ORIGINAL ARTICLE

Reversing the Trend of Antimicrobial Resistance in ICU: Role of Antimicrobial and Diagnostic Stewardship

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Abstract

Background: Increasing antimicrobial resistance (AMR) among common bacteria combined with the slow development of new antibiotics has posed a challenge to clinicians.

Aim and objective: To demonstrate whether antimicrobial and diagnostic stewardship program (ASP and DSP)-related interventions improve antibiotic susceptibilities among common bacteria causing bloodstream infections (BSI) in patients admitted to the intensive care unit (ICU) and whether these resulted in changes in the volume of antimicrobial consumption.

Materials and methods: We compared the susceptibility patterns of gram-negative bacteria (GNB) and gram-positive cocci (GPC) causing BSI and changes in the volume of antibiotics prescribed for the same before and after 2017 by a retrospective analysis.

Results: Postintervention, there was increased susceptibility of all GNBs to aminoglycosides; *Escherichia coli* and *Klebsiella* spp. to beta-lactambeta-lactamase inhibitors (BLBLI) combinations; and *Klebsiella* spp. and *Pseudomonas* spp. to carbapenems. *Acinetobacter* spp., *Klebsiella* spp., and *Pseudomonas* spp. showed improved susceptibility to doxycycline, whereas *E. coli* and *Klebsiella* spp. showed significantly improved susceptibility to fluoroquinolones. Among GPCs, there was increased susceptibility of *Staphylococcus aureus* (levofloxacin, clindamycin, and aminoglycoside), coagulase-negative *S. aureus* (CoNS) (chloramphenicol, levofloxacin, clindamycin, and aminoglycoside), and enterococci (chloramphenicol, levofloxacin, and clindamycin). There was a significant reduction in usage of antimicrobials for the treatment of GPCs (linezolid, doxycycline, chloramphenicol, levofloxacin, BLBLI, macrolide, and cephalosporin) and GNBs (levofloxacin, cephalosporin, carbapenem, and colistin), which caused BSI.

Conclusion: The present study illustrated that combined ASP and DSP interventions successfully reversed the resistance pattern of organisms causing BSI and resulted in a reduction in antibiotic utilization.

Keywords: Antibiotic stewardship, Antimicrobial consumption, Antimicrobial resistance, Carbapenem, Colistin, Gram-negative bacteria, Gram-positive organisms.

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Introduction

Increasing antimicrobial resistance (AMR) among the common bacterial pathogens has become an enormous global concern. The World Health Organization in its October 2020 bulletin reemphasized that AMR is one of the top 10 global public health threats facing humanity.[1] The cost of AMR to the economy is huge and affects it in multiple ways—protracted illness leading to prolonged intensive care unit (ICU) and hospital stays, need for expensive antimicrobial agents and those with enhanced toxicities, financial challenges for the family, and finally, leading to disability and death. The crisis created by AMR became all the more worrisome as the development of new antibiotics has slowed down considerably over the past decades with the emergence of resistance to older as well as newer generations of antibiotics due to injudicious use and increasing hetero resistance among microrganisms.[2]

Antimicrobial stewardship (ASP) has been defined as "coordinated interventions designed to improve and measure the appropriate use of antimicrobials by promoting the selection of the optimal antimicrobial drug regimen, dose, duration of therapy, and route of administration."[2] The results of implementing ASP had been mixed. On one hand, ASP had been associated with improved antibiotic prescribing behavior, significant reductions in total antibiotic use, reduced drug costs, and shorter hospitalizations;[4-6] there were also reports of increasing resistance.[7] In Ireland, it was reported that in spite of 20 years of ASP, there had been a steady increase in antibiotic prescribing and consumption over the past 10 years, with rising AMR, including the advent of carbapenamase-producing Enterobacteriacae (CRE).[8] In a review article published recently, the authors pointed out that there were scant data on ASPs in low- and medium-income countries and deserve urgent attention.[9]

Among the different areas in a hospital, like outpatient departments, wards, and ICUs, the latter poses the gravest AMR

