

Research Article

Analysis of Bloodstream Infections and Their Antibiotic Sensitivity Pattern (Pre- and Post-COVID Lockdown in an Indian Cancer Hospital): A Record-Based Retrospective Cohort Study

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Abstract

Objectives: In cancer centers, various factors influence the type of organism causing bloodstream infection (BSI). Our premise includes the indirect benefits of hand hygiene of healthcare personnel, masking, and distancing practices during lockdown/post-lockdown period on the type of BSI among cancer patients and their antibiotic sensitivity patterns.

Methods: The retrospective cohort study was conducted from November 2020 to July 2021, among cancer patients admitted to Healthcare Global cancer center. Blood culture reports of patients presenting with symptoms of BSI were retrieved and analyzed in the Department of Preventive Oncology, Healthcare Global. Our data were stratified from pre-lockdown (November 2019 to March 24, 2020) and lockdown/post-lockdown (March 25, 2020, to Jul 2020) periods.

Results: The proportion of culture positives during the pre-lockdown (Nov 2019 to March 24, 2020) and post-lockdown period (March 25, 2020, to July 2020) are 21.7% and 21.1%, respectively. However, this small difference did not show a significant association with the difference in hand hygiene during the two periods (<80% and ≥80%). In our study, *Escherichia coli* (23.8%), *Staphylococcus epidermidis* (10.9%), and *Klebsiella pneumoniae* (17.8%) were the most common BSI during the pre-lockdown period. A similar analysis during the post-lockdown period shows a higher prevalence of *E. coli* (20.7%), *Staphylococcus haemolyticus* (12.1%), and *K. pneumoniae* (15.5%). In our study, the isolates showed a greater proportion of resistance (>50%) to Gentamicin, Ciprofloxacin, Tigecycline, and Cephalosporin group of drugs.

Conclusion: During COVID times, some of the preventive interventions which were implemented for reducing the transmission of SARS-CoV-2 could contribute to the reduction of BSI in the hospital setting. For the management of BSI, it is imperative to initiate appropriate antimicrobial treatment at an early stage. It is imperative for customizing the antimicrobial stewardship strategies as per the geographic location.

Keywords: Catheter-related infections, blood culture, medical oncology, bacteremia, COVID-19

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Among hospitalized patients, bloodstream infection (BSI) remains one of the main causes of death with mortality between 30% and 70%.^[1] BSI is caused by the

presence of bacteria or fungi in the bloodstream, which elicits an inflammatory response accompanied by alterations in the biochemical parameters. BSI could be either

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hospital or community acquired, and its etiology could be either primary (where the origin is not identified) or secondary (where the source is documented). If the patient has completed ≥ 48 h of hospital stay or if the central line is present for >48 h, then the BSI is defined as hospital acquired.^[2] Nosocomial BSI is a result of interventions among ill patients, which creates foci for the access of bacteria to the bloodstream. This tends to affect $\sim 1\%$ of all hospitalized patients and represents $\sim 15\%$ of all nosocomial infections.^[2] Apart from the central line as the primary source of infection, secondary foci could be from the respiratory, intraabdominal region, genitourinary tract, or any other source of infection in the body.

The commonest Gram-positive organisms causing BSI include *Staphylococcus aureus*, coagulase-negative *Staphylococci*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, and *Enterococcus faecalis*. Gram-negative bacteria causing BSI include Enterobacteriaceae such as *Escherichia coli*, *Klebsiella pneumoniae*, and *Serratia* species. The organisms implicated more often in BSI include *Staphylococci*, *Enterococci*, and Enterobacteriaceae.^[1] Among the nonfermenting Gram-negative organisms, the commonest include *Pseudomonas* species and *Acinetobacter baumannii*, which are implicated in recent instances of bacteremia. Non-albican *Candida* species followed by *Candida albicans* are the most common fungal organisms.^[2]

Cancer and chemotherapy tend to predispose patients toward acquiring infections in oncology settings. In such centers, various factors that influence the type of organism causing BSI include the presence of central/Peripherally inserted central catheter /peripheral line, duration of catheterization, immune status of the host, underlying comorbidities, prevalent organisms in the center, level of barrier precautions undertaken, and initial antimicrobial therapy.^[2] The immunocompromised state in such settings will predispose the individual to bacterial and fungal BSI. Hospitals could uniquely harbor ecological niches of multidrug-resistant bacteria, and the resultant bacteremia could pose therapeutic challenges.

