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ASSESSMENT AND EVALUATION OF PRESCRIBING PATTERN OF ANTIMICROBIAL AGENTSIN INTENSIVE CARE UNIT OF TERTIARY CARE HOSPITAL

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ABSTRACT

A prospective observational study was conducted to find out prescription pattern of antimicrobial agents (AMA) and its sensitivity pattern in the different intensive care units (ICUs). This study was done at Apollo Hospital International Limited, Ahmedabad by analyzing the prescription and laboratory reports of the patients admitted to the ICUs over a period of six months (October, 2021 to March, 2022). Cephalosporins class (21.43%) and Carbapenem class (16.46%) were commonly prescribed followed by Antifungals (10.40%), Metronidazole (7.45%), Glycopeptide class (6.99%). Prescription pattern of different ICUs hadbeen analyzed. 46.8% patients were prescribed more than two antimicrobial agents. Of the various pathogenic organism isolated, Gram-negative bacteria constituted for 85% (n=99) andGram-positive bacteria constituted for 15% (n=17). Fungal growth had seen in 24 samples consisting candida species (92%) and one sample detected Aspergillus species as well as Rhizopus species. Candida species were sensitive against Amphotericin B, Caspofungin and Flucytosine. Klebsiella Species was found to be most sensitive to Daptomycin, Doxycycline, Linezolid, Moxifloxacin, Glycopeptides, Colistin and Tigecycline and least sensitive to Penicillin, Macrolides and Rifampicin. Acinobacter species and Escheria coli was sensitive toColistin and Tigecycline, while Pseudomonas Species was found to be sensitive to Fosfomycin and Colistin. Enterococcus species was sensitive to Colistin, Daptomycin, Glycopeptides, Netilimycin, and Tigecycline while least sensitive to Penicillin, Cephalosporins and Carbapenem groups. Staphylococcus species was found to be sensitive to Daptomycin, Doxycycline, Glycopeptide, Moxifloxacin, and Linezolid. Need of improving

the prescribing habits through rational prescription is necessary.

KEYWORDS: Antimicrobial Agents, Sensitivity pattern, Intensive care unit, Prescription pattern monitoring studies.

INTRODUCTION

Anti-Microbials are agents that help to reduce the possibility of infection, sepsis, or other illnesses that are caused by harmful microorganisms. The burden of bacterial infections is larger than expected in the healthcare industry. Irrational use of antimicrobial agents could potentially cause antimicrobial resistance amongst the patients, in addition, to increased cost of treatment, adverse effects, and patient mortality, making it a much harder health burden to manage.[1]

Anti-microbials are the most prescribed medications to patients when admitted to the Intensive Care Unit. Bacterial infections are a big problem that is badly underestimated in today's healthcare system. Inappropriate use of antimicrobial agents (AMAs) can lead to antibiotic resistance, which can be detrimental to patients. Furthermore, the field of antimicrobials is constantly developing and introducing new medications, necessitating extensive investigations on their use, effectiveness, and adverse effects.[1] The current study focuses on the prescribing patterns of AMAs in an intensive care unit patient.

Essential elements, here, are to monitor antimicrobial usage and improvement in the knowledge of prescription habits. These strategies are recommended to control resistance to antimicrobials in hospitalized patients.[2] Unnecessary usage of antibiotics can be reduced by monitoring the prescription pattern of antibiotics.[3]

The development of antibiotic-resistant bacteria is a serious problem around the globe, so it's critical to use antibiotics appropriately. Antimicrobial resistance (AMR) develops when bacteria, viruses, fungi, and parasites evolve over time and lose their ability to respond to antibiotics, making infections more difficult to treat and raising the risk of disease transmission, severe illness, and death. Antibiotics and other antimicrobial medications become ineffective as a result of drug resistance, and illnesses become more difficult or impossible to treat.[4]

A thorough understanding of the microorganisms' local susceptibility patterns would allow for a more appropriate and evidence-based antibiotic selection. The goal of this study was to look at the clinical outcomes and in-vitro responses of bacterial isolates to locally accessible and widely prescribed antibiotics in hospitalized individuals.[5]

MATERIALS AND METHODS

Study Size and Population

The study was a prospective, observational study carried out over 6 months from October 2021 to March 2022. This study was conducted at Apollo International Hospital, Bhat, Gandhinagar, India. This hospital provides primary and specialized health care facilities to people in and around Gandhinagar. Patients who are willing to participate in the study with age >18 years of either gender were included. This study excluded patients who are not willing to participate inthe study, pregnant or breast-feeding or lactation women.