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challenge to the clinicians. Many ICUs became sinks for multidrug-resistant (MDR) pathogens, as they are the final destination of patients with treatment failure due to AMR.[2] Moreover, empiric regimens are continued too long or too broadly, inadvertently ending up selecting the resistant pathogen they were intended to treat.[2] In addition to the high incidence of AMR among patients admitted to ICUs, they also provide a defined population of "patients and bacterial isolates" in a confined setting, with high rates of infection (thus higher numbers of clinical isolates to evaluate) and high rates of antibiotic use.[6] ICU demands consideration of various factors unique from those in other areas of the hospital. Two important barriers to a successful ASP in ICUs are diagnostic uncertainty and fear among intensivists of not adequately covering the causative pathogen(s), particularly, in septic shock. These lead to empirical therapy, often prolonged. Both these barriers may be surmounted by accurate and earlier diagnosis.[2]

Implementing diagnostic stewardship (DSP) has a definite role as it envisages the right test for the right patient, generating accurate, clinically relevant results at the right time to optimally influence clinical care and to conserve health-care resources.[10]

We hypothesized that implementation of practices incorporating the principles of ASP and DSP would lead to the reversal of the pattern of AMR among common bacteria isolated from those suffering from bloodstream infection (BSI), which in turn will entail the reduction in the volume of antibiotics used.

The aim of the study was to carry out a retrospective analysis to demonstrate whether ASP- and DSP-related interventions improve antibiotic susceptibility among common organisms causing BSI in patients admitted to ICU. Also, we looked into changes in the volume of antimicrobial consumption following ASP- and DSP-related interventions.

Materials and Methods

The present study is a hospital-based retrospective, cohort study of patients admitted to ICU with bacterial BSI between January 1, 2015, and December 31, 2019. Waiver of consent was approved by the Institute Ethical Committee (IEC 48/20 dated April 20, 2020). Our health-care center is a 500bedded tertiary referral center. As a result, the hospital receives patients, both directly from the community and transferred from other hospitals in the region. All positive blood cultures with recognized bacterial pathogens among patients who were hospitalized in our 14-bedded ICU during the study period were included in the analysis. BSI was defined by positive blood cultures in a patient with systemic signs of infection and may be either secondary to a documented source or primary—that is, without an identified origin.[11]

The present study was divided into two phases; before and during November 2017 when very few or no intervention was implemented, and after November 2017 when we implemented several ASP- and DSP-related interventions.

ASP measures adopted include nominating full-time intensivist for ICU patients, installing electronic medical records (EMR), regular audit and feedback, optimization of dose and duration of antibiotics, educational and reinforcement programs for judicious use of antibiotics, developing protocol for empirical therapy based on local antibiograms, and combined ICU rounds by intensivists and microbiologists. Bundle approach to minimize central line-associated BSI was strictly enforced.[12] Other measures included hands-on training of resident doctors and nurses regarding hand hygiene, sample collection, and biomedical waste disposal.

DSP was implemented in a phased manner. From 2017 onward, blood culture samples were processed using VersaTREK (TREK Diagnostics System, California, USA), and from June 2019 onward in BacTALERT (BioMérieux, France) automated system; before that manual, only blood culture processing was done. Bacterial identification and disk diffusion testing for antimicrobial susceptibility were being done using conventional biochemical tests or disk diffusion method and were performed using VITEK II (BioMérieux, France) from 2017 onward, and antibiotic susceptibility reports with minimum inhibitory concentration (MIC) and breakpoints were initiated. From May 2019 onward, MALDI-TOF (BioMérieux, France) was used for the identification of organisms.[13,14]

Antibiotic susceptibilities were performed using Clinical and Laboratory Standards Institute (CLSI) guidelines with breakpoints as mentioned for respective years.[15] The MIC was promptly communicated to the ICU faculty in charge. Subsequently, annual antibiograms constructed were analyzed for any change in the pattern of antibiotic resistance.

The antimicrobials prescribed by intensivists were purchased from the hospital pharmacy, the record of which is maintained by an inbuilt pharmacy hospital information system (HIS). Data were collected from pharmacy stock regarding prescription, purchase, or consumption of antibiotics in the two phases; using pharmacy prescription uploaded in HIS, units of particular antimicrobials prescribed by an intensivist and its dosage were extracted from the pharmacy portal and evaluated for any changes in antibiotic prescribing habits in ICU.

Data Entry and Statistical Analysis

The data generated in this retrospective study were subjected for analysis with the help of appropriate statistical tools and the interpretation of significant outcome using IBM SPSS (Statistical Package for the Social Sciences) version 21.0. In cases where there were multiple blood cultures positive with the same pathogen, only the first positive blood culture was included in this study. Standard descriptive statistics were calculated for categorical (in percentage) and continuous variables (median and interquartile, interquartile range). *p* value was calculated using the chi-square test for a row-by-column contingency table with appropriate degrees of freedom. $p < 0.05$ was considered statistically significant.

