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Original Research Article

Impact of antibiotic stewardship program on usage of higher range of antibiotics in patients of intensive care units in a tertiary care hospital, India

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ABSTRACT

Background: The aim of the study was to monitor the changes in antimicrobial use after implementation of Antibiotic Stewardship Programmed (ASP) and pattern of use of antimicrobials in the respective ICU's.
Methods: The study was conducted in three ICU's Adult ICU(AICU), Paediatric ICU (PICU), Neonatal ICU (NICU) -Six bedded each) over a period of six months from September 2018 to February 2019 in a tertiary care hospital. Antibiotics monitored over total 155 patients and antibiotics selected for the study are β-lactam inhibitors, Carbapenem derivatives and Colistin
Results: Out of total 155 patients 51% were males and the definitive therapy (Implementation of antibiotics according to the antibiotic policy of the hospital) in the respective ICU's showed increase from 66.7% to 83.3% after implementation of ASP activity in that particular duration. Antibiotic consumption showed fluctuation in the whole duration of the study (p value <0.05).
Conclusions: Analysis of the study shows a positive impact on implementation of ASP programme in intensive care units, brought an effective increase in appropriate use of antimicrobials.

Keywords: Antimicrobial stewardship, Carbapenem derivatives, Colistin, β-lactam inhibitors, Intensive care units

INTRODUCTION

Due to emergence of antimicrobial resistance, a lot of organizations including the Society for Healthcare Epidemiology of America (SHEA), Infectious Disease Society of America (IDSA) and the American Society of Health System Pharmacists (ASHP) had identified that Antibiotic Stewardship Programmed (ASP) carries a vital role in health care environment now a days.[1,2] Antimicrobial stewardship is an emerging field deals with a series of strategies and interventions aimed for improving appropriate prescription of antibiotics in humans in all healthcare setting.[3] Now days, rising concerns about antimicrobial resistance and inadequate development of effective new anti-infective drugs have stimulated universal efforts to strengthen infection-control interventions and antimicrobial stewardship practices.[4,5] The Centres for Disease Control and Prevention (CDC) estimates more than two million people are infected with antibiotic-resistant organisms, resulting in approximately 23000 deaths annually and hence, promoting an efficient antimicrobial stewardship (AMS) program at all levels of healthcare is a global priority.[6]

Antimicrobial stewardship had been promoted for all hospitals to cope up with the challenges of emerging resistance to antibiotics.[7-9] As antimicrobial resistance results in increased morbidity, mortality, and cost of health care, the IDSA initially published guidelines whose main aim was to improve the usage of the antimicrobials in the hospitals in the year 1988.[10] Otherwise, the basic goals of every ASP are similar. It not only includes the attempt to reduce antimicrobial resistance rates, but also to preserve current antibiotics. ASPs also aim to improve patient outcomes, safety and reduce the financial costs associated with inappropriate antibiotic prescription.[11] Therefore, all healthcare services require having an antimicrobial stewardship program (ASP) in practice.[12]

Despite India's commitment to combat antimicrobial resistance by publishing the landmark document "Chennai declaration" reflects the various challenges to be faced - which includes problems like human resource, lack of information technology, higher priorities, lack of awareness, lack of education, misinterpretation of results, prescribing etiquette and medication errors, the consequences of which may increase morbidity, mortality and healthcare costs.[13,16] Antimicrobial consumption data, often reported in Defined Daily Dose (DDDs), but it does not provide a comprehensive analysis of prescribing or explain the reasons of the therapy or changes of therapy, which may result in the misinterpretation of data.[17,18]

Intensive Care Units (ICU) are the most frequently identifiable source of hospital acquired infections with several fold higher infection rates than general hospital wards. Patients admitted to the ICU are at a higher risk of developing hospital acquired infections. Widespread and injudicious use of broad spectrum antimicrobials in the ICUs has led to the emergence of several resistant strains of microbes which contributes significantly to raise the health care costs and also patient morbidity and mortality.[19-22] The present study is directed to achieve optimal use of antimicrobials (in the form of DDD & DOT) with minimal toxicity and other health care infections along with the auditing of the prescriptions – which is one of the key strategies to decrease the preventable health care associated infections.

