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Stewardship Implementation in Intensive Care Unit in a Tertiary Care Unit and the Role of Clinical Pharmacist

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Abstract

We tried to analyse the stewardship interventions in a tertiary care hospital, optimize the antibiotic utility to combact the antibiotic resistance. Clinical pharmacists are trained and engaged in the stewardship management, they have an extensive role in optimizing the rationale use of antibiotics, combact the antibiotic resistance, implement interventions, prevent adverse drug events and improve the patient quality by decreasing the hospital costs and length of stay. As a result, rapid stewardship interventions by clinical pharmacist had significant outcomes.

Keywords: Clinical pharmacists; Antimicrobial stewardship; Intensive care unit; Multidrug resistance; Intervention; Antibiotics; ADR: Adverse Drug Reactions

Abbreviations

MDR: Multi Drug Resistance; ASO: Anti-Biotic Stewardship Programs; CRE: Carbapenem-Resistant Enterobacterales; CNS: Central Nervous System

Introduction

Antimicrobial resistance is the major concern worldwide, India is the hotspot for antimicrobial consumption with an increase in the number of infectious diseases [1]. Hence is crucial to restrict and rationalise the use of antimicrobials to prevent resistance, improve quality care and preserve the utility of last resort drugs available.

WHO defined the inappropriate usage of antimicrobial as; any prescribing antimicrobial agents without need or any improper dosage form, or short or long duration of treatment which usually leads to an increase in the risk of resistance [2].

Antibiotic resistance

The development of MDR gram-negative pathogens is multi factorial [3]. However, experience supports that improving the use of antibiotics in health care settings can play an important role in addressing antimicrobial resistance [4,5]. Although newly approved therapies for CRE infections have been associated with improved patient outcomes compared with older treatment options, their use requires close guidance from ASPs.

Antimicrobial stewardship pharmacists are uniquely positioned to help educate and provide guidance to optimize therapy [6]. It is essential to implement policies like antimicrobial stewardship not only to prevent the resistant strains but also to improve the clinical outcomes and preserve the antibiotic utility. Comprehensive education and resources on guidelines should be disseminated to clinicians to ensure compliance and optimal use in clinical practice [7].

Intensive care units

Various studies have illustrated that antibiotic utilization is maximum in the intensive care units with a wide range of antibiotics prescribed [8,9]. It is due to various factors like nosocomial hospital acquired illness, multiple previous hospitalizations, comorbidities and prescribing privileges of the physicians [10,11]. Although it is necessary to support the clinical judgment and condition of the patient, understanding drug utilization and prescribing factors helps us to achieve rational use, preserve antibiotic utility and also cost saving to the patient [12]. It is also prudent to analyse the local antibiogram, resistance patterns of the microorganisms periodically and modify the antibiotic prescribing patterns [13,14]. In our health care settings we tried to intensify the stewardship policies and recommendations to improve the antimicrobial prescribing patterns in accordance with the hospital's antibiotic policy [15-17].

Materials and Methods

Study design

It is a prospective study of 6 months carried out from September 2019 to February 2020. Both male and female patients of all age groups are taken into consideration. Pregnant and lactating women are not taken into consideration. A total of 531 patients are taken into consideration.

Study instrument

A standard clinical audit form is made which contains all the demographic details and clinical information and evidence for the selection of appropriate antimicrobial therapy.

Study process

List of restricted antibiotics is formulated based on the hospital antibiogram and antibiotic usage. Antibiotics included in this list can be released by the pharmacy for only forty hours after which a justification form for the restricted antibiotic is mandatory. The justification form is filled and signed by the prescribing doctor before the initiation of the antibiotics. It provides evidence for restricting the antibiotics and deters clinicians from prescribing restricted antimicrobials and results in de-escalation of antibiotics. Culture reports are evaluated (usually the culture results are available within 24 hours-48 hours after specimen collection) and the condition of the patient is discussed with the primary consultant. Clinical interventions are documented and discussed with the consultants and culture reports are examined to reassess the initial therapy prescribed and the selection of antibiotics is

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evaluated along with the patient's clinical condition and other clinical investigations. It is ensured that guidelines compliance treatment (rational therapy) is maintained, the duration of the drug and dosage is optimized accordingly.

Results

Patient demographics

The total of 531 patients in Intensive care units in a period of 6 months are considered (Table 1).

Culture sensitivity pattern

Blood and other specimens are collected and sent for microbiology assay and culture sensitivity patterns. The results are reported within forty eight hours of the specimen collection. A total of 489 samples were sent among which respiratory samples were highest with 50.93%. Among 489 samples 255 samples have reported microbial growth which included pathogens, colonisers or contaminents (Table 2).