During the present COVID-19 pandemic, the focus of research should include the determinants of bacteremia in the hospital setting. In recent times, some of the preventive interventions that were implemented for reducing the transmission of SARS-CoV-2 could contribute to the reduction of BSI in the hospital setting. These include hygiene practices in the hospital, hand sterilization, use of masks and other personal protective equipment, social distancing, and limiting the number of people attending the hospital.

In our study, we aim to study the difference in prevalence proportion of BSI during the pre-lockdown period of the

COVID pandemic and the lockdown/post-lockdown period at a tertiary cancer hospital in India.

Objectives

1. To analyze the proportion of hospital-acquired BSI among patients in a cancer center.
2. To assess the benefits of hand hygiene implemented during the period of COVID lockdown/post-lockdown in reducing such BSI.

Literature review

Table 1 lists the literature on BLSI which were reviewed in our study.

Methods

The retrospective cohort study was conducted on data from November 2020 to July 2021, among cancer patients admitted to Healthcare Global cancer center. Blood culture reports of patients presenting with symptoms of BSI were retrieved and analyzed in the Department of Preventive Oncology, Healthcare Global. The nationwide lockdown in India was announced from March 25, 2020, to May 31, 2020. Therefore, our data were stratified from pre-lockdown (Nov 2019 to March 24, 2020) and lockdown/post-lockdown (March 25, 2020, to July 2020) periods. Our premise included the indirect benefits of hand hygiene of healthcare personnel, masking, and distancing practices during lockdown/post-lockdown period on the type of BSI among cancer patients and their antibiotic sensitivity patterns. Blood cultures for diagnosis of BSI were collected based on the classical clinical and laboratory indicators. The WHO guideline^[9] was followed for assessing hand hygiene. In this study, we assessed the changing etiological trend, susceptibility pattern, and the benefits of COVID measures on the prevalence of BSI.

The episodes were analyzed based on the initial entry, and polymicrobial infections were considered as unique BSI for each etiological agent isolated from the blood culture. If the same organism caused multiple BSI events in a patient, then it was considered novel when occurring at least 30 days after the previous positive blood culture. The origin time for BSI was set at 48 hours after hospital admission.

Culture

A quantity of 10 mL of blood was collected either from the peripheral vein or any other port. This was filled to a blood culture bottle with prefilled media, procured from BioMérieux. The green color bottles were for adults and the yellow-colored ones were for the pediatric age group. The samples were loaded to the automated blood processing system called BacT/ALERT 3D.

