



A Study of Drug Utilization Pattern According to Daily Define Dose in Intensive Care Unit (ICU)s at Tertiary Care Teaching Hospital, India

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ABSTRACT

Objective: The goal of study is to identify drug and antimicrobial utilization in ICUs by using daily defined dose. **Material and Methods:** Study was conducted at tertiary care teaching hospital. 100 patients in each medical, surgical and neurosurgical ICU were included. The data were recorded in preformed Case Record Form (CRF). Drugs were classified using the anatomical therapeutic chemical (ATC) classification system and drug utilization was measured as Daily Defined Dose (DDD)/100 bed days. Data were analyzed by Z and χ^2 test. **Results:** DDD/100 bed days of inotropes was 51.44 in medical ICU which was significantly ($p < 0.05$) higher compared to surgical and neurosurgical ICU while DDD/100 bed days of gastrointestinal drugs was 44.52, 38.57 and analgesics was 34.5, 34.41 in surgical and neurosurgical ICU respectively which was significantly ($p < 0.05$) higher as compared to medical ICU. More than two antimicrobials were prescribed in above 70% patients in all ICU. DDD/100 bed days of cephalosporin was 20.76 in medical ICU which was significantly ($p < 0.05$) higher compared to surgical and neurosurgical ICU. DDD/100 bed days of aminoglycosides was 16.01, 17.65 and nitroimidazole was 10.3, 8.4 in surgical and neurosurgical ICU respectively which was significantly ($p < 0.05$) higher compared to medical ICU. Among restricted antimicrobials according to antimicrobial policy of hospital. DDD/100 bed days of piperacillin+tazobactam and cefoperazone+sulbactam were significantly ($p < 0.05$) higher in medical ICU. Levofloxacin and vancomycin were highly sensitive antimicrobials followed by beta lactam antimicrobials with beta lactamase inhibitors in all ICUs. **Conclusion:** Polypharmacy was observed in ICU and antimicrobials widely prescribed in ICUs. Sensitivity of beta lactam along with beta lactamase inhibitors was high.

Key words: Antimicrobial agent, Daily Defined Dose, Intensive Care Unit (ICU), Medical, Neurosurgical, Surgical.

INTRODUCTION

Drug utilization research was defined by WHO as the study of marketing, distribution, prescription, and use of drugs

in a society, with special emphasis on the resulting medical, social and economic consequences.¹ Drug utilization research help in identification of clinical use of drugs in populations and its impact on healthcare system.¹ Intensive care unit (ICU) is special ward of hospital where patients are admitted due to suffering from chronic critical illnesses.² Polypharmacy is common in patient admitted in ICU.² Antimicrobials are the most frequently prescribed drugs in ICU for prophylaxis and management of infections.³ Due to wide spread use and inappropriate use of antimicrobials

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developed multidrug resistant organisms and increase hospital acquired infections.⁴ It can lead to increased morbidity, mortality, length of hospital stay, and healthcare expenditures.^{5,6} Inappropriate use of broad spectrum antimicrobials lead to decreases sensitivity of antimicrobials against microorganisms. Increasing multidrug resistance with limited availability of newer agents there is urgent need for vigilant surveillance, stringent infection control practices, as well as rational anti-biotic prescription.⁷ Our hospital has anti-microbial policy which divide antimicrobials into restricted and unrestricted category. There is limited data from Indian ICUs as well as our hospital on drugs and antimicrobial utilization along with its sensitivity in the ICUs. Hence, we proposed to study the drug utilization pattern into the ICUs.

MATERIAL AND METHODS

Our study was prospective, continuous and observational conducted at tertiary care teaching hospital for a period of 23 months in 2009-2011. Approval from Medical Superintendent of institute and Institutional Ethical Committee (Ref No. EC/Approval/38/10) were taken before starting the study. Investigator visited each medical, surgical and neurosurgical ICU every day. 100 adult patients from each ICU who were prescribed antimicrobials were included in study after obtaining written informed consent. All information like age, gender, prescribed drugs and antimicrobials, report of culture sensitivity test etc. were collected and recorded preformed CRF. Antimicrobials and other drugs were classified using the ATC Classification System and drug utilization was measured as DDD/100 bed-days.

The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults.

The DDD per 100 bed-days was calculated by the formula:

$$\text{DDD/100bed-days} = \frac{\text{No. of units administered in a given period} \times 100}{\text{DDD} \times \text{number of days} \times \text{number of beds} \times \text{occupancy index}}$$

Statistical Analysis

All the data was entered into Microsoft Excel sheet and subjected to statistical analysis test. The data were analyzed by Z test and χ^2 test.