Results

Table 1 shows the characteristics of the study that include the total number of blood samples received in the microbiology laboratory from patients with suspected BSI from ICU, the number of samples that tested positive for BSI, age, and gender of the patients, annually from 2015 to 2019. There has been a gradual increase in the number of cases enrolled every year, due to an increase in the patient population attending this tertiary care hospital.

Table 2 shows the microbiological etiology of BSI. We found that *Acinetobacter* spp. were the commonest bacteria in 2015 and 2016, whereas *Staphylococcus aureus* was the commonest organism in 2017. In 2018 and 2019, *Klebsiella pneumoniae* was the commonest organism detected in the blood. The important thing to note here is that initially (i.e., in years 2015–16) to counteract extended-spectrum beta-lactamase-producing (ESBL) organisms and *Acinetobacter* spp., there was more use of carbapenem group of drugs, as a result, due to selection pressure, there came a surge in cases of CRE, which explains the rise of *K. pneumoniae* in later years.

Table 1: Characteristics of the clinical study

Year	*2015*	*2016*	*2017*	*2018*	*2019*
Total number of blood culture received	188	365	871	957	1492
Total number of cultures positive for BSI	85	51	94	98	158
Age (years), median (IQR)	56 (50–62)	58 (54–62)	60 (53–67)	59 (52–66)	62 (50–74)
Female sex, n (%)	44 (51%)	26 (51%)	49 (52%)	43 (44%)	67 (42%)

Table 2: Etiology of bacterial BSIs

Pathogen	*2015*	*2016*	*2017*	*2018*	*2019*
Gram-negative bacilli					
Enterobacteriaceae					
Enterobacter species	11%	5%	5%	9%	3%
Escherichia coli	18%	11%	12%	13%	14%
Klebsiella species	10%	8%	17%	18%	25%
Proteus species	9%	10%	7%	7%	6%
Providencia species	6%	9%	4%	6%	4%
Salmonella species	0%	0%	0%	0%	0%
Serratia species	0.5%	1%	0%	0%	1%
Non-Enterobacteriaceae					
Acinetobacter species	23%	22%	15%	17%	17%
Aeromonas species	0.5%	0%	0%	0%	0%
Burkholderia species	0%	0%	0%	0%	0%
Stenotrophomonas species	0%	1%	0%	1%	2%
Pseudomonas aeruginosa	10%	10%	11%	12%	13%
Gram-positive cocci					
Enterococcus species	1%	2%	3%	2%	2%
Staphylococcus species	11%	21%	25%	15%	12%
Streptococcus species	0%	0%	1%	0%	0%

Table 3 shows the change in susceptibility of gram-negative bacteria (GNB) to the antimicrobials between pre- and postintervention. There was increased susceptibility for most antibiotics in all the common GNBs (*Acinetobacter* spp., *Escherichia coli*, *K. pneumoniae,* and *Pseudomonas aeruginosa*) postintervention compared to preintervention. The increase was significant for aminoglycosides for all GNBs, for beta-lactambeta-lactamase inhibitors (BLBLI) (like piperacillintazobactam and cefoperazonesulbactam) in *E. coli*, *Klebsiella,* and *Pseudomonas*. *Klebsiella* spp. and *Pseudomonas* spp. also showed a significant increase in susceptibility to carbapenems. *Acinetobacter*, *Klebsiella,* and *Pseudomonas* showed improved susceptibility to doxycycline, whereas *E. coli* and *Klebsiella* showed significantly improved susceptibility to fluoroquinolones.

Table 4 shows the change in susceptibility of common gram-positive cocci (GPC) to antimicrobials. There was increased susceptibility to all the common antimicrobials among GPCs like *S. aureus*, coagulase-negative *Staphylococcus* (CoNS), and *Enterococci*. The increase was significant in the case of *S. aureus* for levofloxacin, clindamycin, and aminoglycoside. For CoNS, there was a significant increase in susceptibility for chloramphenicol, levofloxacin, clindamycin, and aminoglycoside. *Enterococci (E. faecalis* and *E. faecium)* showed increased susceptibility for chloramphenicol, levofloxacin, and clindamycin.