Table 1. List of reviewed literature on BLSI

S. No.	Author/place of study	Study design and sample size	Salient findings	Culture and sensitivity
1	Pandey et al. ^[1] / Nepal	1089 blood cultures	12.6% were bacteriologically positive, Salmonella serotypes were detected in 42.7%, Klebsiella pneumoniae in 19.5%, and Staphylococcus aureus in 15.9%	Gram-negative bacilli (GNB) showed a lower degree of resistance to Amikacin and Ofloxacin and Gram-positive isolates were sensitive to Amikacin, Oxacillin, and Vancomycin
2	Mudshingkar et al. ^[3] / Pune	12 553 blood cultures	13.1% of samples sent for blood culture were positive, predominant bacteria include Gram-negative organisms (Enterobacteriaceae), and Pseudomonas and Acinetobacter were emerging pathogens	Effective antimicrobials against Gram-negative bacteria include Carbapenems and aminoglycosides; for Gram-positive cocci, Vancomycin and Linezolid. During the 4-year period, the prevalence of extended spectrum beta lactamases (ESBL) increased from 61.6% to 66%, Carbapenemase producers from 13.6% to 25%, MRSA from 50% to 60%, and Amp C producers from 69% to 71%
3	Bhat et al. ^[4] / Mangalore	638 cancer patients were diagnosed with an infection	21.9% patients had culture-positive isolates, 36.3% were due to BSI, 69.9% were GNB, and 30.1% were Gram-positive cocci	Among Gram-negative organisms, antibiotic resistance reported to Fluoroquinolones, aminoglycosides, and third-generation Cephalosporins was 45.13%, 39.2%, and 48.58%, respectively. 26.9% of organisms were resistant to all three antibiotics. 11.6% were resistant to β -lactam/ β -lactamase inhibitor concentration. 22.2% were resistant to Carbapenems. 50.4% of Klebsiella species and Escherichia coli produced ESBL. 50% of Staphylococcus species were Methicillin resistant, but all were sensitive to Vancomycin
4	Cataldo et al. ^[5] / Rome, Italy	57 patients in ICU	49% had BSI.	Common agents isolated include Enterococcus species (39.3%), Pseudomonas species (28.6%), and Candida species (17.9%) 2/10 Enterococcus faecium isolates were resistant to Vancomycin. 4/10 Pseudomonas species were resistant to Piperacillin/Tazobactam. 2/6 Enterobacterales produced ESBL
5	Ruiz-Giardin et al. ^[6] / Madrid, Spain	1866 cases with BSI	285 catheter-related bacteremia patients, 77.19% with central and 22.81% with peripheral catheters. Coagulase-negative Staphylococci was the most frequent organism [central (64.1%), peripheral (40.6%)] followed by S. aureus [central (23.4%) and peripheral (9.5%)] and Enterobacteria species [central (15.6%) and peripheral (6.3%)]	

Table 1. CONT.

S. No.	Author/place of study	Study design and sample size	Salient findings	Culture and sensitivity
6	Gasparini et al. ^[7] / Italy	73 patients, with 36 pre-COVID and 47 post-COVID cultures	55.4% cultures reported multidrug resistant (MDR) bacteria. E. coli was the main MDR bacterium. In MDR-infected patients, in-hospital mortality was 37.5% in pre-COVID and 68.8% in post-COVID patients	
7	Giacobbe et al. ^[8] / Italy	78 critically ill COVID patients were included with 45 episodes of ICU-acquired BSI registered in 31 patients	Incidence rate of 47 BSI episodes (95% CI: 35–63) per 1000 patient-days at risk. Estimated cumulative risk of developing at least one BSI episode was ~25% after 15 days at risk and ~50% after 30 days at risk	Incidence rate of BSI was high, and the cumulative risk of developing BSI increased with ICU stay

Sensitivity

In bottles with growth, a preliminary Gram stain was done to identify the probable organism. The organism was extracted through aseptic precautions and inoculated to blood agar and MacConkey agar plates. After overnight incubation at 37 °C, any growth was processed using Vitek strips for identification and sensitivity. The automated Vitek@Compact system provided the results of sensitivity.

Data analysis was done using R i386 4.0.3 software. Categorical data were represented by frequency and percentage. A comparison was done using the proportion test/Fisher's exact test. A value of $p < 0.05$ was considered significant.

Results

As shown in Table 2, during the pre-lockdown period, the proportion of BSI among patients admitted to our Oncology setting was 21.63% when compared with 21.09% during the lockdown/post-lockdown period.

The small difference in the proportion of culture positivity between pre- and post-lockdown periods was not significant ($p=0.8634$).

Table 3 depicts the distribution of bacterial pathogens in the blood culture during the pre-lockdown and post-lock-

down periods. The most prevalent isolates include *E. coli* (23.8%), *K. pneumoniae* (17.8%), and *S. epidermidis* (10.9%).

The various isolates as per their Gram staining status are depicted in Table 4. During the pre-lockdown and lockdown/post-lockdown periods, there is a modest difference in proportion between each group of organisms: Gram-positive (34.7% vs 36.2%), Gram-negative (64.4% vs 58.6%), and fungus (0.9% vs 5.2%).

Table 5 shows the antibiotic resistance (100-sensitivity) pattern to the most prevalent isolates during the year 2020. Of the 1436 blood samples analyzed during 2020, 19% tested positive ($n=267$). The Gram-negative organisms showed greater (>50%) resistance to the Ciprofloxacin and Cephalosporin group of drugs. From the available data for Gram-positive organisms, >60% showed resistance to Gentamicin and Ciprofloxacin drugs.