METHODS

The study was conducted in three ICU's (AICU, PICU, NICU - Six bedded each) over a period of six months from September 2018 to February 2019 in a tertiary care hospital India. According to the inclusion criteria, patients admitted in the respected ICU's received Higher end antibiotics at least for one day had been counted and patients on lower antibiotics or higher end antibiotics for less than a one day had been excluded. Total 155 cases were included on basis of the factors like choice of drugs, dose, frequency, choice of antimicrobials, duration of therapy etc. The antibiotics monitored for the study are β-lactam inhibitors, Carbapenem derivatives and Colistin and the antibiotic usage was calculated by using the software's in the form of DOT/100 Patient days [DOT/100 bed days = Total dose in mg during the study / (DDD of drug × Study duration × bed strength × Average bed occupancy rate)].[23,24] Inclusion criteria of the study includes patients remained admitted in the ICU's for more than 48 hours, going through the higher range of antibiotics like β-lactam inhibitors, Carbapenem derivatives and Colistin individually or in combinations (Patients remained admitted in the ICU's going through some other antibiotics like Amikacin, Ceftriaxone etc. had been excluded from the study). In case of prescription auditing and formulary restriction, one reserved antibiotic usage form had been incorporated in the hospital - which is to be filled by the medical practitioners for each patient undergoing higher range of antibiotics with the proper clarification of using that.

Statistical analysis

Descriptive statistics were used for to find out frequency of different variables and rate of various antimicrobial agents used in Intensive care units (ICU's). Chi square tests were applied to check the antimicrobial pattern after implementation of ASP activity and the results found were statistically significant (p value < 0.05).[22]

RESULTS

Characteristics of patients admitted in ICU's

Out of total 155 cases admitted in ICU's having higher range of antibiotics in that particular period of time, 51% was reported in male patients (Figure 1) Gender wise distribution) and age wise distribution shows that 43% of total population belongs to the age range of >18 years followed by the 42% of cases having age range of 1 month to 18 years (Figure 2). Total 76% of patients were discharged from the ICU's out of 155 patients - where death rate and LAMA (Leave Against Medical Advice) were 22.6% and 1.4% respectively (Table 1).

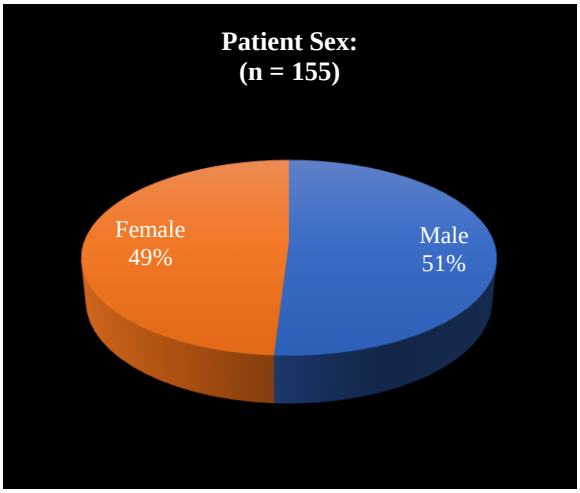

Figure 1: Gender wise distribution.

Impact of 'Empirical' vs 'definitive' therapy after implementation of ASP activity

In the initial two months of Sep - Oct 2018, 66.7% of total ICU patients had gone through the definitive antibiotic therapy (Antibiotics prescribed according to the antibiotic policy) - whereas the percentage of definitive therapy had been raised to 73.2% in the month of Nov-Dec 18 and sharp rise had been found in the month of Jan-Feb 2019 i.e. 83.3% after implementation of ASP activity in the respective ICU's (Table 2).

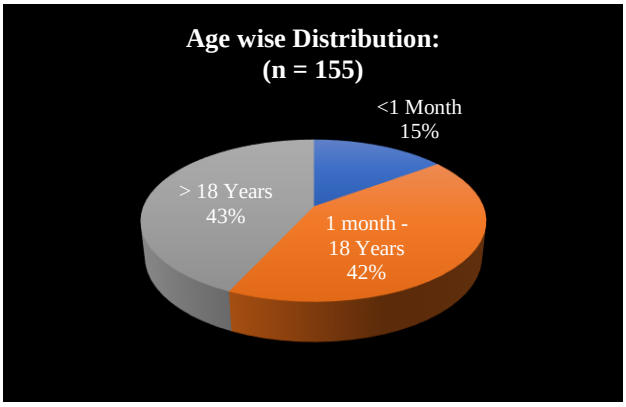

Figure 2: Age wise Distribution.