Data collection

Patients who were admitted in hospital premise in different wards were screened based on the inclusion and exclusive criteria. Subjects who met the inclusive criteria were enrolled for the study. Informed consent was obtained from the patients. Demographic details, final diagnosis, co-morbid condition, date of admission, days in ICU, current therapy, laboratory reports were documented in data collection form. The data collection form also includes WHO prescribing indicator were also documented on the basis of medication prescribed by the physician.

Ethical consideration

The study was started after obtaining clearance from the institutional ethics committee. All the information collected from the patients were strictly used only in research purpose and confidentiality was maintained.

Statistical Analysis and Interpretation

All the statistical analysis were performed using Microsoft excel 2016. Data were entered into Excel (version 2016). Descriptive statistics of socio-demographic and clinical variables included percentage, sum and mean.

RESULT

During study period total 250 patients were evaluated, consisting 145 (58%) male patient and 105 (42%) females. Most common patients' age was between 61 to 70 years. 127 (50.8%) patients were aged more than 60 years of age. All the patients are admitted to different types of ICUs. From this most of the patient admitted in ICU- Intensive Care Unit (n=90, 36%)

followed by MICUMedical ICU (n=75, 30%), SICU- Surgical ICU (n=51, 20.4%), CTPOST (n=19, 7.6%), CCU-Cardiac Care Unit (n=13, 5.2%), and only 2 patients in HDU- High Dependency Unit.

Table (1) shows that Prescription pattern of antimicrobial agents of the different ICUs including MICU, SICU, HDU, CCU, CTPOST describes the most commonly used drugs are from cephalosporin and carbapenem class. Meropenem (n=104) was commonly prescribed from 644 drugs in the 250 patients' prescription. Cefoperazone+sulbactam (n=92) was most commonly prescribed in the class of cephalosporin.

Table 1: Prescription Pattern of AMAs in Different ICUs.

Drugs	Class	Numbers	% Antibiotic
Amikacin, Netilimycin	**Aminoglycoside**	13	2.02
Amoxycillin, Amoxicillin+Clavulanic acid, Ampicillin, Piperacillin, Piperacillin+tazobactam	**Penicillin**	26	4.04
Aztreonam	**Monobactam**	1	0.16
Cefoperazone, Ceftazidime+Avibactam, Ceftriaxone, Ceftriaxone+Sulbactam, Cefoperazone+sulbactam, Cefotaxime, Cefuroxime, Cefpodoxime, Cefixime, Cefadroxil, Ceftriaxone+DSE+Sulbactam, Cefditoren, Ceftaroline, Cefipime+Tazobactam	**Cephalosporin**	**138**	21.43
Colistin, Polymyxin B	**Polymyxin**	41	6.37
Meropenem, Doripenem, Imipenem+cilastatin	**Carbapenem**	**106**	16.46
Levofloxacin, Moxifloxacin, Levonadifloxacin	**Fluoroquinolones**	46	7.14
Trimethoprim/Sulfamethoxazole	**Trimethoprim/Sulphonamides**	2	0.31
Minocycline, Tigecycline, Doxycycline	**Tetracycline**	40	6.21
Fosfomycin	**Fosfomycin**	8	1.24
Clindamycin	**Lincosamides**	12	1.86
Azithromycin	**Macrolide**	13	2.02
Linezolid	**Oxazolidinones**	29	4.50
Teicoplanin, Vancomycin	**Glycopeptide**	45	6.99
Daptomycin	**Lipopeptide**	6	0.93
Nitrofurantoin	**Nitrofuran**	1	0.16

Metronidazole	**Nitroimidazole**	48	7.45
Fluconazole, Voriconazole, Posaconazole, Micafungin, Caspofungin, Anidulafungin	**Antifungal**	67	10.40
Oseltamivir	**Antiviral**	2	0.31
	Total	**644**	**100**

191 Patient (76%) culture study was done by collecting specimens. From that calculation total specimen collected from 191 patients, 244 specimens are collected for the culture sensitivity test. Highest specimen collected is respiratory culture (n=77, 32%) (includes tracheal secretion, swab, sputum, BAL). In this study, out of 244 sample positive growth were seen in 152 culture sample (62.30%) and 37.7% (n=92) of total sample had negative growth. Enterococcus Sps (n=10, 58%), Staphylococcus Sps (n=5, 29%) and Streptococcus Sps (n=2, 11%) are the gram-positive bacteria detected from the positive growth (n=152) of culture test. Klebsiella Sps (n=33, 33%) and Acinobacter Sps (n=22, 22%) are detected more than half infected from gram-negative bacteria. Information of bacterial growth is seen in figure (1, 2, 3).