Table 6 shows the resistance pattern of the four isolates stratified by the pre- and post-lockdown periods. A Chi-squared test was performed for testing the significance of the difference between two proportions (from independent samples). For the four isolates, the Chi-squared test of significance for the difference between proportions showed a significant difference in the resistance pattern to various antibiotics during the post-lockdown period when compared with the pre-lockdown period.

Table 2. Association of hand hygiene with culture positivity

	Pre-lockdown (<80% hand hygiene)		Post-lockdown (≥80% hand hygiene)	
	Count	%	Count	%
Culture positivity	101	21.63	58	21.09
Culture negativity	366	78.37	217	78.91
Total blood culture drawn	467		275	

Table 3. Distribution of bacterial pathogens in blood culture

Organism	Pre-lockdown		Post-lockdown	
	n	%	n	%
<i>Escherichia coli</i>	24	23.8	12	20.7
<i>Klebsiella pneumonia</i>	18	17.8	9	15.5
<i>Ralstonia mannitolilytica</i>	5	5	8	13.8
<i>Staphylococcus epidermidis</i>	11	10.9	7	12.1
<i>Staphylococcus haemolyticus</i>	5	5	9	15.5
<i>Burkholderia cepacia</i>	4	4	1	0.01
<i>Enterobacter cloacae</i>	4	4	1	0.01
Others*	30	29.7	11	19
Total	101	100	58	100

*Others include *Pseudomonas aeruginosa*, *Klebsiella oxytoca*, *Staphylococcus lentus*, *Proteus mirabilis*, *Candida tropicalis*, *Enterococcus faecalis*, *Streptococcus mutans*, *Streptococcus mitis*, *Acinetobacter baumannii*, *Enterococcus faecium*, *Staphylococcus aureus*, *Staphylococcus hominis*, *Streptococcus pneumoniae*, *Enterobacter faecalis*, *Candida parapsilosis*, *Staphylococcus warneri*, and *Candida famata*.

The difference in culture positivity of organisms based on their Gram staining status is depicted in Figure 1. However, Fischer's exact test does not show a significant difference in the prevalence of these organisms during the pre-lockdown and post-lockdown periods ($p=0.2987$).

Table 4. Bacterial pathogens with their Gram staining status

Organism	Gram staining	Pre-lockdown	Post-lockdown
<i>Staphylococcus epidermidis</i>	Gram-positive	11	7
<i>Staphylococcus haemolyticus</i>		5	9
<i>Staphylococcus aureus</i>		4	1
<i>Streptococcus pneumoniae</i>		2	0
<i>Staphylococcus capitis</i>		2	0
<i>Staphylococcus lentus</i>		1	0
<i>Enterococcus faecalis</i>		2	1
<i>Streptococcus mutans</i>		1	0
<i>Streptococcus mitis</i>		2	0
<i>Enterococcus faecium</i>		2	0
<i>Staphylococcus hominis</i>		3	2
<i>Staphylococcus warneri</i>		0	1
<i>Enterobacter cloacae</i>		Gram-negative	4
<i>Escherichia coli</i>	24		12
<i>Pseudomonas aeruginosa</i>	4		2
<i>Burkholderia cepacia</i>	4		1
<i>Klebsiella oxytoca</i>	1		0
<i>Proteus mirabilis</i>	1	0	
<i>Klebsiella pneumonia</i>	18	9	
<i>Acinetobacter baumannii</i>	2	1	
<i>Ralstonia mannitolilytica</i>	5	8	
<i>Enterobacter faecalis</i>	2	0	
<i>Candida tropicalis</i>	Fungus	1	0
<i>Candida parapsilosis</i>		0	2
<i>Candida famata</i>		0	1
Total		101	58

Discussion

Among immunocompetent adults, evidence shows that community-acquired BSI is characterized by drug-susceptible bacteria and healthcare-associated BSI^[10] is a result of multidrug resistant (MDR) strains. The key for improving BSI outcomes includes early initiation of antibiotic therapy (following examination of samples) based on the available guidelines. For therapeutic management of BSI, appropriate therapy should be ideally administered within 6 h of the onset of symptoms preferably within the first critical hour.^[2] Serial levels of biomarkers such as procalcitonin and C-reactive protein will differentiate infective sepsis from noninfective forms, as well as determine the effectiveness of the intervention.