Factors for prescribing antibiotics

Culture report was taken into consideration and infectious diseases diagnosis is made. Among the patients admitted in ICUS, the majority of the patients had been diagnosed with sepsis and septic shock (34.5%) with underlying comorbidities. The other conditions were lung infections 25.61% Intra Abdominal infections 8.47%, Meningitis and CNS infections 5.46%, RTA 5.46%, Urinary tract infections 4.51%, Immunocompromised with carcinoma and neutropenic sepsis 4.13%, Bloodstream infections 3.89%, Skin and soft tissue infections 2.44%, Bone and joint infections 2.25%, Bedsore infections 0.94% , cellulitis 1.88% (Figure 1).

Prescribing patterns of restricted antibiotics

We analysed a category of 18 antibiotics marked as restricted. A total of 1186 restricted antibiotics were prescribed for the above conditions. The average consumption of restricted antibiotics for a patient was 2. It is similar to the study done by Williams RM, et al. where in a mean (± SD) of 2.09 (± 1.27) antibiotics/prescription has been reported [15]. Study done by Hanssens Y, et al. reported an average of almost three antibiotics/prescription in MICU [18]. A study conducted in Southern India reported the mean of 1.60 (± 0.77) antibiotics/prescription which is lower than current study [19,20]. Meropenem (38.44%) consumption is highest among the restricted antibiotic usage in our study with empirical pssrescription of 84.64(%). Although carbapenem usage against nosocomial gram negative bacteria can be considered as an effective antibiotic therapy in life threatening conditions [21], the rampant emergence of carbapenem resistant enterobacteriaceae is worrisome [22]. It may limit the antibiotic therapy and furthermore worsen the patient's condition. Hence it is advisable to restrict the empiric usage of carbapenems to prevent the emergence of widespread carbapenemase producing enterobacteriaceae [23,24]. In our study we identify that meropenem was given empirically in 49 cases (56.97%) in 86 MDR cases which might be a major probability of development of multi drug resistant organisms [25,26]. The other restricted antibiotics prescribed are in Figure 2.

Multidrug resistant organisms

Out of 255 samples that reported microbial growth 33.72% had multidrug resistant organisms. Among them respiratory samples had 70.87% of multi drug resistant organisms. *Klebsiella pneumoniae* is the most common gram negative organism with multi drug resistance in our hospital settings with 44.66%.

Although multiple factors favours the development of multi drug resistant organisms [27,28]. The antibiotic resistance should be managed by the rationale antibiotic usage, other factors responsible for MDR's are older age, chronic pathologies, trauma, surgery and persistent infections which may cause acquired immune suppression that involves both innate and adaptive immunity [29,30] (Table 3).

Interventions

In a period of 6 months of 531 studied cases drug interventions were noticed in 116 cases (21.84%). The total number of drug interventions in 116 cases were 189 (61.37%). The average drug intervention observed per case is +/- 1.6. Stewardship interventions were accepted in 88 cases (75.86%) and not accepted in 28 cases (24.13%) (Tables 4 and 5).

S.No	Demographics	Total number of patients	Percentage
I	Age		
	0-20 years	45	8.47%
	20-40 years	92	17.32%
	40-60 years	177	33.33%
	60-80 years	198	37.28%
	80-100 years	19	3.57%
II	Gender		
	Male	342	64.40%
	Female	189	35.50%

Table 1: Patient demographics in percentage (%).

S.No	Lab cultures	Total number of patients	Percentage
I	Total cultures		
	Culture sent	489	92.09%
	Culture positive	255	52.14%
	No growth	234	47.85%
II	Culture samples		
	Respiratory samples	164	50.93%
	Blood samples	84	26.08%
	Urine samples	43	13.35%
	Fluid samples	24	7.45%
	CSF cultures	5	1.55%
	Clostridium difficle	2	0.62%

Table 2: Culture sensitivity patterns in percentage (%).