RESULTS

Analysis of demographic criteria

It was observed that 60%, 64% and 68% patients in age group of 40-60 years and 58%, 61% and 64% patient

were male in medical, surgical and neurosurgical ICU respectively. Mortality after 14 days of ICU was significantly ($p < 0.05$) higher in medical ICU as compared to surgical and neurosurgical ICU. Duration of stay in ICU was significantly ($p < 0.05$) higher in medical and neurosurgical ICU as compared to surgical ICU. It was observed that 5 to 14 drugs were prescribed with mean of 13.48 ± 1.64 , 11.52 ± 1.32 and 12.30 ± 1.46 in medical, surgical and neurosurgical ICU respectively. In medical ICU 46%, surgical ICU 86% and neurosurgical ICU 77% patients were prescribed either 3 or 4 antimicrobials. There was statistically significance in prescribing antimicrobials by generic name as compared to brand name in all ICUs. Average duration of antimicrobial agent was significantly ($p < 0.05$) higher in neurosurgical and medical ICU as compared to surgical ICU (Table 1).

Analysis Daily Defined Dose (DDD) per 100 bed days of drugs

DDD/100 bed days of inotropes (adrenaline, noradrenaline, dopamine), anticholinergic drugs (atropine) cardiovascular drugs (aspirin, clopidogrel, digoxin, atorvastatin etc) and respiratory drugs (salbutamol, Etofylline+theophylline hydrate) were significantly ($p < 0.05$) higher in medical ICU as compared to surgical and neurosurgical ICU. DDD/100 bed days of corticosteroids (beclomethasone, dexamethasone,) drugs acting on central nervous system (phenytoin, sodium valproate, diazepam, lorazepam) and diuretics (furosemide) were significantly ($p < 0.05$) higher in neurosurgical ICU as compared to medical and surgical ICU. DDD/100 bed days of gastrointestinal drugs (ranitidine, pantoprazole, omeprazole, ondansetron) and analgesics (diclofenac, tramadol) were significantly ($p < 0.05$) higher in surgical ICU and neurosurgical ICU as compared to medical ICU. DDD/100 bed days of antimicrobials was similar to all ICUs (Table 2 a, b).

Analysis of DDD/100 bed days of antimicrobials group

DDD/100 bed days of penicillin, aminoglycosides, nitroimidazole and macrolide were significantly ($p < 0.05$) higher in surgical and neurosurgical ICU as compared to medical ICU. DDD/100 bed days of cephalosporin and fluoroquinolone were significantly ($p < 0.05$) higher in medical and neurosurgical ICU as compared to surgical ICU (Table 3).

DDD/100 bed days of antimicrobials according to antimicrobial policy of hospital

Among unrestricted antimicrobials of policy DDD/100 bed days of ceftriaxone, ciprofloxacin and ofloxacin were significantly ($p < 0.05$) higher in medical ICU as compared to surgical and neurosurgical ICU. DDD/100 bed days of amoxicillin-clavulanate, cefotaxime, amikacin and

Table 1: Analysis of demographic data and drug prescription in ICU

ICU		MICU (n=100)	SICU (n=100)	NSICU (n=100)
Age group (years)	20-40	24	22	15
	40-60	60	64	68
	More than 60	16	14	17
Male/ Female		58/42	61/39	64/36
Mortality before 14 days		22	18	14
Mortality after 14 days		57*	21	19
Transfer to ward		16	54	59
Duration of stay in ICU		9.2±1.29 [#]	5.7±1.04	11.2±1.16 [#]
Average no. of drugs prescribed(Mean±SEM)		13.48±1.64	11.52±1.32	12.30±1.46
No of antimicrobial agents	1 and 2	12	03	09
	3 and 4	46	86	77
	More than 4	42	11	14
Average duration of antimicrobial agents		8.03±1.53 [#]	6.72±1.12	10.8±1.31 [#]
Antimicrobials prescribed by generic/brand name		273 (66.26%)** /139 (33.74%)	232** (68.63%) /106 (31.37%)	233 (64.90%)** /126 (35.10%)

*p<0.05 (Z test) significantly higher as compared to surgical and neurosurgical ICU; **p<0.05 (X² test) significantly higher as compared to brand name in all ICU; [#]p<0.05 (Z test) significantly higher as compared to surgical ICU.

