IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

STUDY ON PRESCRIBING PATTERN OF ANTIBIOTICS IN PATIENTS ADMITTED TO INTENSIVE CARE UNITS.

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Abstract:

Objective
To study prescribing patterns of antibiotics by WHO prescribing indicators in intensive care unit patients in mehsana city.

Experimental work:
Prospective, observational, multi centric study was carried out at Astha ICU and Lions general hospital at Mehsana, Gujarat. Sample size was calculated using formula n = (Z^2 × P(1-P))/e. Study was performed on 400 ICU patients. The WHO prescribing indicators were used. The data was analyzed using Microsoft excel.
Results and discussion:
A total of 400 prescriptions were encountered with the total of 16,452 drugs prescribed. The average number of drug per prescription was 4.11. Only 15.49 % (n=16,452) of drugs were prescribed by generic name. Percentage of drug prescribed from NLEM model list of Essential drugs was 53 % (n=8722). Antibiotics and injections encountered were 96%(n=384) and 100% (n=400) respectively. Ceftriaxone was most frequently prescribed 234 (25%), followed by Amikacin, Piperacillin-Tazobactam, Amikacin-Clavulanic acid prescribed in 156(17%), 94(10%), 82(8%) respectively. Maximum 320 (27.6%) times third generation cephalosporin were prescribed.
Conclusions:
On the basis of the finding of this study, the prescribing practices for antibiotics shows deviation from the standard recommended by WHO. Antibiotics & injections were commonly overused and costly forms of drug therapy need to be regulated closely. Drug use evaluation should be done for some of the antibiotics to check whether they were appropriately prescribed or not. On the other hand, polypharmacy, generic prescribing and prescribing from EDL were also found to be a problem in this study.

Keywords:
Antibiotics, Cephalosporins, WHO core drug use indicators

I. INTRODUCTION

Antibiotics substances which are produced by microorganisms, they suppress the growth or kill microorganisms at low concentrations. [1]
Intensive care unit or critical care unit is designated special area of hospital where medical equipment and services are provided for serious patient. [1]

Prescription pattern
Prescription monitoring studies (PPMS) are a tool for assessing the prescribing, dispensing and distribution of medicines. The main aim of PPMS is to facilitate rational use of medicines (RUM). [1]

Indicators that focus general prescribing quality:
National Patient Safety Agency (NPSA) documents – the NPSA has produced a number of documents that are relevant to the safety of prescribing in primary care. [2] For example, the fourth report from the Patient Safety Observatory highlighted medication incidents in the community and at the interface between community and hospital care and also suggested ways in which risks of harm could be reduced. In addition, the NPSA has highlighted a number of specific safety issues relevant to primary care including

anticoagulant prescribing, dosing errors with opioid medicines and the prescribing of methotrexate (NPSA 2009). [3] A number of these issues could be incorporated into indicators. [2]

WHO prescribing indicators: The World Health Organization (WHO) in 1993 has formulated a set of "Core drug use indicators" namely prescribing indicators, patient care indicators and facility indicators. Among them, for this study only "prescribing indicators" were taken which measure the performance of prescribers. The core prescribing indicators are average number of drugs per prescription, percentage of drugs prescribed by generic name, percentage of encounters with an antibiotic prescribed, percentage of encounters with an injection prescribed and percentage of drugs prescribed from essential drug list or formulary. [4]

Some additional indices are percentage of encounters with a NSAID prescribed, percentage of encounters with an antiulcerant prescribed, percentage of encounters with a calcium preparation prescribed and the data was expressed as percentage, mean and total numbers. Selected WHO/INRUD drug use indicators for primary health care facilities (WHO, 1993). [4]

Prescribing Indicators:
Average number of medicines prescribed per patient encounter
% medicines prescribed by generic name
% encounters with an antibiotic prescribed
% encounters with an injection prescribed
% medicines prescribed from essential medicines list or formulary
Patient Care Indicators:
Average consultation time
Average dispensing time
% medicines actually dispensed
% medicines adequately labeled
% patients with knowledge of correct doses
Facility Indicators:
Availability of essential medicines list or formulary to practitioners
Availability of clinical guidelines
% key medicines available
Complementary Drug Use Indicators:
Average medicine cost per encounter
% prescriptions in accordance with clinical guidelines

II. RESEARCH METHODOLOGY

2.1 Study design

Observational, Prospective and multicenter study
Duration of study: Dec-2018 to March-2019
The study is being conducted according at two different ICUs.

1. Astha ICU, Mehsana.
2. Lions General Hospital, Mehsana.

2.2 Study population

Patient population was enrolled who admitted to ICU longer than 24 hrs.
The sample size was calculated using the formula [5]

$$n = (Z^2 \times P(1-P))/e^2$$

Where,
Z = value from standard normal distribution corresponding to desired confidence level (Z=1.96 for 95% CI)
P is expected true proportion
e is desired precision (half desired CI width).
Estimated Proportion P = 0.1
Desired precision of estimate e = 0.05
Confidence level = 0.95
So, Population size is 400

2.3 Subject eligibility

2.3.1 Inclusion Criteria:

Patient of either sex and age above 18 years
Who are willing to provide inform consent
Who are admitted longer than 24 hrs in ICU

2.3.2 Exclusion criteria:

Age below 18 years
Patient who are not co-operative
Patient admitted in ICU longer than 15 days
Pregnant women

2.4 Ethical consideration:

A detailed study protocol, case record form (CRF) and informed consent form was prepared and the same were approved by Independent Ethical Committee of SSPC-IEC.