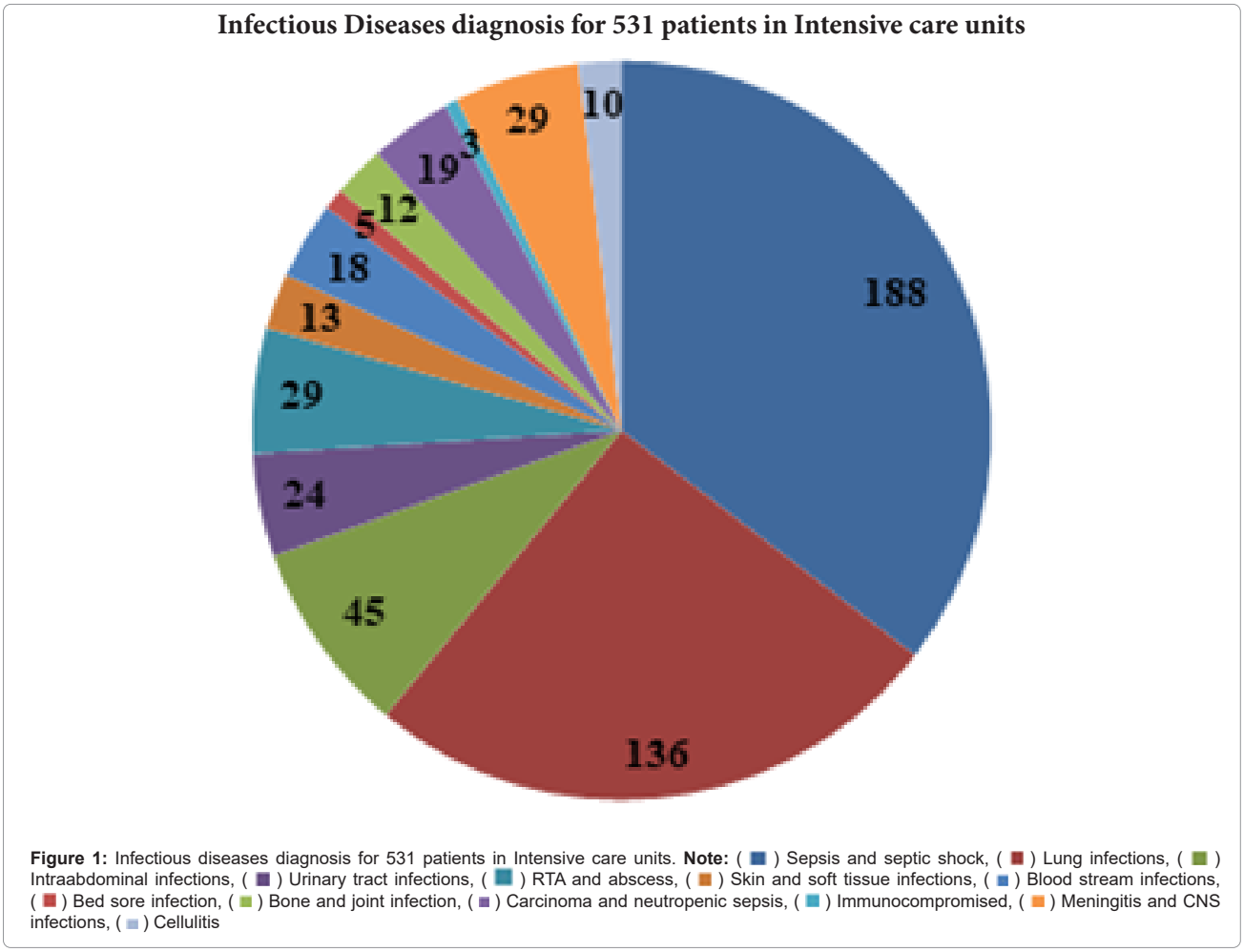

Figure 1: Infectious diseases diagnosis for 531 patients in Intensive care units. **Note:** ( ) Sepsis and septic shock, ( ) Lung infections, ( ) Intraabdominal infections, ( ) Urinary tract infections, ( ) RTA and abscess, ( ) Skin and soft tissue infections, ( ) Blood stream infections, ( ) Bed sore infection, ( ) Bone and joint infection, ( ) Carcinoma and neutropenic sepsis, ( ) Immunocompromised, ( ) Meningitis and CNS infections, ( ) Cellulitis