Table 2: a) Analysis DDD of group of drugs

Drugs	Medical ICU DDD/100 bed days	Surgical ICU DDD/100 bed days	Neurosurgical ICU DDD/100 bed days
Inotropes	51.54*	29.43	28.32
Anticholinergic	35.33*	23.74	25.64
Gastrointestinal drugs	14.13	44.52**	38.17**
Corticosteroids	7.63	17.87	62.86 [#]
Analgesics	13.76	34.5**	34.41**
CNS drugs	15.43 [#]	8.32	28.53 [#]
Cardiovascular drugs	13.54*	8.55	7.8
Diuretics	5.24	11.21**	16.33 [#]
Respiratory drugs	9.02*	5.33	7.21
Electrolytes	4.24	4.07	3.91
Antimicrobial agents	48.42	46.57	52.81

metronidazole were significantly ($p<0.05$) higher in surgical and neurosurgical ICU as compared to medical ICU while DDD/100 bed days of ceftazidime was significantly ($p<0.05$) higher in neurosurgical ICU as compared to medical and surgical ICU. Among restricted antimicrobials of policy DDD/100 bed days of piperacillin+tazobactam, cefoperazone+sulbactam were significantly ($p<0.05$) higher in medical ICU as compared to surgical ICU and neurosurgical ICU. DDD/100 bed days of vancomycin was significantly ($p<0.05$) higher in surgical ICU as compared to medical and neurosurgical ICU while DDD/100 bed days of linezolid was significantly ($p<0.05$) higher in neurosurgical ICU as compared to medical and surgical ICU (Table 4 a,b).

Sensitivity of most commonly prescribed antimicrobials

For culture sensitivity test 129 samples were collected from all ICUs. No micro-organisms found in 76 samples and sensitivity of antimicrobials was observed in remaining 53 samples. Sensitivity percentage to beta lactam antimicrobials with beta lactamase inhibitors was significantly ($p<0.05$) higher as compared beta lactam alone in all ICUs. Vancomycin and levofloxacin more than 80% sensitive in all ICUs which was significantly ($p<0.05$) higher as compared to beta lactam anti-microbials with beta lactamase inhibitors. Sensitivity of linezolid was higher as compared to beta lactam antimicrobials but lower as compared to beta lactam anti-microbial with beta lactamase inhibitors (Figure 1).

Table 2: b) Analysis of DDD per 100 bed days individual drugs

Drugs	ATC DOE	DDD by WHO	Medical ICU		Surgical ICU		Neurosurgical ICU	
			Units prescribed	DDD/100 bed day	Units prescribed	DDD/100 bed days	Units prescribed	DDD/100 bed days
Atropine	A03BA01	1.5 mg	1710	32.57*	788	22.51	864	24.51
Nor adrenaline	C01CA03	6 mg	464	2.14*	241	1.43	118	0.7
Adrenaline	C01CA24	0.5 mg	1674	39.85*	892	21.23	734	21.84
Dopamine	C01CA04	0.5 gm	1056	5.02*	424	3.02	367	2.62
Dobutamine	C01CA07	0.5 gm	745	4.43*	421	3.75	354	3.16
Beclomethasone	H07AC01	1.5 mg	37	1.17	12	0.57	298	14.19#
Dexamethasone	H02AB02	1.5 mg	53	0.84	43	1.02	936	22.85#
Hydrocortisone	H02AB09	30 mg	134	5.31	236	14.04	329	19.58#
Salbutamol	R03AC02	0.8 mg	452	0.67*	132	0.29	159	0.35
Etofylline+theophylline hydrate	R03DA54	0.4 gm	408	8.01*	134	3.94	237	6.98##
Aspirin	B01AC06	75 mg	184	2.19*	82	1.46	85	1.51
Atorvastatin	C10AA05	20 mg	192	2.28*	98	1.75	86	1.53
Clopidogrel	B01AC04	75 mg	183	2.17*	89	1.58	86	1.54
Amlodipine	C08CA01	5 mg	182	2.16*	45	0.8	56	1
Metoprolol	C07AB02	0.15 mg	195	0.77*	36	0.21	33	0.19
Digoxin	C01AA05	0.25 mg	102	2.42*	24	0.85	14	0.5
Furosemide	C03CA01	40 mg	764	5.54	824	6.25	1146	12.38##
Ranitidine	A02BA02	0.3 gm	2320	4.6	2870	8.54**	2389	7.11**
Pantoprazole	A02BC02	40 mg	602	7.16	1056	18.85**	982	17.53**
Ondansetron	A04AA01	16 mg	468	1.39	1656	7.39**	1076	4.8**
Omeprazole	A02BC01	20 mg	20	0.23	473	8.44**	305	5.44**
Phenytoin	N03AB02	0.3 gm	898	3.56##	364	2.16	1686	10.03#
Sodium valproate	N03AG01	1.5 gm	1022	0.81##	142	0.16	1287	1.53#
Diazepam	N05BA01	10 mg	289	3.44##	117	2.08	343	6.12#
Lorazepam	N05BA06	2.5 mg	219	3.98##	93	2.65	213	6.08#
Midazolam	N05CD08	15 mg	764	3.03##	214	1.27	802	4.77##
Tramadol	N02AX02	0.3 gm	876	3.47	1022	6.08**	1084	6.45**
Diclofenac	M01AB05	0.1 gm	1025	9.15	1685	22.56**	1588	21.26**
Sodium chloride	A12CA01	1 gm	252	1.35	130	1.04	63	0.5
Magnesium Sulphate	A12CC02	1 gm	198	2.35	89	1.58	103	1.83