Some of the factors influencing BSI include prolonged duration of admission, immunocompromised status of the patient, pathogens in the bloodstream acquiring virulence status, and prevention measures directed toward the control of infection. In our study, the key reason for the higher prevalence (21.63%) of BSI during the pre-lockdown peri-

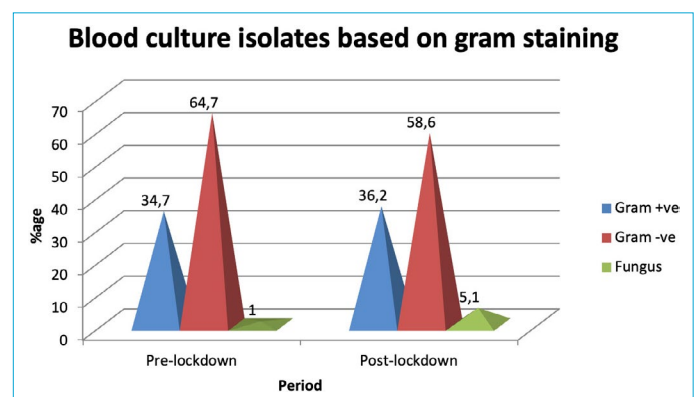
**Figure 1.** Gram stain of blood culture isolates.

Table 5. Resistance pattern of the most prevalent isolates during 2020

Antimicrobial drug	<i>Escherichia coli</i> % resistant	<i>Klebsiella pneumoniae</i> % resistant	<i>Staphylococcus epidermidis</i> % resistant	<i>Staphylococcus haemolyticus</i> % resistant
Amikacin	15	40		
Gentamicin	34	40	62	77
Ciprofloxacin	85	65	75	86
Piperacillin/Tazobactam	51	42		
Ceftriaxone	83	65		
Ceftazidime	95	98		
Cefepime	78	53		
Polymyxin				
Tigecycline	2	53	0	5
Imipenem	27	42		
Meropenem	29	40		
Ertapenem	100	100		

od was the lower adherence to infection control and prevention measures. The small difference in the proportion of culture positives observed in our study between the pre-lockdown (21.63%) and lockdown/post-lockdown periods (21.09%) did not show a significant association with the difference in hand hygiene during the two periods (<80% and ≥80%). One of the frequent causes of BSI is catheter related, which results in morbidity, increased hospital stay, and healthcare costs. Evidence^[6] shows that although the usage of peripheral catheters is relatively higher, the rate of bacteremia related to peripheral catheters is lower than those due to central catheters.

Blood culture of the specimen is the commonly used diagnostic method, along with an assessment of the antibiotic sensitivity pattern. However, the sensitivity of some of these culture-based tools is variable. Some of the nonculture techniques such as combined detection of mannan and anti-mannan antibodies, D-glucan detection, and other molecular techniques are characterized by lack of standardization and moderate levels of sensitivity and specificity.^[2]

The proportion of culture positives during the pre-lockdown (Nov 2019 to March 24, 2020) and post-lockdown periods (March 25, 2020, to July 2020) are 21.7% and 21.1%, respectively. In Pandey et al.'s^[1] study, 12.6% of the blood cultures were bacteriologically positive. Mudshingkar et al.,^[3] Bhat et al.,^[4] and Cataldo et al.^[5] showed a culture positivity rate of 13.1%, 21.9%, and 49%, respectively. A study by Gasperini et al.^[7] shows that during the post-COVID period, the prevalence of BSI was 34%, which was significantly more than the pre-COVID period (13.9%, $p=0.036$).

In our study, *E. coli* (23.8%), *Staphylococcus epidermidis* (10.9%), and *Klebsiella pneumoniae* (17.8%) were the most common BSI during the pre-lockdown period. A similar analysis during the post-lockdown period shows a higher prevalence

of *E. coli* (20.7%), *Staphylococcus haemolyticus* (12.1%), and *K. pneumoniae* (15.5%). In Pandey et al.'s^[1] study, *Salmonella* serotypes were detected in 42.7%, *K. pneumoniae* in 19.5%, and *S. aureus* in 15.9%. In Mudshingkar et al.'s^[3] study, the predominant bacteria include Gram-negative organisms (Enterobacteriaceae), and the emerging pathogens include *Pseudomonas* and *Acinetobacter*.