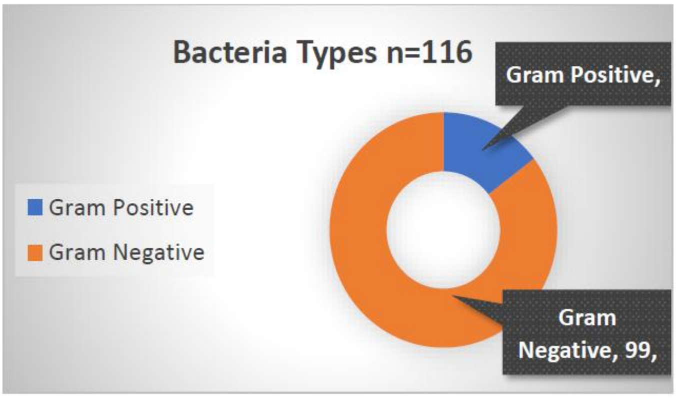

Figure 1: Isolation of bacterial organism.

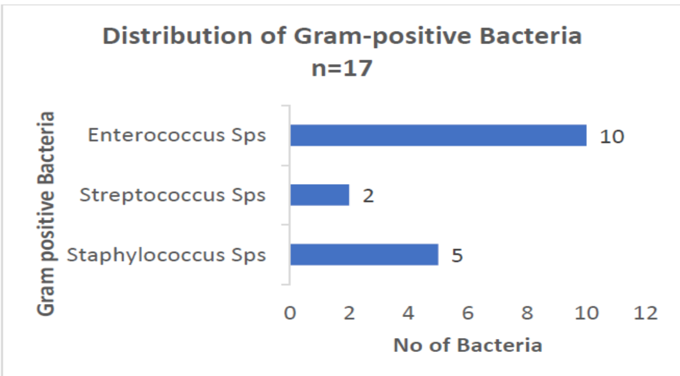

Figure 2: Distribution of Gram-Positive Bacteria.

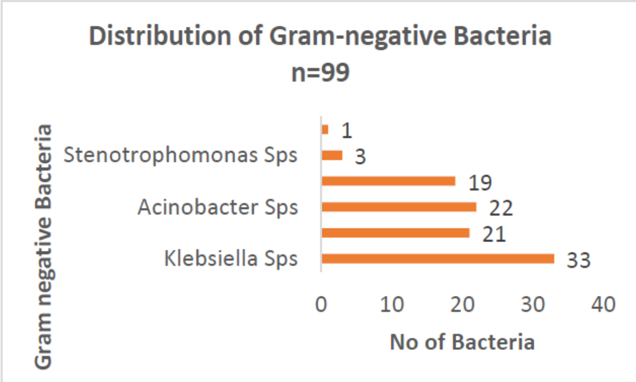

Figure 3: Distribution of Gram-Negative Bacteria.

Figure (4, 5, 6) shows the data of sensitivity pattern of different microorganism detected in different specimens.

In Respiratory samples, klebsiella species was most commonly detected. Sensitivity patternof this microorganism indicated that 100% sensitive with moxifloxacin, doxycycline, linezolid, daptomycin and 95% sensitive with colistin. Fosfomycin showed 100% sensitive against e. coli and pseudomonas species. These newer drugs were most commonly sensitive to the different microorganism and used for respiratory tract infections. Growth of different microorganism in blood culture showed the complete sensitivity with antibiotics such as ceftazidime+avibactam, glycopeptide group, linezolid, tetracyclines, colistin against gram-negative bacteria and daptomycin against gram-positive bacteria. Tigecycline was 100% sensitive against both gram-negative and gram-positive bacteria.

Urinary tract infection was caused by gram-negative bacteria including klebsiella species and pseudomonas species. Both species were sensitive against colistin. Tigecycline had also sensitive with klebsiella and e. coli but pharmacokinetics of tigecycline indicates that there is no metabolism in urine. For fluid culture examination, klebsiella, e. coli and acinobacter were shown the growth. Sensitivity pattern of these bacteria indicates that both species had a sensitivity towards tigecycline, fosfomycin, and colistin. The study results that resistance was increasing in most commonly used antibiotics which are penicillin, 1st, 2nd generation cephalosporins group. Carbapenem group showed the sensitivity against minimal microorganism as the resistance was increasing against this antibiotic group.