*p<0.05 (Z test) significantly higher as compared to surgical and neurosurgical ICU; **p<0.05 (Z test) significantly higher as compared to medical ICU

#p<0.05 (Z test) significantly higher as compared to medical and surgical ICU; ##p<0.05 (Z test) significantly higher as compared to surgical ICU

Table 3: Analysis of DDD per 100 bed days in antimicrobial groups

Antimicrobial groups	MICU	SICU	NSICU
	DDD/ 100 bed days	DDD/ 100 bed days	DDD/ 100 bed days
Cephalosporin	23.76##	8.05	12.71##
Penicillin	6.1	7.51**	7.22**
Fluroquinolones	5.9##	2.71	5.8##
Aminoglycosides	4.98	16.01**	17.65**
Nitroimidazole	3.72	10.3**	8.04**
Macrolides	0.35	0.74**	1.12**
Monobactam	0.06	0.23	0.17
Others	3.55*	0.72	0.1

*p<0.05 (Z test) significantly higher as compared to surgical and neurosurgical ICU; **p<0.05 (Z test) significantly higher as compared to medical ICU; ##p<0.05 (Z test) significantly higher as compared to surgical ICU.

Table 4: a) DDD per 100 bed days in unrestricted antimicrobials according to antibiotic policy of hospital

Name of antimicrobial agents	ATC CODE	DDD by WHO (gms)	Medical ICU		Surgical ICU		Neurosurgical ICU	
			Prescribed dose in gms	DDD/100 bed days	Prescribed dose in gms	DDD/100 bed days	Prescribed dose in gms	DDD/100 bed days
Crystalline penicillin	J01CE01	3.6	36	0.11	0	0	0	0
Amoxicillin-Clavulanate	J01CR02	3	956.4	3.79	1152	6.85**	1072.8	6.38**
Cefoperazone	J01DD62	4	0	0	0	0	78	0.34
Cefotaxime	J01DD01	4	316	0.94	438	1.95**	711	3.17**
Ceftriaxone	J01DD04	2	2096	15.47*	146	1.3	170	1.51
Cefatazidime	J01DD02	4	116	0.34	80	0.35	414	1.84#
Cefixime	J01DD08	0.4	0	0	1.2	0.05	0.8	0.03
Ciprofloxacin	J01MA02	0.5	24.2	0.57*	1	0.03	0.2	0.01
Ofloxacin	J01MA01	0.4	10	0.29*	0.2	0.01	0.2	0.01
Levofloxacin	J01MA12	0.5	21.1	5.02##	75	2.67	162	5.78##
Gatifloxacin	J01MA16	0.4	0.8	0.02	0	0	0	0
Amikacin	J01GB06	1	418.5	4.98	897	16.01**	988.5	17.65**
Azithromycin	J01FA10	0.5	16	0.64	3	0.1	0	0
Metronidazole	J01XD01	1.5	469	3.72	865.5	10.3**	676	8.04**

Table 4: b) DDD per 100 bed days in restricted antimicrobials according to antibiotic policy of hospital

Name of antimicrobial agents	ATC CODE	DDD by WHO (gms)	Medical ICU		Surgical ICU		Neurosurgical ICU	
			Prescribed dose in gms	DDD/100 bed days	Prescribed dose in gms	DDD/100 bed days	Prescribed dose in gms	DDD/100 bed days
Piperacillin+Tazobactam	J01CR05	14	2592	2.2*	522	0.66	666	0.84
Cefoperazone + sulbactam	J01DD62	4	2358	7.01*	987	4.4	1086	4.84
Imipenem	J01DH51	2	10.5	0.06	9	0.08	0	0
Imipenem+cilistatin	J01DH51	2	0	0	17	0.15	20	0.17
Vancomycin	J01XA01	2	10.5	0.06	54	0.48@	13.5	0.12
Linezolid	J01XX08	2	21.2	0.12	18	0.16	112.8	1#
Clindamycin	J01FF01	1.8	6	0.03	0	0	0	0

* p<0.05 (Z test) significantly higher as compared to surgical and neurosurgical ICU; ** p<0.05 (Z test) significantly higher as compared to medical ICU; # p<0.05 (Z test) significantly higher as compared to medical and surgical ICU; ## p<0.05 (Z test) significantly higher as compared to surgical ICU; @ p<0.05 (Z test) significantly higher as compared to medical and neurosurgical ICU.