2.5 Study Methodology

Prospective, observational, multi centric study is being carried out at Astha ICU and Lions general hospital at Mehsana, Gujarat. Study was performed on 400 ICU patients to determine the antibiotics prescribing pattern in ICU patients.

Prescription analysis is studied as per inclusion and exclusion criteria

The information such as name, age, sex, weight, date of admission, diagnosis, and name of antibacterial agent, dosage form, and route of administration, total duration and total dose of antibiotic agent administered is recorded in paper CRF and converted in to Microsoft excel sheet. [6]

The WHO prescribing indicators were used in this study.

The prescribing indicators that were measured included:

1. The average number of drugs prescribed per encounter was calculated to measure the degree of polypharmacy. It was calculated by dividing the total number of different drug products prescribed by the number of encounters surveyed. Combinations of drugs prescribed for one health problem were counted as one.
2. Percentage of drugs prescribed by generic name is calculated to measure the tendency of prescribing by generic name. It was calculated by dividing the number of drugs prescribed by generic name by total number of drugs prescribed, multiplied by 100.
3. Percentage of encounters in which an antibiotic was prescribed was calculated to measure the overall use of commonly overused and costly forms of drug therapy. It was calculated by dividing the number of patient encounters in which an antibiotic was prescribed by the total number of encounters surveyed, multiplied by 100.
4. Percentage of encounters with an injection prescribed was calculated to measure the overall level use of commonly overused and costly forms of drug therapy. It was calculated by dividing the number of patient encounters in which an injection was prescribed by the total number of encounters surveyed, multiplied by 100.
5. Percentage of drugs prescribed from an essential drug list (NLEM) was calculated to measure the degree to which practices conform to a national drug policy as indicated in the NLEM. Percentage is calculated by dividing number of products prescribed which are in essential drug list by the total number of drugs prescribed, multiplied by 100. [7]

2.6 Data Analysis

The data was analyzed using Microsoft excel.

III. RESULTS AND DISCUSSION

3.1 Patients demographic details

Total 400 patients who meet inclusion and exclusion criteria during the study period, December-2018 to March-2019 are being in the study.

3.1.1 Classification of patients by gender

The study population comprised of 319(80%) male and 81(20%) female in prescriptions as shown in table. 1 and figure. 1

table 1. classification of patients by gender

Gender	Frequency	Percentage
Male	319	80%
Female	81	20%
Total	400	100%

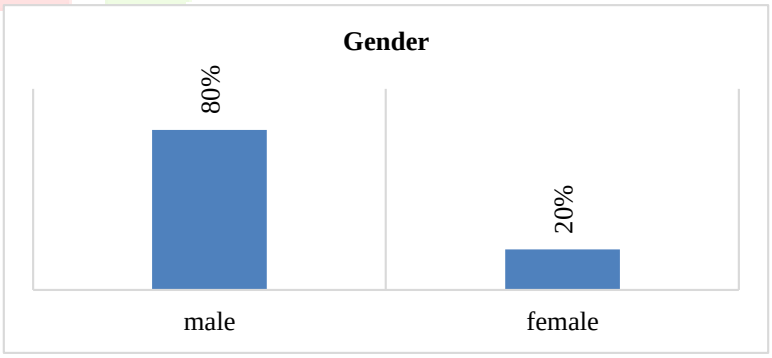

figure 1. classification of patients by gender

3.1.2 Classification of patients by age

Patients have been divided in different age groups in years as follows 18-38, 39-58, 59-78, 79-98, >98 years.
It was found that 36% of patients belonged to age group of 18-38 years, 39% of patients belonged to age group 39-58 years, 241% of patients belonged to 59-78 years, 3% of patients belonged to 79-98 years and 0% of patients belonged to >98 years as shown in table 2 and figure 2. It was observed that higher number of patients was found in age group 39-58 years and age group 18-38 years

table 2. classification of patients by age

Age	Frequency	Percentage
18-38	142	36%
39-58	154	39%
59-78	94	24%
79-98	10	3%
Total	400	100%