Gasperini et al.'s^[7] study on blood culture infections also report that *E. coli* was the most prevalent (38.6%) organism, with the rate rising from 36.1% during the pre-COVID period to 40.4% during the post-COVID period. Ruiz-Giardin et al.'s^[6] study on catheter-related bacteremia patients reports that coagulase-negative *Staphylococci* was the most frequent organism [central (64.1%) and peripheral (40.6%)], followed by *S. aureus* [central (23.4%) and peripheral (9.5%)] and Enterobacteria species [central (15.6%) and peripheral (6.3%)]. In Cataldo et al.'s^[5] study, the most common agents isolated include Enterococcus species (39.3%), *Pseudomonas* species (28.6%), and *Candida* species (17.9%).

In our study, out of the 159 blood culture-positive specimens, 99 were Gram-negative (62.3%), 56 were Gram-positive bacteria (35.2%), and 4 were fungal organisms (2.5%). Bhat et al.'s^[4] study on BSI reports that 69.9% were Gram-negative bacilli (GNB) and 30.1% were Gram-positive cocci. Among cancer patients, evidence from developed countries shows a ~70% incidence of infections due to Gram-positive bacteria,^[4] unlike in developing countries which report a high incidence of Gram-negative infections. This difference could be because of the varied usage of antimicrobial prophylactic regimens among neutropenic patients and the duration of indwelling catheters and devices across various healthcare settings. Evidence shows that patients are more susceptible to MDR microorganisms in ICU settings than in medical wards.^[7]

Table 6. Resistance pattern of the isolates stratified by the pre- and post-lockdown periods

Anti-microbial drug	Escherichia coli % resistant		Klebsiella pneumoniae % resistant		Staphylococcus epidermidis % resistant		Staphylococcus haemolyticus % resistant	
	Pre-lockdown	Post-lockdown	Pre-lockdown	Post-lockdown	Pre-lockdown	Post-lockdown	Pre-lockdown	Post-lockdown
Amikacin	9.7	9	14.8*	50*	-	-	-	-
Gentamicin	12.9*	54.5*	14.8*	43.75*	50	-	33.3	-
Ciprofloxacin	67.7*	100*	96.3*	81.25*	80	-	100	-
Piperacillin/Tazobactam	35.5*	63.6*	22.22*	50*	-	-	-	-
Ceftriaxone	60.7*	100*	44.44*	87.5*	-	-	-	-
Ceftazidime	62.5	-	42.8	-	-	-	-	-
Cefepime	51.6*	100*	23.04*	81.25*	-	-	-	-
Tigecycline	0	0	14.8	0	30*	71.42*	60	45.45
Imipenem	12.9*	45.4*	18.51*	50*	-	-	-	-
Meropenem	12.9*	36.4*	14.8*	50*	-	-	-	-
Erythromycin	-	-	-	-	100	100	83.3*	100*
Clindamycin	-	-	-	-	90*	42.85*	71.4	83.33
Linezolid	-	-	-	-	40*	71.42*	66.6*	83.33*
Teicoplanin	-	-	-	-	70*	50*	57.14*	83.33*
Vancomycin	-	-	-	-	30*	85.71*	57.14*	100*
High-level gentamycin	-	-	-	-	00	28.71	00	00

*Statistically significant (p<0.05).

Ruiz-Giardin et al.^[6] report that bacteraemias due to central catheters were more frequent when compared to peripheral catheters (77.19% vs 22.81%). The peripheral catheters are changed every 48–72 h because the risk of phlebitis is high on the second or third day of catheter insertion and stabilizes thereafter. Giacobbe et al.^[8] report a high incidence rate of ICU-acquired BSI among critically ill patients with COVID-19, and the cumulative risk of contracting a BSI increased with the duration of ICU stay. The study^[8] found an independent association between receiving anti-inflammatory agents and developing an episode of BSI.