DISCUSSION

Analysis of demographic criteria

In our study age group of 40-60 (years) was more than 60% patients in all ICUs which was higher to study at Kuwait where 45% patients in same group.⁸ More than 55% patients were male in all ICUs which was similar to study by Biswal *et al.*⁹ In contrast to our study, Smythe *et al.*, reported equal number of male and female patients.¹⁰ In the Indian scenario it is noticed that female populations are reluctant to utilize health care faculties even if they are critically ill.² Mortality after 14 days was significantly high in medical ICU (57%) as compared to surgical (21%) and neurosurgical (19%) ICU that similar to study by Blot *et al.*, where 61% death occurred after 14 days.¹¹ Average duration of stay was more than 9 days in medical and neurosurgical ICU significantly higher compared to surgical ICU. Study from Bangalore reported that an average length of stay in ICU of 6 days which was lower as compared to our study.¹²

Majority patients in medical ICU were on ventilator support and mortality as well as length of stay was observed higher in patients on ventilator. In neurosurgical ICU patients were admitted for post operative care. Average more than 11 drugs was prescribed in all ICUs which was similar to study by Smythe *et al.*, where mean number of drugs was 12.6 ± 7.6 .⁹ Polypharmacy was common in ICU due to critical and comorbid illness. In all ICUs above 75% patients were prescribed more than 2 antimicrobials which was contrast to study conducted at Puducherry where only 17% patients were given a more than 2 antimicrobials.¹² Prescribing more than two antimicrobials may be due to critical illness and longer duration of stay. In all ICUs more than 60% antimicrobials prescribed by generic name as compared to brand name while study conducted at South India reported that 29.20% antimicrobials were prescribed in generic names.¹² Antimicrobials were supplied from state government and drugs were prescribed by brand name in unavoidable circumstance in our study. Average duration

