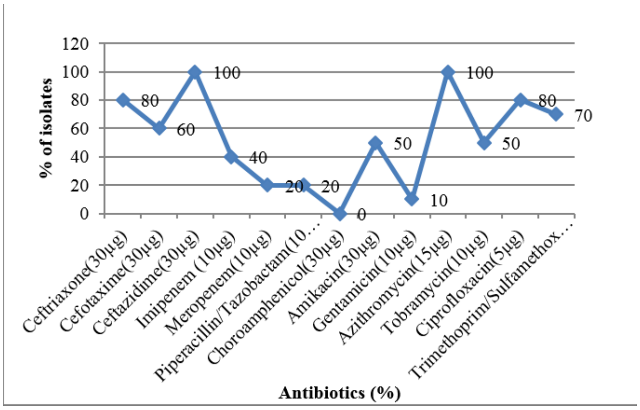

Fig. 3: Antimicrobial-resistant pattern of Gram-negative microorganism of bloodstream infection amongst COVID-19 patients (n=711).

4. Discussion

Bloodstream infections are one of the most severe complications witnessed in COVID-19 patients. Despite administering empirical antibiotics during the illness, BSIs in such patients contribute to sepsis leading to higher mortality rates. Bacterial co-infections in COVID-19 patients are scarce and conflicting, even more so with BSIs.[17]

In April 2021, there was a surge in COVID-19 patients presenting to our hospital which served as one of the epicenters of the global COVID-19 pandemic, which led to a dramatic increase in the using up blood cultures in BSIs patients. As In patients presenting with severe febrile illness, sepsis and septicemia, blood cultures are the mainstay in ruling out bacterial infection and guiding towards appropriate antibiotic usage. Early identification of bloodstream pathogens and their antimicrobial susceptibility profile is necessary to improve patient management and clinical outcome.[18]

In the present study. Blood culture positivity was 16.9% isolated in COVID-19 patients. Our study finding was higher as compared to the study reported by Rajni et al from Jaipur 2021; where they reported a positivity rate close to 9.4%.[19] A higher positivity rate could be attributed to our higher burden of seriously ill patients requiring decisive and intensive care admissions. The maximum number of blood culture positivity was observed amongst 33-55 years (33%) of age and males were involved more than females in the present study. This was similar to another study, where a similar age group and gender predominance was seen.[20]

Table 1: Frequency distribution of the microorganism Location wise in bloodstream infection of COVID -19 positive patients. (n=711)

Location	N=711	%	Total N=711 (%)	P value
NICU	121	17	394 (55.4)	0.001
MICU	112	15.7		
PICU	106	14.9		
CCU	55	7.7		
Medicine ward	109	15.3	268 (37.6%)	0.231
Surgery ward	70	9.8		
Gynecology ward	89	12.5		
OPDs	49	6.8	49 (6.8%)	0.520

Note: NICU: Neonatal Intensive Care, MICU: Medical Intensive Care Unit, PICU: Paediatric Intensive.
Care Unit; CCU: Cardiac care unit, OPD: Outpatient department.

There is limited availability of data that provides numbers and statistics of secondary BSIs in COVID -19 ICU admissions related to paediatric patients. The incidence rates of secondary BSIs were more observed in ICUs patients (NICU > MICU > PICU > CCU) follow by in-patients and out-patients. Our finding coincided with the study published with Shafran et al in which Intensive care units has comprised 17% BSIs rate.[20]

There was extensive variant in the microorganisms causing BSIs in COVID-19 patients along with an elevated fraction of multi-drug-resistant organisms. In the present study, gram-positive microorganisms were more prevalent than gram-negative ones. A study reported from the southern part of the country showed the prevalence of gram-positive microorganisms over gram-negative microorganisms in causing BSIs in COVID-19 patients.[21]

Amongst gram-positive microorganisms, the most common isolated was *Staphylococcus aureus* (48.9%) followed by coagulase-negative *staphylococcus* (CONS; 6.4%). *Staphylococcus aureus* microorganism prevalence from 44 to 79.6% in COVID-19 intensive care patients reported by Elabaddi et al.[22] A study from India, reported a high proportion of organisms to be belonging to skin commensals mostly coagulase-negative *Staphylococcus* (70%) as compared to our study in which CONS was isolated 6.4%.[19] Amongst gram-negative *Klebsiella pneumoniae* (11.8%) followed by *Acinetobacter baumanii* (10.8%) were the most commonly isolated microorganisms. Our finding was correlated with the study done by Zeno et.al and Palani Samy et al. from the Northern and Southern parts of the country.[23,24] This heterogeneity in prevalence and distribution of microorganisms may attribute to different patient settings, depending upon the number of patients on mechanical ventilation, duration of hospital stays, and follow-up and isolation of the pathogen from other specimens from different parts of the body, in addition to BSIs. A study from Asia reported that more than 70% of patients received antimicrobial treatment despite less than 10% had bacterial or fungal coinfections.[25,26]

The antimicrobial susceptibility testing of BSIs with COVID-19 paediatrics patients were showed, 100% resistance to amoxicillin and 80% resistance to ampicillin in gram-positive microorganisms, whereas macrolides (100%) and third-generation cephalosporins (60-80%) were resistant amongst gram-negative microorganisms. This resistance could be attributed to the irrational misuse of antibiotics as a part of treatment for COVID-19.

5. Conclusion

A better understanding of the BSI trends, causative factors including re-evaluation of existing infection control measures and reinforcement of antimicrobial stewardship principles will be critical to mitigating future outbreaks. Antibiotic prophylaxis may be used with caution, and prompt discontinuation should be done based on clinical judgment and Laboratory results. More such studies are needed to know the outcome of BSI's as the pandemic continues to evolve every minute on a global level. The blood culture positivity along with their antimicrobial susceptibility is the need of the hour in order to aid hospitals to formulate and implement antimicrobial stewardship guidelines.

6. Acknowledgement

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7. Conflict of Interest

The authors declare no relevant conflicts of interest.

8. Source of Funding

None.

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