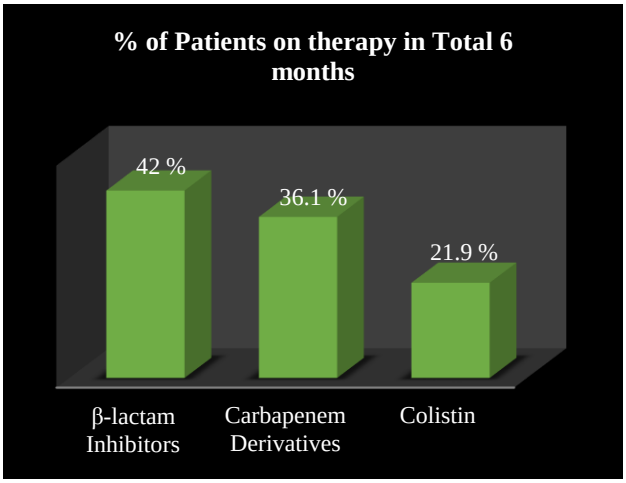

Figure 3: β-lactam inhibitors are the antimicrobials mostly used in the ICU's followed by the usage of carbapenem derivatives. Most of the patients had undergone combination of antimicrobials in the entire range of their ICU stay.

Restricted antibiotics used in ICU's

In the total study duration, 42% of total patients had undergone through β-lactam inhibitors followed by the 36.1% patients having carbapenem derivatives followed by 21.9% patients had received colistin (Figure 3). Most of the patients had undergone the combination of therapies in the six months of study period.

Table 1: Discharge wise patient distribution.

Discharge Details	Patient No	Percentage
Normal Discharge	118	76%
Death	35	22.6%
LAMA	2	1.4%

Antibiotic usage in the form of DOT/100 Patient days

Everyday data had been collected from the respective ICU's in terms of patients undergoing through the antibiotics (β-lactam Inhibitors, Carbapenem Derivatives and Colistin) and the daily data had been transcribed into the monthly sheet of DOT/100 patients by using ICMR automated software and finally DOT/100 patients data had been compared in monthly basis (Figure 4, Figure 5 and Figure 6).

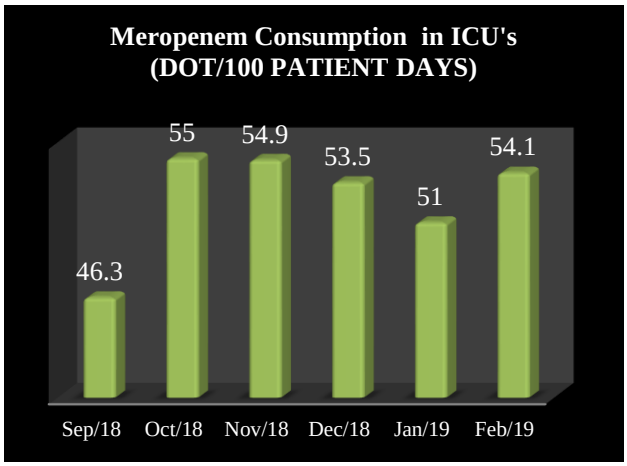

Figure 4: DOT/100 patient days for Meropenem shows a fluctuation of data – which is due to the number of severity of cases admitted in the ICU's in that particular duration.

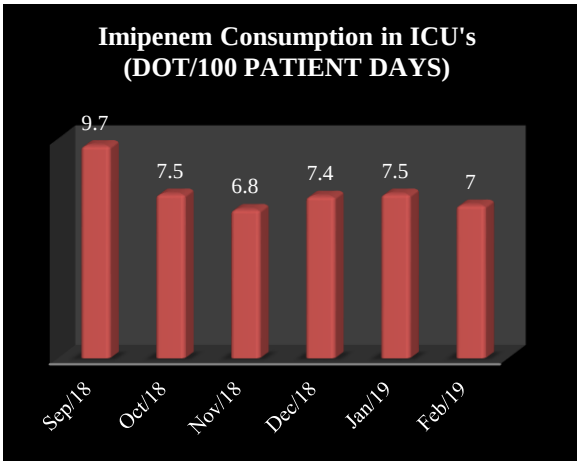

Figure 5: DOT/100 patient days for Imipenem shows a rapid fall in the month Oct-18 after implementation of ASP in the respective ICU's followed by the slight fluctuation in the consecutive months.

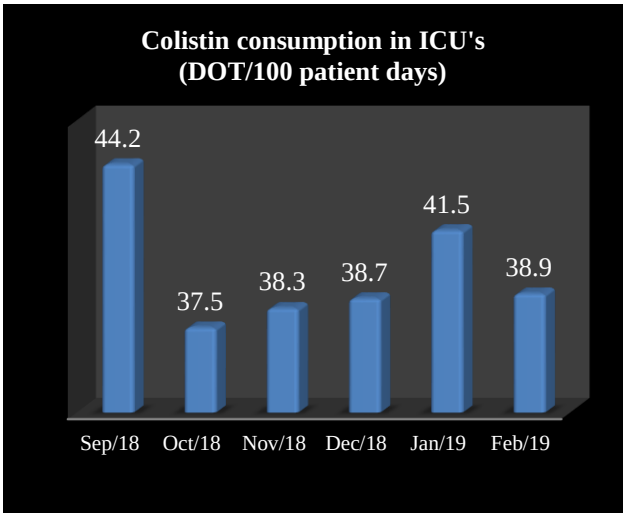

Figure 6: DOT/100 patient day's shows a drastic fall of usage of Colistin in the month of Oct 18 in respect to the Sep-18 – which is due to implementation of ASP activity in the ICU's. Slight fluctuation of data is due to the number of severity of cases admitted in the ICU's in that particular duration.