Table 5A shows there was a significant reduction in usage of linezolid, doxycycline, chloramphenicol, levofloxacin, BLBLI, macrolide, and cephalosporin, whereas there was an increase in usage of aminoglycoside for treating BSI caused by GPCs.

Table 5B showed that there was a significant reduction in usage of levofloxacin, cephalosporin, carbapenem, and colistin.

Flowchart 1 shows schematically the decrease in turnaround time (TAT) of blood culture samples after the introduction of DSP. Earlier using conventional biochemical identifications and AST methods, laboratory TAT was 72 to 96 hours, which was significantly decreased to 24–48 hours once automated methods for identification and AST were being used.

Discussion

This is the first study, to our knowledge, which explored the combined role of implementation of ASP and DSP on changes in susceptibility patterns of common microorganisms and also the changes in volume of antibiotics prescribed or consumed.

India carries one of the largest burdens of drug-resistant pathogens worldwide and alarmingly high resistance among GNB and GPCs. India is also one of the largest consumers of antibiotics worldwide, and antibiotic sale continues to increase rapidly,

Table 3: Change in susceptibility of microorganisms to antimicrobials between pre- and postintervention periods for GNB

Organisms												
	Acinetobacter spp.			*Escherichia coli*			*Klebsiella spp.*			*Pseudomonas aeruginosa*		
Antimicrobial	*Pre*	*Post*	*p value*	*Pre*	*Post*	*p value*	*Pre*	*Post*	*p value*	*Pre*	*Post*	*p value*
Gentamicin	20%	35%	0.01*	28%	42%	0.03*	26%	41%	0.025*	24%	37%	0.04*
Piperacillintazobactam	10%	18%	0.1	15%	36%	0.009*	14%	29%	0.011*	9%	25%	0.003*
Imipenem	22%	34%	0.06	35%	47%	0.08	37%	58%	0.003*	27%	41%	0.03*
Ceftriaxone	5%	15%	0.02*	11%	33%	0.003*	9%	37%	0.001*	12%	34%	0.003*
Doxycycline	30%	45%	0.02*	56%	65%	0.19	53%	68%	0.03*	42%	58%	0.02*
Levofloxacin	33%	38%	0.46	30%	46%	0.02*	32%	51%	0.006*	36%	49%	0.06
Colistin	76%	83%	0.22	78%	92%	0.008*	75%	89%	0.01*	68%	75%	0.27

*Significance observed in antimicrobial susceptibility, in post-intervention period; *p* value was calculated using a paired *t*-test for a row-by-column contingency table with appropriate degrees of freedom. $p < 0.05$ was considered statistically significant

Table 4: Change in susceptibility of microorganisms to antimicrobials between pre- and postintervention periods for GPC

Organism												
	S. aureus			*CoNS*			*E. faecalis*			*E. faecium*		
Antimicrobial	*Pre*	*Post*	*p value*	*Pre*	*Post*	*p value*	*Pre*	*Post*	*p value*	*Pre*	*Post*	*p value*
Linezolid	98%	99%	0.6	98%	98%	1	98%	99%	0.6	97%	99%	0.3
Doxycycline	80%	78%	0.7	83%	77%	0.3	85%	82%	0.6	81%	76%	0.4
Chloramphenicol	55%	65%	0.15	50%	70%	0.04*	52%	70%	0.09*	51%	68%	0.01*
Levofloxacin	20%	36%	0.01*	21%	35%	0.03*	19%	37%	0.005*	19%	41%	0.009*
Clindamycin	18%	29%	0.07*	19%	31%	0.05*	21%	38%	0.009*	20%	35%	0.01*
Gentamicin	35%	53%	0.01*	31%	48%	0.01*	33%	39%	0.4	34%	37%	0.7

*Significant, *S. aureus: Staphylococcus aureus, CoNS: Coagulase-negative staphylococci, E. faecalis: Enterococcus faecalis*, and *E. faecium: Enterococcus faecium*; *p* value was calculated using a paired *t*-test for a row-by-column contingency table with appropriate degrees of freedom. *p* <0.05 was considered statistically significant

Table 5A: Change in antimicrobial consumption for BSI between pre- and postintervention in GPC causing BSI