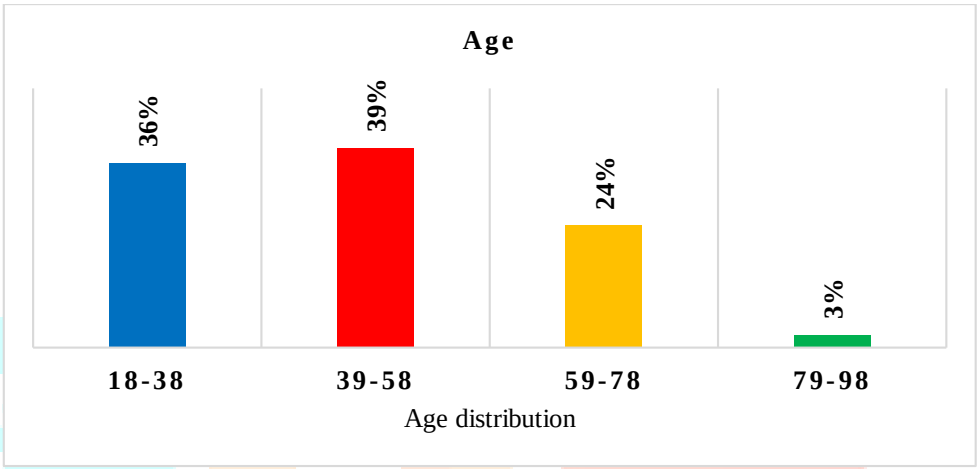

figure 2. classification of patients by age

3.1.3 Patients distribution by Length of Stay

It was observed that 316 number (79%) of patients had 1-5 treatment days, 67 (17%) patients were found in 6-10 treatment days and 17(4%) patients were 11-15 treatment days as shown in table 3 and figure 3.

table 3. patient's distribution by length of stay

Length of Stay	Frequency	Percent
1-5	316	79%
6-10	67	17%
11-15	17	4%
Total	400	100%

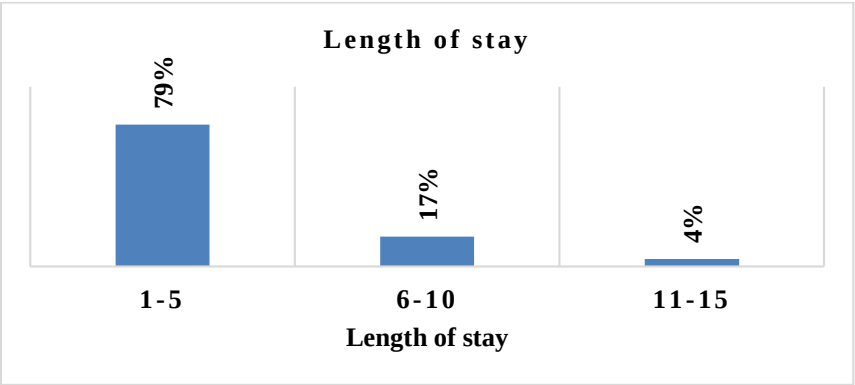

figure 3. patient's distribution by length of stay

3.2 Patients distribution by diagnosis

It was observed that 171 (20%) patients were found in accident patients. CNS disorders were seen in 167 (19%) patients. 155 (18%) patients were found with CVS disorders. Respiratory related ailments were seen in 126 (14%) patients.
Hormonal disorders were found in 80 (9%) patients. Gastro Intestinal disorders were seen in 54 (6%) patients. Infectious disease & Muscular disease were seen in 35(4%), 27(3%) patients. <18 patients were found in other disorders like Renal disease, Hepatic disorders, Poisoning etc as shown in table 4 and figure 4.

table 4. patient's distribution by diagnosis

Provisional Diagnosis	Frequency	Percent
CVS disorders	155	18%
CNS disorders	167	19%
Respiratory disorders	126	14%
Renal disorders	28	3%
Hepatic disorders	8	1%
GIT disorders	54	6%
Blood disorders	7	1%
Infections	35	4%
Hormonal disorders	80	9%
Muscular disorders	27	3%
Surgery	1	0%
Poisoning	3	0%
Cancer	5	1%
Bone disorders	4	0%
Accidents	171	20%
Total	871	100.00%

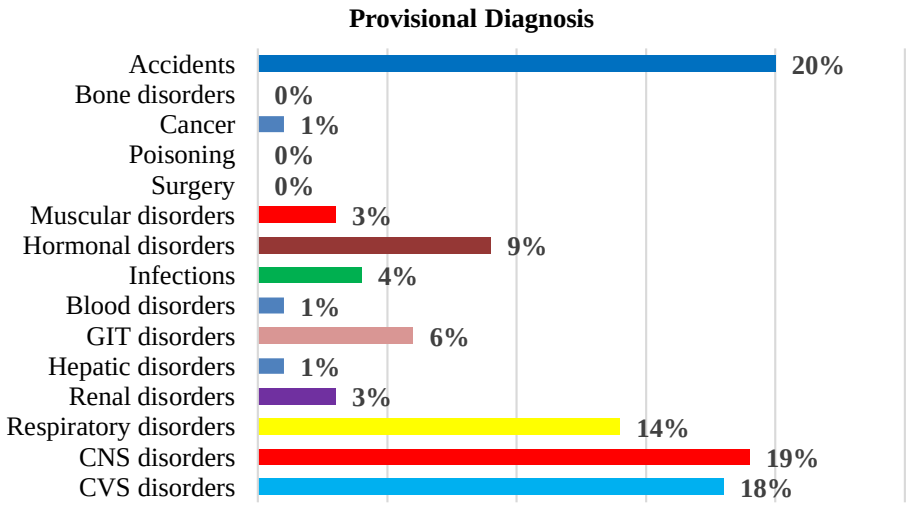

figure 4. patient's distribution by diagnosis

3.3 Drug prescribed by Generic and Brand name

It was found that 2550 (37%) drugs were prescribed by Generic name and 4355 (63%) drugs were prescribed by Brand name as shown in table 5 and figure 5.