DISCUSSION

'Restricted antibiotics' are the antimicrobials responsible for development of Multi resistant organisms - which must be used according to the 'Antibiotic Policy' of that particular organization.[25] Its usage must be permitted after determining the infection, risk stratification in the patient and sending a sample for culture and sensitivity. In the literature review conducted by Patel MK et al, cephalosporins, metronidazole and penicillins were the most commonly prescribed antimicrobials in critical care unit of that particular organization.[26]

In the study of 2013, fluoroquinolones were prescribed in 8.8% and doxycycline was prescribed in 0.9% of prescriptions of Intensive Care Units.[27] Among the antimicrobial agents β-lactam antibiotics namely piperacillin+tazobactam (45%) and ceftriaxone (38%) were more commonly prescribed as seen in other studies.[28] Metronidazole was most commonly prescribed followed by ceftriaxone in a study conducted in Western Nepal.[29] But there might not be any rationality o compare utilization of each antimicrobial agent in the ICU's.

Table 2: Definitive and empirical therapy wise distribution.

Month of Study	Department	Definitive therapy	Empirical therapy	Total patients with definitive therapy (X)	Total patients with empirical Therapy (Y)	% of Definitive therapy [X / (X+Y)] *100 (According to antibiotic policy)
Sep-Oct 2018	AICU	22	9	44	22	66.7%
	PICU	14	8			
	NICU	8	5			
Nov-Dec 2018	AICU	15	4	30	11	73.2%
	PICU	11	4			
	NICU	4	3			
Jan-Feb 2019	AICU	21	1	40	8	83.3%
	PICU	11	5			
	NICU	8	2			

In the present study, gender distribution of the patients was almost same in case of male and females - whereas in respect to age distribution, 43.2% of total cases having in the adult and elder age group (>18 years). Normal discharge rate in the entire duration of the study was 76% in respect to the death rate of 22.6%. The Mean±SD of the stay duration of the patients receiving higher range of antibiotics were 5.4(±1.9), where lengths of stay were found shorter than 5.7 days per medical patient, shown in the study done by Williams A et al.[30]

Culture sensitivity tests were done in all (100%) the cases admitted to the ICU's-out of them more than 50% culture reports were found to be positive. In a study done by Banerjee T et al, microbiological investigations had been sent for only in 51.2% of the patients following admission to the ICU where majority of the cases (60/87) were culture positive.[31] Most of the times, patients admitting to the ICU's come from tertiary care centres after taking prior medications at the previous hospitals. Out of total 155 patients in ICU's where 42% β-lactam inhibitors were the highest prescribed, followed by Carbapenem derivatives of 36.1% and colistin was continued only on 21.9% of patients in the entire study duration. Entire calculation of Defined Daily Dose (DDD) and Duration of Therapy (DOT) had been calculated using the ICMR software.[26,32] The study conducted by Patel MK, reported piperacillin-tazobactam was the highest prescribed critical care unit - while cefoperazone-sulbactam (30.8%) were the most common prescribed in ICU in a study conducted by John LJ et al.[33]

According to the findings of the present study, Definitive therapy prescriptions had significantly improved from 66.7% to 83.3% in the entire duration of six months after implementation of ASP activity. The study conducted by Amer MR et al., the ASP implementation in medical ICU improved appropriateness of empirical antibiotics utilization from 30.6% to 100% in the proactive ASP arm.[34] DOT/100 patient days for Carbapenem derivatives and colistin show a fluctuation of data - which is due to the number of severity of cases admitted in the ICU's in that particular duration.

CONCLUSION

After implementation of Antimicrobial Stewardship Programme (ASP), unnecessary use of higher range of antibiotics had been prevented up to a great extent and definitive therapy prescriptions had shown a significant improvement from 66.7% to 83.3% in the entire duration study. A bit of fluctuation of antibiotic consumption had been noticed - which was due to the number of critical cases admitted in the phase of study. Overall in depth, analysis of the study shows a positive impact on implementation of ASP programme in intensive care units, brought an effective increase in appropriate use of antimicrobials.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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