	100% of isolates susceptible
	Intrinsic Resistance
	Gram-negative bacteria
	Gram-positive bacteria

Figure 4: Sensitivity Pattern in Respiratory and Blood culture.

Specimen		Respiratory Sample *56/77								Blood *27/75							
	Organism	Klebsiella Sps (19)	E.Coli (7)	Pseudomonas Sps (13)	Acinobacter Sps (13)	Stenotrophomonas (2)	Enterococcus Sps (2)	Staphylococcus Sps (0)	Streptococcus (0)	Klebsiella Sps (5)	E.Coli (3)	Pseudomonas Sps (4)	Acinobacter Sps (7)	Stenotrophomonas (1)	Enterococcus Sps (5)	Staphylococcus Sps (2)	Streptococcus (0)
β-lactam	Amoxycillin+Clavulanic Acid	6	16.66				0	NIL	NIL	0	0				0	0	NIL
	Ampicillin		17				0				0				0	-	
	Ampicillin+sulbactam		17				-				0				0	-	
	Piperacillin	13	17	67	0		-			0	0	25	0		0	-	
	Piperacillin+tazobactam	31	17	75	0		-			20	67	25	14		0	-	
	Ticarcillin	12	17	58	0		-			0	0	25	0		0	-	
	Ticarcillin+clavulanic acid	38	17	67	0		-			25	67	25	14		0	-	
Carbapenem	Doripenem	40	33	77	8		-			20	67	67	14		0	-	
	Ertapenem	23	33	-	0		-			20	67	-	17		0	-	
	Imipenem	44	33	77	0		-			20	67	50	14		0	-	
	Meropenem	31	33	77	0		-			20	67	50	14		0	-	
Monobactam	Aztreonam	11	16.66	77		-				0	0	25		-			
Cephalosporins	Cefazolin	11	0		0	-				0	0		0	-		0	
	Cefoxitin	29	0		0	-				20	33		0	-		0	
	Cefoperazone	40	0	58	0	-				0	-	25	-	-		-	
	Cefoperazone+sulbactam	25	33	75	0	-				20	67	25	14	-		-	
	Cefotaxime	-	-	-	-	-				-	-	-	-	-		-	
	Ceftazidime	11	17	58	0	50				0	0	25	14	100		-	
	Ceftazidime+Avibactam	23	20	66	0	-				25	67	100	0	-		-	
	Ceftriaxone	7.7	0		0	-				0	0		0	-		0	
	Cefepime	11	17	58	0	-				0	0	25	14	-		0	
	Cefepime+tazobactam	29	33	67	0	-				20	67	25	14	-		-	
Aminoglycosides	Amikacin	39	57	77	8					0	67	50	14			-	
	Gentamicin	39	17	69	0					0	67	50	14			0	
	Netilimicin	38	83	83	8					0	100	25	14			-	
Quinolones	Ciprofloxacin	19	0	62	15		0			0	0	25	14		0	0	
	Levofloxacin	18.75	16.66	66.66	15.38		0			0	0	25	14.29		0	0	
	Moxifloxacin	100	-	-	-		0			-	-	-	-		0	100	
	Ofloxacin	19	17	67	8.3		-			0	0	50	14		0	-	
Tetracyclines	Doxycycline	100	-		-	-	50			-	-		-	-	50	100	
	Minocycline	33	50		46	100	-			40	67		50	100	0	0	
	Tetracycline	13	67		11	-	s			0	0		0	-	0	0	
	Linezolid	100	-			-	50			-	-			-	100	100	
Macrolides	Azithromycin	-				-	0			-				-	-	-	
	Erythromycin	0				-	0			-				-	0	0	
Glycopeptides	Teicoplanin						50								100	100	
	Vancomycin						50								100	100	
Lincosamides	Clindamycin	-	-			-	0			-	-			-		0	
Others	Chloramphenicol	67	67			50	50			-	-			100	75	50	
	Colistin	95	83	92	100	-				100	-	75	100	-			
	Co-trimoxazole	31	50			100				20	0			100		0	
	Daptomycin	100	-	-	-	-	100			-	-	-	-	-	100	100	
	Fosfomycin	40	100	100	0	-	-			0	33.3	-	0	-	-	-	
	Rifampicin	0	-			-	0			-	-			-	50	0	
	Tigecycline	94	83		92	-	-			100	100		100	-	100	-	

Figure 5: Sensitivity Pattern in Urine and Fluid culture.