table 5. drug prescribed by generic and brand name

Category	Number of drugs	Percentage
Brand name	4355	63%
Generic name	2550	37%
Total	6905	100%

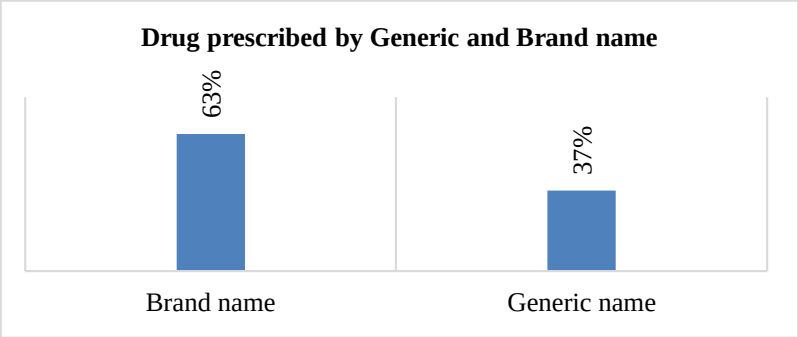

figure 5. drug prescribed by generic and brand name

3.4 Patients distribution by number of prescribed drugs

It was found that maximum 46% of patients were prescribed by 21-40 number of drugs, 18% prescribed by 0-20 number of drugs, least 3% of patients were prescribed by 81-100 number of drugs and 5% of patients were prescribed by maximum 101-120 number of drugs.

table 6. patient's distribution by number of prescribed drugs

Class limit	Frequency	Percentage
0-20	70	18%
21-40	183	46%
41-60	67	17%
61-80	47	12%
81-100	10	3%
101-120	21	5%
121-140	1	0%
141-160	1	0%
Total	400	100%

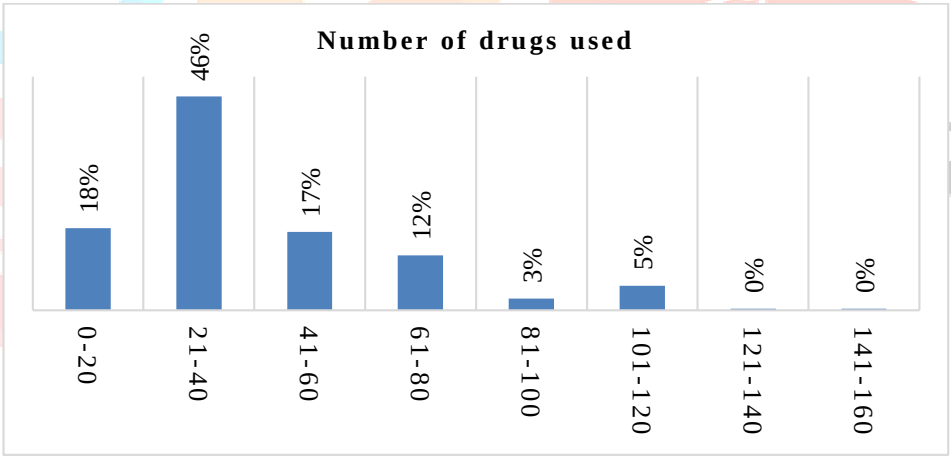

figure 6. patient's distribution by number of prescribed drugs

3.5 Patients distribution by number of antibiotics used

It was found that 0-10 number of antibiotics were prescribed in maximum 299(75%) number of patients, Maximum 30-40 number of antibiotics were prescribed to least 12(3%) number of patients, 11-20 number of antibiotics were prescribed to 60(15%) and 21-30 number were prescribed to 29(7%) of patients as shown in figure 7.

table 7. patient's distribution by number of antibiotics used

Class limit	Frequency	Percentage
0-10	299	75%
11-20	60	15%
21-30	29	7%
30-40	12	3%
Total	400	100%

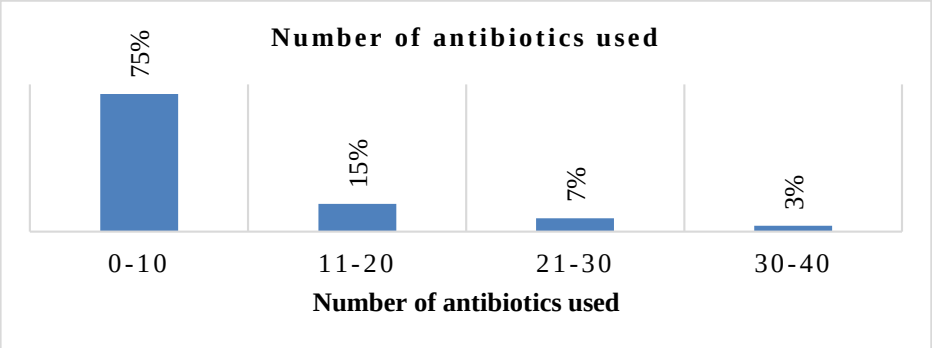

figure 7. patient's distribution by number of antibiotics used

3.6 Patients distribution by number of injections used

It was found that 1-20 number of injections prescribed to maximum 169 (42%) number of patients, following 21-40 number of injections prescribed to 136 (34%) number of patients, Maximum 101-120 injections prescribed to 14 (4%) number of patients as shown in figure 8.