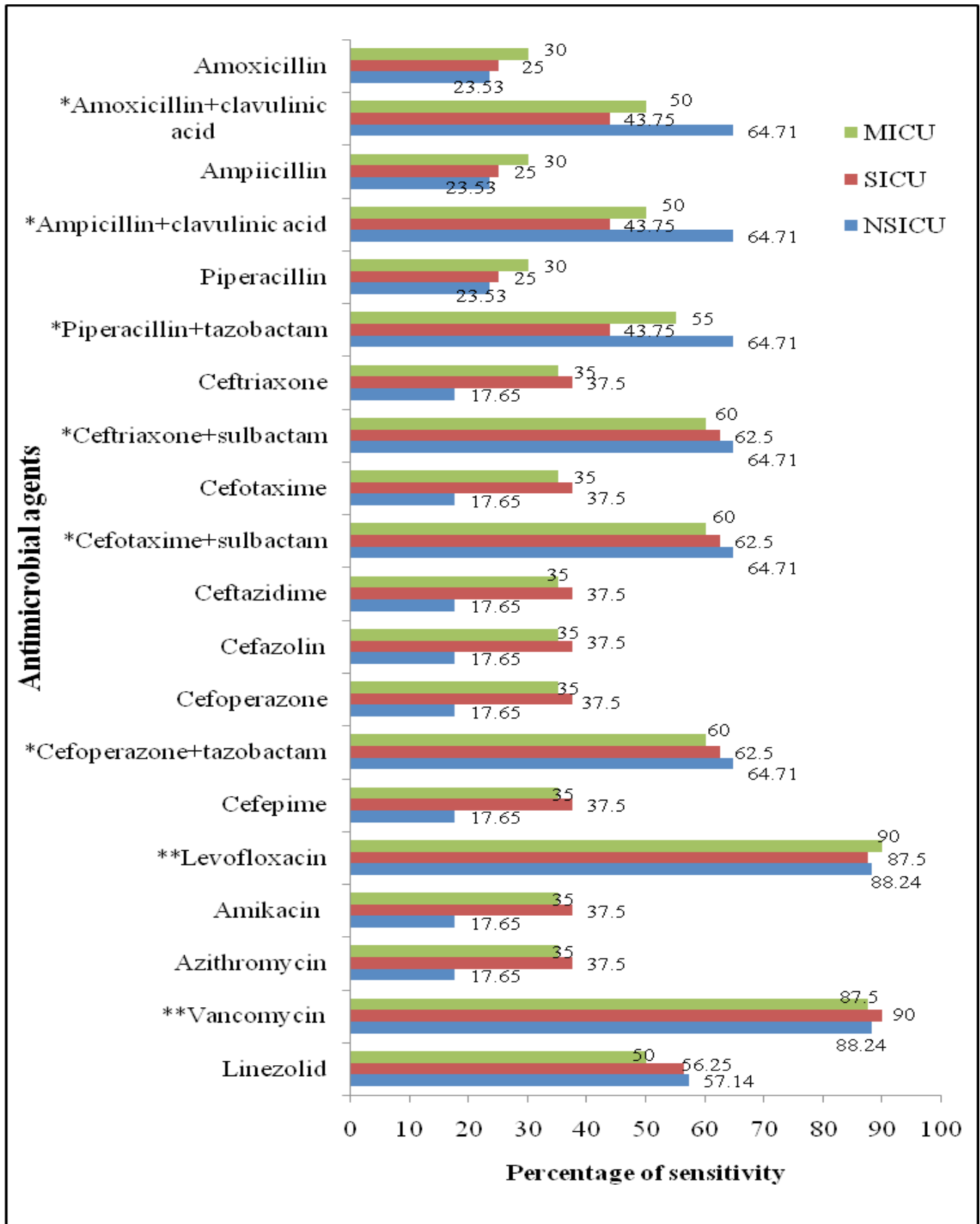


Figure 1: Sensitivity of antimicrobial agents in medical, surgical and neurosurgical ICU (n=53)

*p<0.05 (Z test) significantly higher as compared to beta lactam antimicrobials; **p<0.05 (Z test) significantly higher as compared to others antimicrobials.

of antimicrobial agent was more than 8 days significantly higher in neurosurgical and medical ICU while it was 6 days in study conducted at Mangalore.⁴ Patients of critical illness required longer duration of antimicrobial therapy.

Analysis Daily Defined Dose (DDD) per 100 bed days of drugs

Among anti-cholinergic drugs DDD/100 bed days of atropine was significantly ($p < 0.05$) higher in medical ICU. Atropine was prescribed in patients of organophosphate poisoning, and to decrease heart rate in critically ill patients. In inotropes, DDD/100 bed days of adrenaline, noradrenaline, dopamine was significantly ($p < 0.05$) higher in medical ICU. Adrenaline was mainly used for cardiac resuscitation and cardio respiratory arrest. Dopamine, dobutamine and noradrenaline were used to restore cardiac output, tissue perfusion and oxygenation.¹³ Among cardiovascular drugs DDD/100 bed days of aspirin, clopidogrel, digoxin, atorvastatin etc. were significantly ($p < 0.05$) higher in medical ICU which was similar to studies reported by Smythe *et al.*, and Biswal *et al.*^{9,10} In respiratory drugs DDD/100 bed days of salbutamol, etofylline+theophylline hydrate was significantly ($p < 0.05$) higher in medical ICU. Salbutamol and theophylline were prescribed in case of respiratory failure or difficulty in breathing which was more observed in medical ICU and similar report observed by Shankar *et al.*³ In corticosteroids, DDD/100 bed days of beclomethasone, dexamethasone were significantly ($p < 0.05$) higher in neurosurgical ICU. Corticosteroids have proven to be beneficial in controlling tumor-associated pain and limiting nausea and vomiting in operated neurosurgical patients.¹⁴ DDD/100 bed days of phenytoin, sodium valproate, diazepam, lorazepam were significantly ($p < 0.05$) higher in neurosurgical ICU as anticonvulsant and sedatives were prescribed neurosurgical patients to prevent and management of convulsive episodes. DDD/100 bed days of furosemide was also significantly ($p < 0.05$) higher in neurosurgical ICU. Furosemide was required to maintain body fluid level which was more concerned in neurosurgical patients. DDD per 100 bed days of proton pump inhibitors and analgesics like diclofenac, tramadol were significantly ($p < 0.05$) higher in surgical ICU and neurosurgical ICU. Proton pump inhibitors can be prescribed for prophylaxis and management of stress induced and drug induced ulcers among critically ill patients.¹² Analgesics were commonly prescribed in both surgical and neurosurgical ICU for management of postoperative pain.