Specimen		Urine *12/57								Fluid *10/24							
	Organism	Klebsiella Sps (5)	E.Coli (2)	Pseudomonas Sps (4)	Acinobacter Sps (0)	Stenotrophomonas (0)	Enterococcus Sps (0)	Staphylococcus Sps (1)	Streptococcus (0)	Klebsiella Sps (2)	E.Coli (4)	Pseudomonas Sps (0)	Acinobacter Sps (1)	Stenotrophomonas (0)	Enterococcus Sps (3)	Staphylococcus Sps (0)	Streptococcus (0)
β-lactam	Amoxycillin+Clavulanic Acid	20	0					100		0	0				0		
	Ampicillin		0					0			0				0		
	Ampicillin+sulbactam		0					-			0				-		
	Piperacillin	0	0	25				-		0	0		0		-		
	Piperacillin+tazobactam	20	0	25				-		0	25		0		-		
	Ticarcillin	0	0	25				-		0	0		0		-		
	Ticarcillin+clavulanic acid	20	0	25				-		0	25		0		-		
Carbapenem	Doripenem	20	0	33				-		0	33		0		-		
	Ertapenem	20	0	-				-		0	33		0		-		
	Imipenem	20	0	25				-		0	25		0		-		
	Meropenem	20	0	25				-		0	25		0		-		
Monobactam	Aztreonam	0	0	50						0	0						
Cephalosporins	Cefazolin	0	0					100		0	0		0				
	Cefoxitin	20	0					100		-	25		0				
	Cefoperazone	-	0	25				-		-	0		-				
	Cefoperazone+sulbactam	20	0	-				-		0	33		0				
	Cefotaxime	-	-	-				-		-	-		-				
	Ceftazidime	0	0	25				-		0	0		0				
	Ceftazidime+Avibactam	-	100	33				-		-	50		0				
	Ceftriaxone	0	0					-		0	0		-				
	Cefepime	0	0	25				-		0	0		0				
	Cefepime+tazobactam	0	0	25				-		0	33		0				
Aminoglycosides	Amikacin	40	50	25				0		0	50		0				
	Gentamicin	20	50	25	NIL	NIL	NIL	100	NIL	0	50	NIL	0	NIL		NIL	NIL
	Netilimicin	40	50	25				-		0	25		0				
Quinolones	Ciprofloxacin	20	0	25				0		0	0		0		0		
	Levofloxacin	20	-	25				0		0	0		0		0		
	Moxifloxacin	-	-	-				100		-	-		-		66.7		
	Ofloxacin	20	0	25				100		0	0		0		-		
Tetracyclines	Doxycycline	-	-					100		-	-		-		33.3		
	Minocycline	50	-					100		0	50		-		0		
	Tetracycline	25	-					100		100	0		-		0		
	Linezolid	-	-					100		-	-				100		
Macrolides	Azithromycin	-						-		-					-		
	Erythromycin	-						0		-					0		
Glycopeptides	Teicoplanin							100							100		
	Vancomycin							100							100		
Lincosamides	Clindamycin	-	-					0		-	-						
Others	Chloramphenicol	0	-					100		-	0				100		
	Colistin	100	100	100						100	100		100				
	Co-trimoxazole	0	50					100		0	0						
	Daptomycin	-	-	-				100		-	-		100		100		
	Fosfomycin	66.7	100	100				-		100	100		-		-		
	Rifampicin	-	-					100		-	-				50		
	Tigecycline	100	100					-		100	100		100		-		

DISCUSSION

It was observed that high tendency of prescribing class of antimicrobial agents was cephalosporins class (n=138, 21.43%) and carbapenem class (n=106, 16.46%). More than 50% drugs are from the class of cephalosporins, carbapenem, metronidazole (n=48, 7.45%), and fluoroquinolones (n=46, 7.14%). Total antimicrobial agents prescribed among 250 patients were 644 drugs. Meropenem (n=104) was most commonly prescribed as it showed the sensitivity in some patients' culture reports. Cefoperazone+sulbactam (n=92) was the second most prescribed antibiotics followed by metronidazole (n=47), and colistin (n=39). One study done by Vandana et al concluded that most commonly prescribed antibiotics were cefotaxime (32%), metronidazole (24%) and ampicillin (17.29%).[2] This showed the similar results.