table 8. patient's distribution by number of injections used

Class limit	Frequency	Percentage
1-20	169	42%
21-40	136	34%
41-60	47	12%
61-80	28	7%
81-100	5	1%
101-120	14	4%
121-140	1	0%
Total	400	100%

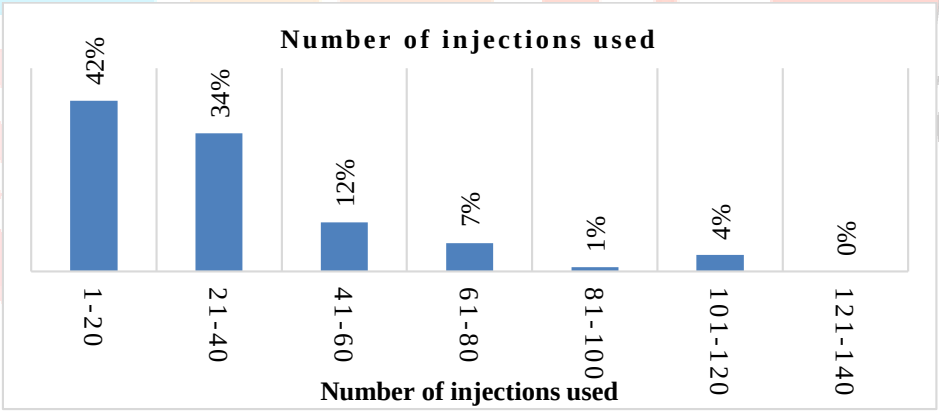

figure 8. patient's distribution by number of injections used

3.7 Essentiality status of prescribed drugs from National List of Essential Medicine (NLEM-2015)

The extent of essential and non-essential drug from NLEM-2015 was found to be 8722 (53%) and 7730 (47%) prescribed respectively as shown in table 9 and figure 9.

table 9. essentiality status of prescribed drugs from nlem

Category	Frequency	Percentage
Essential drug	8722	53.01%
Nonessential drug	7730	46.99%
Total	16452	100%

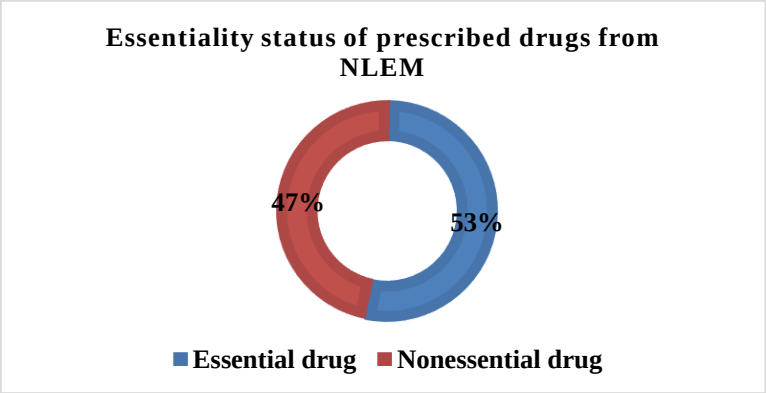

figure 9. essentiality status of prescribed drugs from NLEM

3.8 Antibiotics used

It was found that ceftriaxone is in maximum frequently prescribed in 234 (25%) number of patients, followed by Amikacin, Piperacillin-Tazobactam, Amikacin-Clavulanic acid prescribed in 156(17%), 94(10%), 82(8%) number of patients respectively. Sulbactam, Ciprofloxacin, Colistin, Erythromycin, Methicillin, Clindamycin, Netilmicin, Azithromycin were least used as shown in table 10 & figure 10(a) and 10(b).

table 10. antibiotics used

Antibiotics used	Frequency	Percentage
Ceftriaxone	234	24.9%
Amikacin	156	16.6%
Amikacin + Clavulanikacid	82	8.7%
Piperacillin + Tazobactam	94	10.0%
Linezolid	33	3.5%
Metronidazole	53	5.6%
Meropenem	49	5.2%
Moxifloxacin	18	1.9%
Imipenem	36	3.8%
Cefotaxime + Sulbactam	23	2.4%
Ceftazidime	40	4.3%
Netilmicin	5	0.5%
Cefuroxime	12	1.3%
Cefixime	4	0.4%
Cefepime + Sulbactam	1	0.1%
Ofloxacin + Ornidazole	9	1.0%
Ofloxacin	6	0.6%
Benzathine Penicillin	4	0.4%
Clarithromycin	9	1.0%
Tobramycin	4	0.4%
Cefadroxil	4	0.4%
Cefoperazone + Sulbactam	5	0.5%
Cefpodoxime	3	0.3%
Levofloxacin	12	1.3%
Azithromycin	2	0.2%
Ceftriaxone + Tazobactam	1	0.1%
Ceftriaxone + Sulbactam	2	0.2%
Sulbactam	2	0.2%
Amoxicillin	6	0.6%
Vancomycin	6	0.6%
Ciprofloxacin	4	0.4%
Colistin	2	0.2%
Erythromycin	2	0.2%
Methicillin	4	0.4%
Cefepime	4	0.4%
Clindamycin	2	0.2%
Cefpodoxime + proxetil	8	0.9%
Total	941	100%