Analysis of DDD of antimicrobials group

Total antimicrobial usage DDD/100 bed day was 44.42, 46.27 and 52.81 in medical, surgical and neurosurgical ICU respectively which was lower as compared to study

carried out at Germany where the total antibiotic usage DDD/100 bed day was 133.7. Germany study was carried out in 35 ICUs while our study was carried out in three ICUs.¹⁵ DDD/100 bed days of penicillin, aminoglycosides and nitroimidazole were significantly ($p < 0.05$) higher in surgical (7.51, 16.01 and 10.3) and neurosurgical (7.22, 17.65 and 8.4) ICU as compared to medical ICU (6.1, 4.98 and 3.72) respectively. Shankar *et al.*, reported that utilization of penicillin was 55.1 DDD/100 bed days which was higher as compared to our study.³ Study conducted at Czech Republic reported that DDD/100 bed days of aminoglycosides was 8.79 which was lower as compared to surgical and neurosurgical ICU.¹⁶ Biswal *et al.*, documented metronidazole as the commonly prescribed antimicrobial agent in their study.⁹ Variation was observed in antimicrobials prescribed in different region and ICU in the world may be due to sensitivity pattern of antimicrobials.

DDD/100 bed days of antimicrobials according to antimicrobial policy of hospital

DDD/100 bed days of amoxicillin-clavulanate, amikacin and metronidazole were significantly ($p < 0.05$) higher in surgical (6.85, 16.01, 10.03) and neurosurgical ICU (6.38, 17.65 and 8.04). Santosh EF *et al.*, reported that DDD/100 bed days ampicillin+sulbactam was 41.74.¹⁷ Williams *et al.*, reported that DDD/100 bed days of amikacin and metronidazole were 8.15 and 14.65 respectively which was higher compared to our study.⁵ Due to amoxicillin-clavulanate as broad spectrum anti-microbial, amikacin effective against abdominal *enterobacteria* and metronidazole effective against anaerobe they were prescribed significantly in surgical and neurosurgical ICU to prevent post operative infections.

DDD/100 bed days of cephalosporin and fluoroquinolone were significantly ($p < 0.05$) higher in medical (20.76 and 5.9) and neurosurgical ICU (12.71 and 5.8) as compared to surgical ICU (8.05 and 2.71) respectively. Shankar *et al.*, reported that the utilization of cephalosporins and fluoroquinolones, were 13.74 and 5.34 DDD/100 bed-days respectively which was similar to our report.³ DDD/100 bed days of ceftriaxone was significantly ($p < 0.05$) higher in medical ICU (15.47) and DDD/100 bed days of cefotaxime was significantly ($p < 0.05$) higher in surgical (1.95) and neurosurgical ICU (3.17) while DDD/100 bed days of ceftazidime was significantly ($p < 0.05$) higher in neurosurgical ICU (1.84). Patel *et al.*, reported that DDD/100 bed days of ceftriaxone and cefotaxime were 7.41 and 5.53 respectively which was higher compared to our study.¹⁸ Vojtova V *et al.*, reported that DDD/100 bed days of ceftazidime was 2.19 which was higher as compared

to our study.¹⁶ Ceftriaxone, cefotaxime and ceftazidime were prescribed as empirical therapy due to their broad spectrum in our study. DDD/100 bed days of levofloxacin was significantly ($p < 0.05$) higher in medical ICU (5.02) and neurosurgical ICU (5.78). Williams *et al.*, reported that DDD/100 bed days of levofloxacin was 15.97 which was higher as compared to our study.⁵ Levofloxacin was most commonly prescribed for the treatment and prevention of hospital acquired pneumonia in medical and neurosurgical ICUs.

Among the restricted antimicrobials DDD/100 bed days of piperacillin+tazobactam (2.2), cefoperazone+sulbactam (7.01) were significantly ($p < 0.05$) higher in medical ICU. Vojtova V *et al.*, reported that DDD/100 bed days of piperacillin+tazobactam and cefoperazone+ sulbactam was 3.17 and 0.21 which was higher and lower compared to our study respectively.¹⁶ Sensitivity of cefoperazone+sulbactam and piperacillin+tazobactam were high at our set up. DDD/100 bed days of vancomycin was higher in surgical ICU (0.48) while study carried out at Brazil reported that DDD/100 bed days of vancomycin was 13.13 which was higher compared to our study.¹⁷ Vancomycin was prescribed against methicillin resistant *Staphylococcus aureus* which was observed in more in surgical ICU. DDD/100 bed days of linezolid was one (1) in neurosurgical ICU. Garcia MS *et al.*, reported that linezolid use decreased from 202 to 25 DDD/100 bed days still it was higher as compared to our study.¹⁹ In their study resistant to lizezolid against *Staphylococcus aureus* was observed while in our study linezolid was sensitive against *Staphylococcus aureus*.