The first-line antibiotics include Ampicillin, Gentamicin, and Cefuroxime. The extended-spectrum Cephalosporins include Ceftriaxone. In our study, the organisms showed a greater proportion of resistance (>50%) to Gentamicin, Ciprofloxacin, Tigecycline, and Cephalosporin group of drugs. Among the four major isolates (*E. coli*, *K. pneumoniae*, *S. epidermidis*, and *S. haemolyticus*), a significant difference in the proportion of resistance for various antibiotics (Table 6) was found between the post-lockdown and pre-lockdown periods. The ability of microbes for evolving mechanisms for antimicrobial resistance has been facilitated during Covid period, possibly due to the sustained exposure to disinfectants and non-pharmacological agents. The concept of MDR includes nonsusceptibility to at least one agent in three or more antimicrobial categories.^[7] This resistance could be due to the presence of extended spectrum beta lactamases (ESBL), Methicillin-resistance, and production of Carbapenemase. One of the known risk factors for MDR GNB infection includes previous use of antimicrobials, especially resistance concerning Cephalosporins, Fluoroquinolones, and Carbapenems.

Gasperini et al.^[7] study reports that ~55.4% of cultures reported MDR infections. The most prevalent MDR bacteria include ESBL producing bacteria, which was 41.7% during pre-COVID compared with 38.3% in the post-COVID period. In MDR infections, more than one antibiotic was used (48.6% vs 66.7%). Since the past few decades,^[11] *K. pneumoniae* is recognized as a leading cause of hospital-acquired infections. This organism tends to accumulate and transfer the determinants of drug resistance. Leal et al.^[11]

study reports that 28.7% of patients with BSI were due to MDR pathogens. This study^[11] reports a 74% prevalence of resistance genes among *K. pneumoniae* microbial species. The resistance shown by *K. pneumoniae* was 52% for Cephalosporins and 10% for Carbapenems. *A. baumannii* showed a resistance of 66.7% for both Cephalosporins and Carbapenems, and 83.4% for Sulfamethoxazole/Trimethoprim. This study^[11] also documented that ~50% of isolates from community-acquired infections presented with β -lactamase genes, which indicates their spread outside of the hospital environment.

The misuse of antibiotics is the root cause of resistance, which could be mapped with an antibiogram. The inappropriate usage of broad-spectrum antibiotics for non-severe COVID-19 infection could result in the development of MDR bacteria, as accumulated evidence shows that only a small proportion of Covid-19 patients suffered from bacterial co-infections (7% hospitalized and 14% patients admitted to mixed ward/ICU setting).^[12] However, 70-97% of hospitalized Covid-19 patients received antibiotic therapy. Initially, the treatment guidelines for COVID patients from the Centers for Disease Control and Prevention (CDC) did not recommend the use of antibiotics.^[13] Prescribing narrow spectrum and pathogen-specific antibacterial agents can mitigate some drawbacks of the broad spectrum antibiotics, which includes antimicrobial resistance (among both pathogenic and non-pathogenic commensals) and detrimental effect on the host microbiome. The resistance genes can persist among non-pathogenic bacteria, and over the years are potentially transferred to pathogenic bacteria. Disruption of host microbiome is detrimental to its vital functions such as synthesis of vitamins, supply of nutrients and protection from pathogens. In addition to the rise in antibiotic resistance, many studies have noted a change in the pattern of microbial pathogens in the hospital environment. Within the hospital environment, resistant microbes could be transmissible among vulnerable patients. It is imperative for customizing the antimicrobial stewardship strategies as per the geographic location. The impact of the COVID pandemic on antimicrobial resistance needs to be further elucidated.

Limitations of the study

- Among cancer patients with suspicion of infection, only those with positive cultures were included in the study. We did not study the characteristics of other patients, among whom the blood culture was negative.
- This study was performed in a tertiary care center, which provides healthcare to cancer patients. However, the BSI events among cancer patients may not simulate the prevalence among all hospitalized patients.