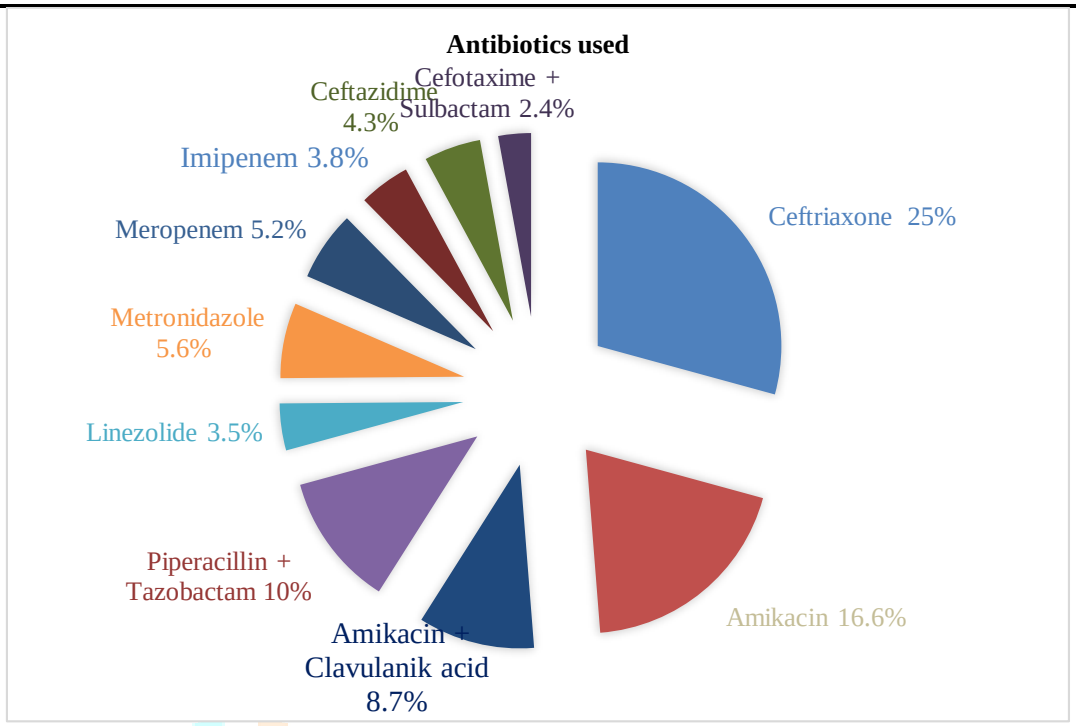

figure 10. (a) antibiotics used

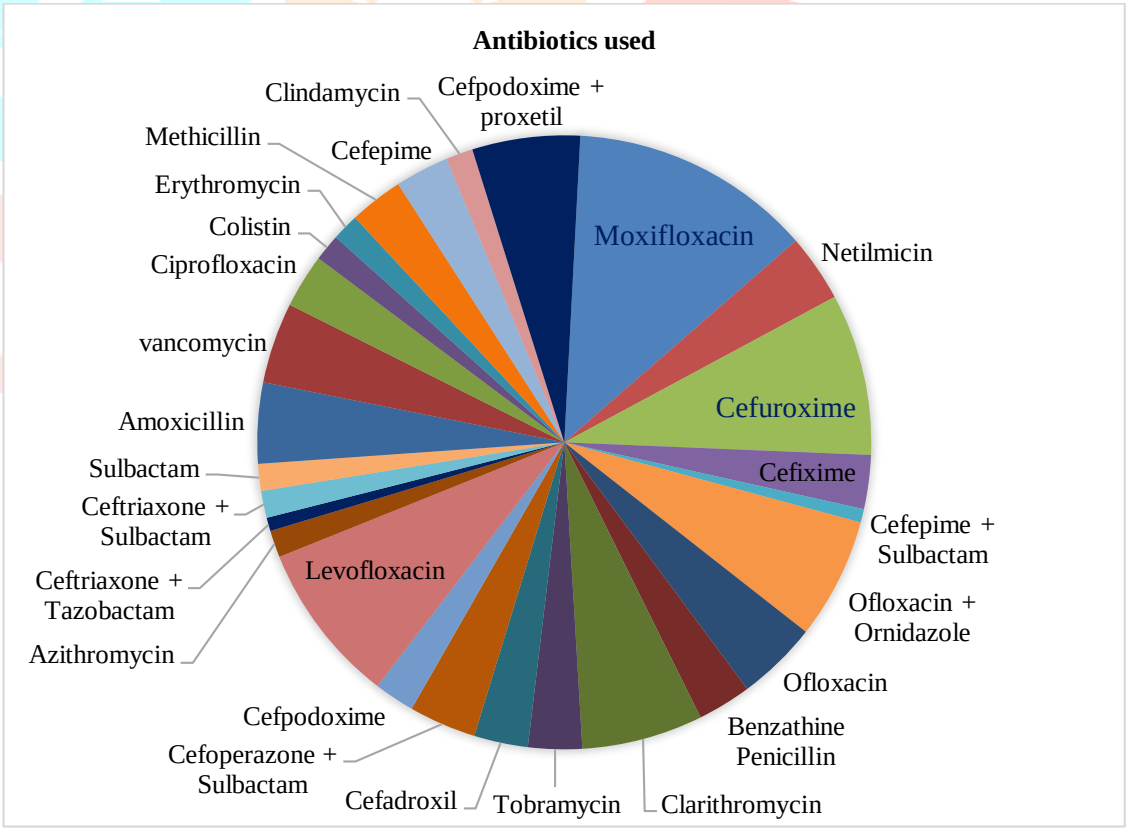

figure 10. (b) antibiotics used

3.9 Patients distribution by number of prescribed Antibiotics

It was found that one antibiotic was prescribed in 129 (32%) patients, two antibiotics were prescribed in 73 (18%), three antibiotics were prescribed in 99 (25%), four antibiotics were prescribed in 48 (12%), five antibiotics were prescribed in 33 (8%) of patients and six antibiotics were prescribed in 2(1%) of patients as shown in table 11 and figure 11.

table 11. patient's distribution by number of prescribed antibiotics

Number of antibiotics used	Frequency	Percent
0	16	4%
1	129	32%
2	73	18%
3	99	25%
4	48	12%
5	33	8%
6	2	1%
Total	400	100%

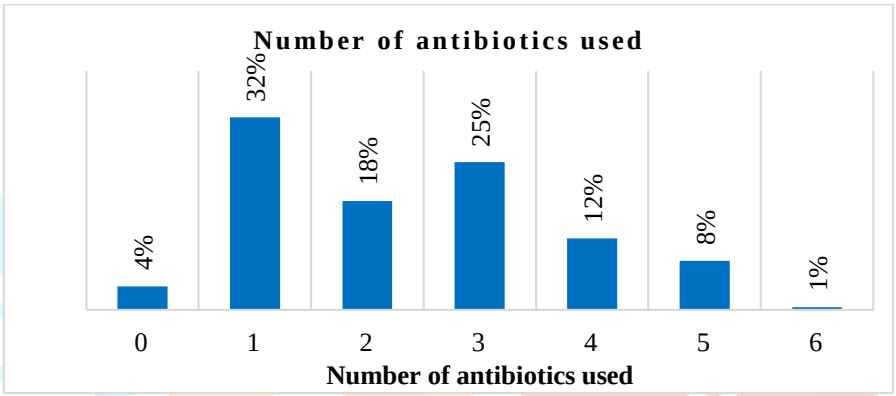

figure 11. patient's distribution by number of prescribed antibiotics

3.10 Class of Antibiotics used

Maximum 320 (27.6%) patients were prescribed by third generation cephalosporin, followed by beta lactamase inhibitors were prescribed in 210 (18%) number of patients, aminoglycosides and penicillins were prescribed in 165(14.2%) and 190 (16.4%) of patients. First generation cephalosporin, fourth generation cephalosporin, glycopeptides, polymyxin, lincosamides were least prescribed as shown in table 12 and figure 12.

table 12. class of antibiotics used

Class of Antibiotics used	Frequency	Percentage
First Generation Cephalosporin	4	0.3%
Second Generation Cephalosporin	12	1.0%
Third Generation Cephalosporin	320	27.6%
Fourth Generation Cephalosporin	5	0.4%
Aminoglycoside	165	14.2%
Penicillin	190	16.4%
Beta Lactamase Inhibitors	210	18.1%
Oxazolidinones	33	2.8%
Nitroimidazole Derivative	62	5.4%
Carbapenems	85	7.3%
Second Generation Fluoroquinolones	19	1.6%
Third Generation Fluoroquinolones	12	1.0%
Fourth Generation Fluoroquinolones	18	1.6%
Macrolides	13	1.1%
Lincosamides	2	0.2%
Glycopeptides	6	0.5%
Polymyxins	2	0.2%