Sensitivity of most commonly prescribed antimicrobials

Sensitivity percentage of amoxicillin+clavulanic acid, ampicillin+clavulanic acid, piperacillin+tazobactam (55, 43.75 and 64.71) was significantly higher as compared to sensitivity percentage of amoxicillin, ampicillin and pipracillin (30, 25 and 23.53) in medical, surgical and neurosurgical ICU respectively. Jones ME, *et al.*, reported that sensitivity of ampicilin was 6.7 and 12.6 in USA and Canada respectively which was lower compared to our study.²⁰ Shakibaie MR *et al.*, reported that all strain were fully resistant to piperacillin, while 6.7% strain was sensitive to piperacillin + tazobactam which was lower as compared to our study.²¹ Sensitivity percentage to cefotaxime+sulbactam, ceftriaxone+sulbactam and cefoperazone+sulbactam (60, 62.5 and 64.71) was significantly higher as compared to sensitivity percentage cefotaxime, ceftriaxone and cefoperazone (35, 37.5 and 17.65) in medical, surgical and neurosurgical ICU respectively. Neil *et al.*, reported that 20% strain was sensitive to the third-generation cephalosporins which was lower as compared to our

study.²² Beta lactam along with in combinations with beta lactamase inhibitors were prescribed highly as compared to beta lactam alone at our set up.

Sensitivity percentage of vancomycin and levofloxacin were more than 80% in all ICUs. Study by Thati *et al.*, reported that 93.57% strain was sensitive for vancomycin similar to our study while study carried out at Turkey reported that sensitivity percentage of levofloxaicn was 60-75 which was lower as compared to our study.^{23,24} Vancomycin was prescribed when infection occurred due to methicillin resistant *Staphylococcus aureus* while levofloxacin was prescribed in the patients when penicillin and cephalosporins with beta lactamase inhibitors were resistant.

Sensitivity percentage of linezolid was more than 50% in all ICUs. Zhanel GG *et al.*, reported that sensitivity rate of linezolid was above 90% which was higher as compared to our study.²⁵ In neurosurgical ICU linezolid was prescribed due to its high sensitivity and reduce intracranial tension in post operative neurosurgical patients.

In our study, inotropes and cardiovascular drugs prescribed higher in medical ICU while gastrointestinal drugs and analgesics were prescribed higher in surgical and neurosurgical ICU. Corticosteroids and antiepileptic drugs were prescribed higher in neurosurgical ICU. Antimicrobials were prescribed most commonly and more than 2 antimicrobials prescribed in majority of the patient in all ICUs. Although antimicrobial policy of our hospital is available but some of the restricted antimicrobials are used in all ICUs. Hence we recommended following suggestion to improve rational use of antimicrobial agents:

- Education of prescriber by encourage to attend seminar, medical workshop, conference etc.
- Availability of antimicrobial policy in each ward, ICU and to prescriber
- Strict evaluation of implementation of antimicrobial policy

In our study limitation we did not study those patient who were shift from ward to ICU for critical care management and pregnant women as well as children.

CONCLUSION

In conclusion, our study reveals that antimicrobials are widely prescribed in critically ill patients and form a significant proportion of the total drugs consumed in the ICU. This study will helpful for education to prescribers, rational prescription of antimicrobials and better management of patients.

ABBREVIATION

ATC: Anatomical Therapeutic Chemical
 CRF: Case Record Form
 DDD: Daily Defined Dose

ICU: Intensive Care Unit
 NSICU: Neurosurgical ICU
 MICU: Medical ICU
 SICU: Surgical ICU

Highlights of Paper

- DDD/100 bed days of inotropes was higher in medical ICU while DDD/100 bed days of gastrointestinal drugs and analgesics were higher in surgical and neurosurgical ICU.
- DDD/100 bed days of cephalosporins was higher in medical ICU while DDD/100 bed days of aminoglycosides and nitroimidazole were higher in surgical and neurosurgical ICU.
- Among restricted antimicrobials according to antimicrobial policy of hospital DDD/100 bed days of piperacilli+tazobacatm and cefoperazon+sulbactam were higher in medical ICU.
- Levofloxacin and vancomycin were highly sensitive antimicrobials followed by beta lactam antimicrobials with beta lactamase inhibitors in all ICUs.

Author Profile



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