		Gram-positive organisms		
		Number of prescribed units		
Antimicrobial	*Dose*	*Pre-ASP*	*Post-ASP*	*p value*
Linezolid	2 mg/mL	198	195	0.001*
Doxycycline	100 mg	810	748	0.0001*
Chloramphenicol	1 g	1091	686	0.021*
Gentamicin	40 mg/2 mL	151	164	0.001*
Levofloxacin	25 mg/mL	706	415	0.03*
Piperacillintazobactam	4.5 g	761	462	0.01*
Azithromycin	500 mg	1150	660	0.007*
Ceftriaxone	1 g	670	481	0.001*

*Significant decrease in prescription units after initiation of MIC-based antimicrobial therapy

Table 5B: Change in antimicrobial consumption for BSI between pre- and post-intervention in GNB causing BSI

		Gram-negative organisms		
		Number of prescribed units		
Antimicrobial	*Dose*	*Pre-ASP*	*Post-ASP*	*p value*
Doxycycline	100 mg	802	542	0.07
Gentamicin	40 mg/2 mL	564	421	0.05
Levofloxacin	25 mg/mL	547	443	0.008*
Piperacillintazobactam	4.5 g	761	457	0.07
Ceftriaxone	1 g	670	342	0.01*
Imipenem	1 g	944	683	0.04*
Colistin	3 MIU	382	210	0.02*

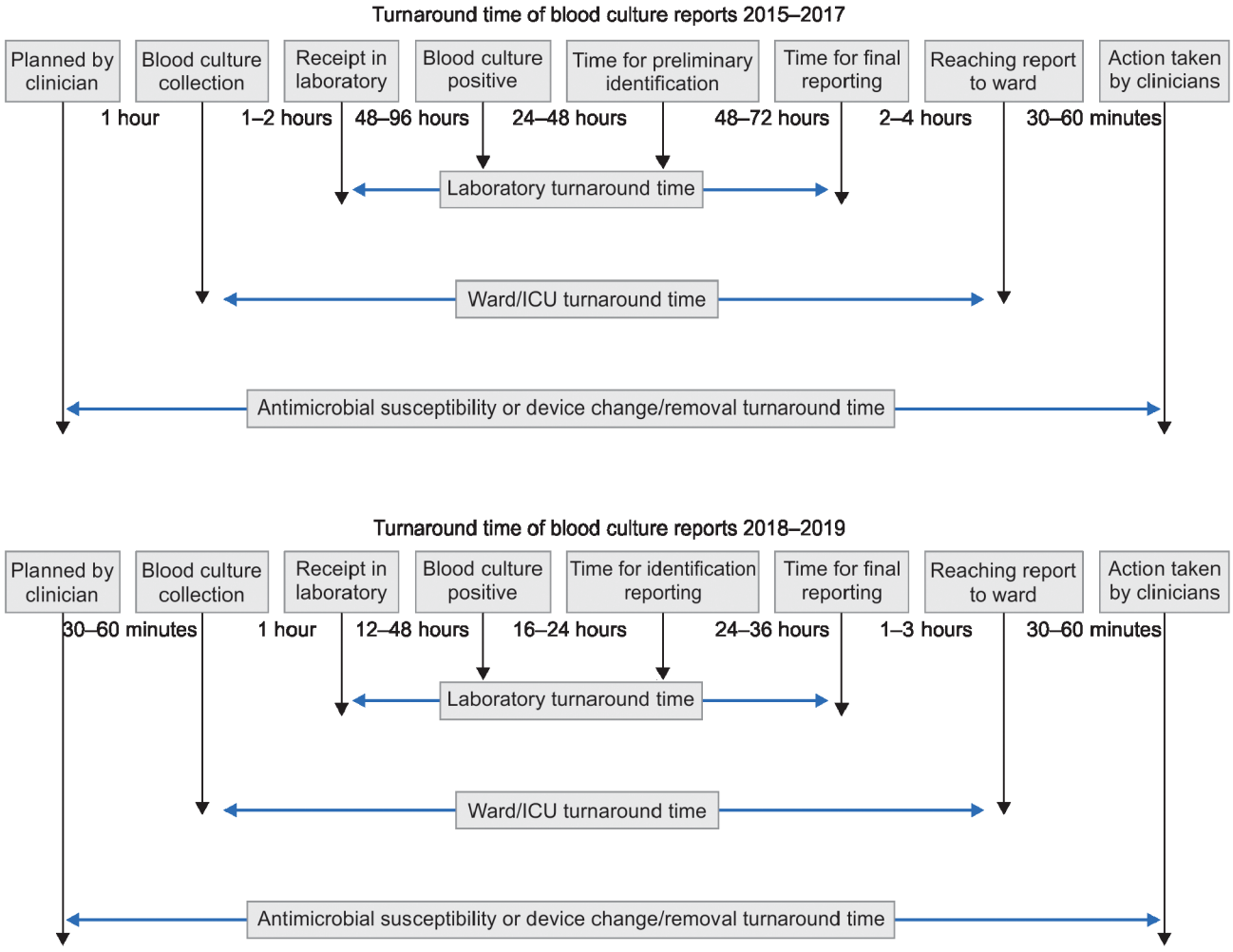
*Significant decline was noted in the prescription of antimicrobials for GNB causing BSI; Data were collected from pharmacy stock regarding purchase or consumption of antibiotics in the two phases; using pharmacy prescription uploaded in HIS, and units of particular antimicrobials prescribed by an intensivist, and its dosage was extracted from the pharmacy portal and evaluated for any changes in antibiotic prescribing habits in ICU.
p value was calculated using the Chi-square test for a row-by-column contingency table with appropriate degrees of freedom. p <0.05 was considered statistically significant