Conclusion

In our study, we assessed hospitalized cancer patients by comparing the proportion of BSI during the COVID pre-lockdown period and the lockdown/post-lockdown period. Oncology settings are characterized by the wide usage of indwelling catheters. Early reports suggest that ~70% of COVID patients were treated with antibiotics, although bacterial superinfection was detected only among 10% of such patients. Given the changing patterns of antimicrobial usage and the increasing rates of resistance, there is a compelling need to formulate an antibiotic policy according to the local susceptibility pattern and effective implementation of the same. It is alarming to note the emerging trend of resistance among Gram-negative organisms toward routine empirical therapy. Thus, it is imperative to use narrow-spectrum antibiotics in clinical practice based on the culture reports.

Some measures to prevent BSI include training of health-care staff, barrier precautions for cancer patients on central/peripheral lines, and aseptic measures while inserting the central venous catheter through the skin of the patient. Some innovations which are being tried include medicated catheter-lock solutions, sponge dressings coated with Chlorhexidine, and antibiotic-impregnated central venous catheters. The findings from our study will facilitate the prognosis of cancer patients with BSI and enable the prudent use of antibiotics.

Disclosures

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4. Dr.Priyank Tripathi, Clinical Pharmacist, HCG, KR Road, Bangalore.

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References

1. Pandey S, Raza S, Bhatta CP. The aetiology of the blood-stream infections in the patients who presented to a tertiary care teaching hospital in kathmandu, Nepal. *J Clin Diagn Res* 2013;7:638–41.

2. Bharadwaj R, Kapila K. Blood stream infections. *BioMed Research International* 2014;2014:515273.
3. Mudshingkar SS, Palewar M, Dohe V, Bharadwaj RS. Blood stream infections: Changing trends in etiology and susceptibility pattern. *IJID* 2016;45:106.
4. Bhat S, Muthunatarajan S, Mulki SS, Bhat KA, Kotian KH. Bacterial infection among cancer patients: Analysis of Isolates and Antibiotic sensitivity pattern. *Int J Microbiol* 2021;2021:8883700.
5. Cataldo MA, Tetaj N, Selleri M, Marchioni L, Capone A, Caraffa E, et al; INMICOVID-19 Co-infection Group. Incidence of bacterial and fungal bloodstream infections in COVID-19 patients in intensive care: An alarming "collateral effect". *J Glob Antimicrob Resist* 2020;23:290–1.
6. Ruiz-Giardin JM, Ochoa Chamorro I, Velázquez Ríos L, Jaqueti Aroca J, García Arata MI, SanMartín López JV, et al. Blood stream infections associated with central and peripheral venous catheters. *BMC Infect Dis* 2019;19:841.
7. Gasperini B, Cherubini A, Lucarelli M, Espinosa E, Prospero E. Multidrug-resistant bacterial infections in geriatric hospitalized patients before and after the COVID-19 outbreak: results from a retrospective observational study in two geriatric wards. *Antibiotics (Basel)* 2021;10:95.
8. Giacobbe DR, Battaglini D, Ball L, Brunetti I, Bruzzone B, Codda G, et al. Bloodstream infections in critically ill patients with COVID-19. *Eur J Clin Invest* 2020;50:e13319.
9. WHO. Observation form. Available at: https://www.who.int/gpsc/5may/Observation_Form.doc. Accessed Feb 17, 2021.
10. Timsit JF, Ruppe E, Barbier F, Tabah A, Bassetti M. Bloodstream infections in critically ill patients: an expert statement. *Intensive Care Med* 2020;46:266–84.
11. Leal HF, Azevedo J, Silva GEO, Amorim AML, de Roma LRC, Arraes ACP, et al. Bloodstream infections caused by multidrug-resistant gram-negative bacteria: epidemiological, clinical and microbiological features. *BMC Infect Dis* 2019;19:609.
12. Pelfrene E, Botgros R, Cavaleri M. Antimicrobial multidrug resistance in the era of Covid-19: a forgotten plight? *Antimicrobial resistance & infection control* 2021;10(21). <https://doi.org/10.1186/s13756-021-00893-z>.
13. NIH COVID-19 treatment guidelines. Available at: [covid19treatmentguidelines.nih.gov](https://www.covid19treatmentguidelines.nih.gov), last accessed on 20th Oct 2021.