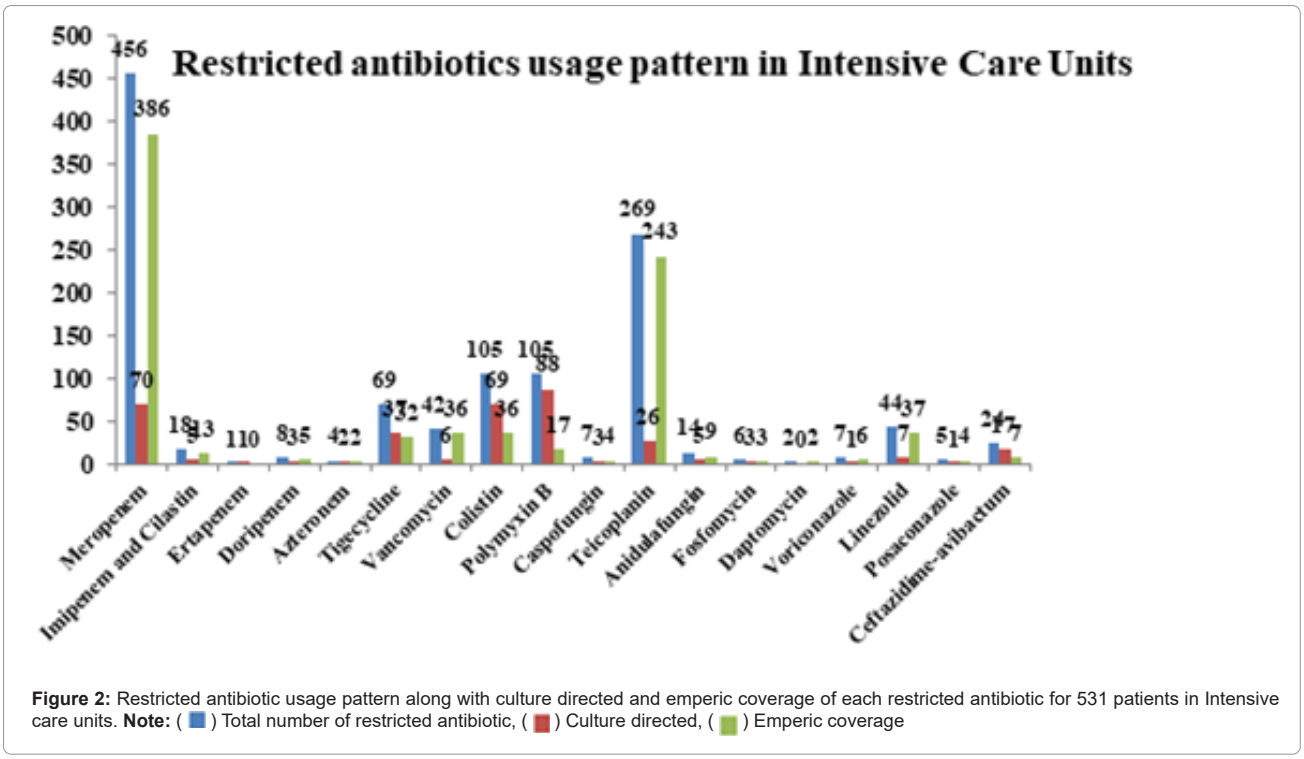

Figure 2: Restricted antibiotic usage pattern along with culture directed and emperic coverage of each restricted antibiotic for 531 patients in Intensive care units. **Note:** ( ) Total number of restricted antibiotic, ( ) Culture directed, ( ) Emperic coverage

Mdr samples and micro organisms	No of sample	Percentage
Sample		
Respiratory samples	73	70.87%
Blood samples	13	12.62%
Urine samples	6	5.82%
Fluid samples	9	8.73%
CSF cultures	2	1.94%
Organism type		
Acinetobacter	34	33%
Klebsiella pneumoniae	46	44.66%
Serratia	1	0.97%
Pseudomonas aeruginosa	11	10.67%
Gram negative bacilli	2	1.94%
E.coli	6	5.82%
Enterobacter	3	2.91%

Table 3: MDR samples and organisms in percentage (%).

Intervention characteristics	Total percentages among interventions	Accepted percentages
De-escalation	35.97%	94.10%
Escalation	11.10%	71.40%
Dose adjustment	7.40%	100%
Prolonged duration	2.60%	20%
Wrong indication	20.60%	51.10%
Dual coverage	15.30%	44.80%
Drug interaction	2.10%	100%
ADR	4.70%	100%

Table 4: Intervention characteristics among interventions in percentage (%).

Outcome parameters	Accepted cases	Not accepted cases
Improved	60.22%	21.42%
Readmitted (within 30 days of admissions)	0.45%	17.85%
LAMA	13.63%	32.14%
Death	21.59%	28.57%

Table 5: Study of outcome measures of stewardship intervention.

Discussion

It is evident from our study that in spite of widespread awareness of antibiotic resistance, physicians continue to prolong the duration of therapy for greater than 14 days in the absence of infection parameter [31], dual coverage of antibiotics is widely practised which is not advisable [32], Use of multiple drugs active against anaerobes is not necessary and puts the patients at risk for additional drug toxicities [33]. No data or guidelines support the use of two anti anaerobic drugs in clinical practice [34]. Dual coverage de-escalation were accepted in only 15.3% commonly observed dual coverage include: Carbapenems and metronidazole (dual anaerobic) clindamycin and teicoplanin (dual MRSA coverage), linezolid and clindamycin (dual GPC, dual anaerobic coverage). However rapid de escalation was observed in 94.1% and escalation of organism specific antibiotics was observed in 71.4%.

Conclusion

In conclusion, the implementation of antimicrobial stewardship by clinical pharmacist significantly reduced antimicrobial use and improved the patient outcomes. Hence there is a requirement of antimicrobial stewardship program in Intensive care units to reduce the emerging antibiotic resistance and for a better patient outcome. Life threatening adverse drug reactions and drug-drug interactions are carefully observed and notified. ADR intervention acceptance rate is 100%, drug-drug interactions were analysed and necessary substitution of the other category of drug or time gap between the administration of the drugs is maintained.

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