despite a decline in the incidence of communicable diseases.[16] In spite of this, there are very few published studies from India that evaluate the role of ASP on AMR of common microbes and on the consumption of antibiotics.

In a retrospective study published in 2012 from India, the impact of ASP activities on the prevalence of CRE in the hospital was investigated. Authors reported that the incidence of CRE *E. coli* dropped from 3.7 to 1.6%, whereas CRE *Klebsiella* spp. reduced from 6 to 3.6%. ESBL-producing *E. coli* rate increased from 70 to 82%, while for ESBL *Klebsiella* spp., the rate reduced from 80 to 75%. The average usage of carbapenem group of antibiotics reduced from 955 vials to 745 vials.[17] In a recent prospective cohort study carried out over 18 months involving two ICUs of a tertiary care hospital, infectious diseases (ID) physicians reviewed all prescriptions and gave alternate recommendations if the antibiotic use was inappropriate. Antimicrobial use decreased from 831.5 to 717 days of therapy per 1,000 (<0.000) patient days. De-escalation according to culture sensitivity improved significantly. They found that 73.3% of antibiotic prescriptions were inappropriate indicating that an effective inpatient ASP would make a substantial impact.[18] They used a consultative-based stewardship, which would be difficult to implement in most Indian hospitals because of the lack of ID specialists.[19] Moreover, the authors did not investigate changes in resistance patterns as a result of the ASP program. In another recent study, the authors reported a decrease in the mean monthly cost of consumption of restricted antibiotics and a decreasing trend of defined daily dose of colistin.[20] Our study, spanning over a period of over 5 years, examined the change in resistance patterns of a number of GPCs as well as GNBs to several commonly used antibiotics, including colistin.

Adoption of an EMR can improve ASP by providing a centralized location for microbiology results and other relevant clinical data.[21] Absence of EMR had been recognized as one of the barriers to an effective ASP.[22] Multidisciplinary rounds with guideline-based antibiotic recommendations for specific infections have been found to decrease the use and duration of both broad-spectrum and high-end, reserve antibiotics.[23] Since there is a paucity of ID specialists, medical microbiologists play an important role in promoting DSP and supporting common tracking and reporting practices, and making hospital antibiograms.[19] Thus, we believe the combined rounds of intensivists and microbiologists and collective decision taken (on basis of MIC obtained) to start appropriate treatment as well as de-escalation made a huge impact on the rational use of antibiotics in our study.

Flowchart 1: Comparative decrease in TAT before and after the introduction of ASP and DSP: (A) From 2015 to 2017; (B) From 2018 to 2019



The presence of a prompt microbiology laboratory, high level of understanding of ASP among staff, an easily accessible antibiogram, and established guidelines for empiric prescribing were identified as important facilitators of an effective ASP in a hospital.[22]

We chose BSI because it was associated with a 40–60% increase in the risk of mortality[24,25] and is considered one of the most devastating entity in ICU with far-reaching consequences, like a prolonged length of hospital stay, high cost to the family and exchequer, and in many instances, death. They represent 15% of all nosocomial infections.[26] It is important to initiate prompt and adequate antimicrobial therapy as it impacted mortality.[24,25]We found that *Acinetobacter* spp. were the commonest bacteria in 2015 and 2016, whereas *S. aureus* was the commonest organism in 2017. In 2018 and 2019, *Klebsiella* species were the commonest organism detected in blood (Table 2). The findings of our study compare well with those described in a recent study from a premier institute of India. The authors reported that the predominant pathogen in BSI was GNBs (*Acinetobacter* spp. being the commonest followed by *Klebsiella*) in 82% of cases with *S. aureus* being the most common pathogen among GPCs.[27]