In the present study, prescription pattern of individual intensive care unit has been done. According to the result, prescription pattern of antimicrobial agents in ICU, Medical ICU, and Surgical ICU had shown the same pattern (meropenem, followed by cefoperazone+sulbactam, and metronidazole was used in these different ICUs). One study concluded that in ICU cefotaxime was the most commonly used AMA by 32 % patients, followed by metronidazole 24% patients, and ampicillin by 17.29% patients which was different from the present study.[2] Levofloxacin was more commonly prescribed in CTPOST and cardiac care unit patients as they had been treated for infection as prophylactic therapy.

The prescribing frequency of AMA combinations in the present study was low (19%) compared to past study as that study had observed the 73% of AMA combinations used. 127 AMA combination were prescribed from 644 prescribed AMAs. Cefoperazone+sulbactam (n=92, 72%) followed by Piperacillin+tazobactam (n=14, 11%) were most commonly used combinations of antimicrobial agents. Previous study also showed the similar use of AMA combination.[1]

Among the culture grown samples, 116 samples show the growth of bacterial species and remaining 36 samples have fungal or any other microorganism growth. From bacterial samples, 99 samples were gram-negative and 17 were gram-positive organisms. The most common isolates were klebsiella species (n=33) as the three previous study showed common growth of pseudomonas species.[3,6-8] The majority of isolates obtained from ICU patients in Asian nations, including India, are gram-negative organisms like e. coli, klebsiella, and acinobacter, followed by gram-positive species like staphylococcus, similar to our findings.[9-11]

One past Brazilian study done by Ferreira et al showed the resistance pattern in all βlactam antibiotics.[12] In this study, 33 samples of Klebsiella Sps were isolated from the culture test. This species was sensitive to daptomycin, doxycycline, linezolid, moxifloxacin, teicoplanin (100% sensitive) while resistance to penicillin, cefazolin, cefepime, ceftazidime, ceftriaxone (more than 90% resistance).

Current study showed that 22 samples of Acinobacter Sps were isolated from the culture test. This species was sensitive to only colistin and tigecycline (100% and 95% sensitive respectively) while resistance to penicillin, almost all cephalosporins, fosfomycin, imipenem, tobramycin (100% resistance). Past study done by Chakravarty et al concluded that acinobacter species was resistance to cephalosporins (96%) followed by Piperacillin+tazobactam (84%).[13]

For the present study, 21 samples of Pseudomonas Sps were isolated from the culture test. This species was sensitive to colistin, fosfomycin (90% and 100% sensitive respectively) while resistance to penicillin, cefazolin, cefoxitin, ceftriaxone and trimethoprim/sulfamethoxazole (100% resistance). One study showed the contrast in resistance pattern with ceftazidime and Piperacillin+tazobactam.[14]

In the present study, 19 samples of E. Coli were isolated from the culture test. 7 respiratory culture and 4 fluid sample indicated the growth of e. coli. This species was sensitive to Colistin, tigecycline (94% sensitive) while resistance to penicillin, almost all cephalosporins, levofloxacin, ofloxacin, ciprofloxacin (more than 90% resistance). Similar resistance pattern showed in one study done by Sneha et al.[14]

3 samples of Stenotrophomonas Sps were isolated from the culture test. This species was sensitive to all of the mentioned antibiotics including levofloxacin, minocycline and trimethoprim/sulfamethoxazole (100% sensitive) while resistance to ceftazidime, chloramphenicol, Ticarcillin+Clavulanic acid (nearly only 33% resistance). The sample size for the sensitivity pattern was less in this study so cannot get a precise pattern of the microbiological sensitivity.

CONCLUSION

Multiple antibiotic resistance was most frequently reported in 2nd generation cephalosporins and penicillin. Antibiotic prescribing patterns and resistance patterns for the same drugs were identical. According to the analysis, the prescription habit for infection should be modified.

The frequency of sensitive pattern analysis report was low, but it may be increased to improve infection therapy. As a result, physicians must get a thorough understanding of how to use antibiotics in a safe and effective manner. They must be aware of the presence of different infections and resistance patterns in their hospital and use clinical judgement when choosing antibiotic regimens. Antibiotic prescription pattern monitoring study must be carried out to study the rational use of antimicrobials. For safety and drug monitoring, clinical pharmacists should actively participate in clinical ward rounds and report Pharmacist observations on prescriptions in the patient folder.

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