Carbapenem resistance affects both nonfermenters and fermenters in all regions; however, the rates of carbapenem resistance were higher in nonfermenters than in fermenters. It has posed a huge challenge in the management of several types of life-threatening infections caused by nonfermenters because of the low permeability of the outer bacterial membrane to several antibiotics, including carbapenems.[28] In a recent report, it was found that *K. pneumonia* and *E. coli* were the most common CRE among Enterobacteriaceae. These CREs pose the greatest risk to public health because of their high prevalence, high potential for causing a wide range of clinical infections, coresistance to BL as well as other antimicrobial agents (such as aminoglycosides and fluoroquinolones).[29] The present study showed that there was significantly improved sensitivity of *Klebsiella* spp. and *Pseudomonas aeruginosa* (a nonfermenter) to not only carbapenems but also cephalosporins, BLBLI combinations, aminoglycosides, and doxycycline, thus, reversing the trend prevalent worldwide (Table 3). Significant improvement in susceptibility of *Pseudomonas* spp. to imipenem and gentamycin was reported after intervention with ASP-related measures by others too.[6]

Polymyxin E or colistin was withdrawn from clinical use in mid-1970s, on account of its adverse effects, particularly, nephrotoxicity and neurotoxicity. It reemerged in mid-1990s, as a last resort treatment against MDR and extended drug-resistant GNBs.[30] With

time, the overuse and misuse of these last resort drugs have also led to the emergence of colistin-resistant bacteria.[31] The results of our study showed that there was significantly increased sensitivity of *E. coli* and *Klebsiella* spp. and nonsignificant increase in sensitivity of *Acinetobacter* spp. and *P. aeruginosa* to colistin (Table 3).

The high prevalence of resistance of GPC to several commonly used antimicrobials (Table 2) may be ascribed to increasing incidence of community-associated methicillin-resistant *S. aureus* (CA-MRSA) in causing infections in the hospitals, thus, fading the distinction between CA-MRSA and healthcare-associated MRSA. There had been reports of outbreaks of infections caused by CA-MRSA and also reports of CA-MRSA-associated BSI in significant numbers.[32]

There was a significant reduction in consumption of linezolid, doxycycline, aminoglycoside, levofloxacin, macrolide, and cephalosporin for management of BSI caused by GPCs (Table 5A). We found that there was a significant reduction in usage of levofloxacin, cephalosporin, carbapenem, and colistin, whereas there was an increase in usage of aminoglycoside for treating BSI caused by GNBs. (Table 5B). Several previous studies had reported that ASP had positively impacted the antibiotic utilization and susceptibilities.[4,5,17,18,20,33] In the present study, it is not only the ASP intervention that played a vital role, but DSP too. DSP was the first step toward the effective implementation of ASP. With the advent of automated machines, the culture and antibiotic sensitivity result can be available 24–48 hours earlier than the usual conventional and manual techniques. Diminished TAT gave an advantage to intensivist for prompt and appropriate action including de-escalation and removal or change of central line where possible. It was proved that rapid diagnostics only improve clinical outcomes if they are accompanied by stewardship teams that properly interpret results and apply them to treatment decisions.[34]

Limitations of the Study

We understand that the present study suffers from several limitations. This is the experience of the ICU of a single center. We did not differentiate primary from secondary BSI. Two years postintervention is a short time, and it needs to be seen whether the benefit accrued will sustain over a longer time. We have reported only the total number of organisms and not the BSI episodes. Study of BSI episodes classified into community- and hospital-acquired BSIs would have led to a more comprehensive analysis. In spite of these limitations, the present study definitely adds to the scanty data on the implementation of ASP and DSP in India.

Conclusion

The present study illustrates that effectively implemented ASP and DSP interventions can help in successfully controlling and reversing the AMR in gram-negative and gram-positive organisms associated with BSI in an ICU setup and also result in a reduction in antibiotic prescription or consumption. The study further emphasizes building and strengthening of other components, such as information technology in monitoring and surveillance, use of automated methods and sensitizing staff, and broadening the role of different staff members to develop an effective team.

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