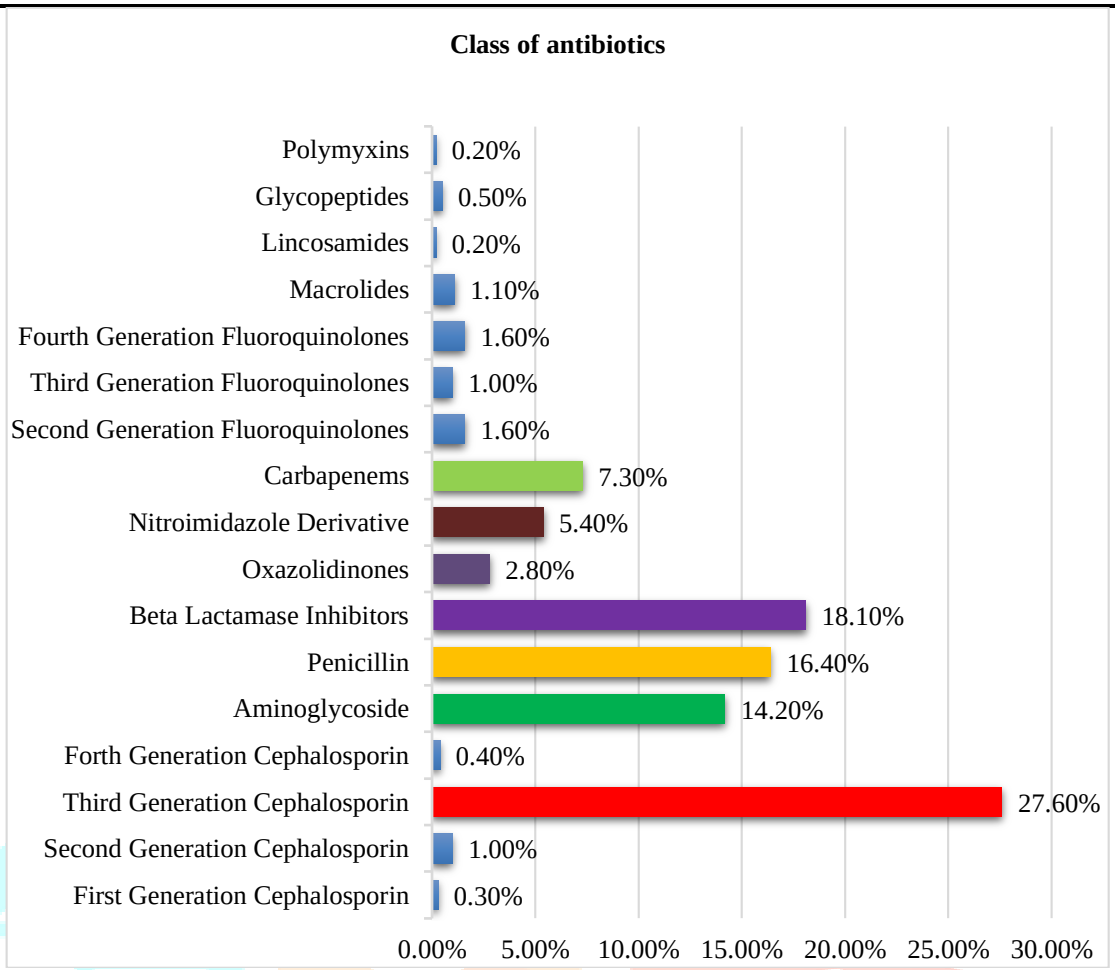

figure 12. class of antibiotics used

3.11 Summary of results obtained

table 13. summary of results obtained

Prescribing Indicators Assessed	Total drugs /encounter	Average/Percent	Standard derived or ideal
• Average number of drugs per encounter	16,452	4.11	(1.6-1.8)
• Percentage of encounter with antibiotics	384	96 %	(20.0-26.8%)
• Percentage of encounters with injection	400	100 %	(13.4%-24.1%)
• Percentage of drugs prescribed by generic	2550	15.49 %	100%
• Percentage of drugs from essential drug list	8722	53 %	100%

3.12 Discussion

This observational, prospective and multicenter research study was conducted on 400 ICU patients prescriptions. The prescription demographic details showed higher male 319(80%) to female 81(20%) proportion with mean age of 39-58 years, Similar to study done in South India by Pandiamunian et al [8] where male female ratio was 63:37 & average age was 53 years, in Dharmapuri medical college hospital in South India (174:126) [9] average age 59.2 years, other than that in study done in Qatar by yolande Hassens et al [10] where female patiets 68% where greater compared to male 31.5%. The probable reasons may be the sociological factors in this part of the country or could be the male to female ratio is higher in the Mehsana city, Gujarat. it is noticed that female populations are reluctant to utilize health care facilities even if they are critically ill.

The higher number of patients (79%) were found shorter length of stay 1-5 days compared to for example 5.8 days in Qatar by yolande Hassens et al, [10] 6-10 days in Kerala, India by Lekshmi B Chandran et al [9] might be due to relative short study period.

The common provisional diagnosis in our study were Accidents, CNS disorders, CVS disorders. The most common illnesses which required ICU admission in our study was Accidents, CNS disorders, CVS disorders which was different from a previous study where the most common cause of admission in ICU settings were cerebrovascular accident followed by chronic kidney disease, road traffic accident and heart ailments. [9]

With regard to the average number of drugs per prescription, the value found in the present study was 4.11. On the other hand, average number of drugs in the study of Dharmapuri medical college hospital in South India was less, [9] 1.9 at Hawassa University Hospital, South Ethiopia, [11] found 10.4 by Pandiamunian at South India. The variation in results may be due to difference in characteristics of health care delivery system, socioeconomic profile, and morbidity and mortality characteristics in the population. Since, WHO has recommended that average number of drug per prescription should be 2.0, [12] the results of our study reflects polypharmacy which may lead to adverse drug reactions, decrease adherence to drug regimens and unnecessary drug expenses. In contrast, since the medical department encountered highest number of prescriptions with a larger number of drugs prescribed for chronic clinical conditions like hypertension, and diabetes, the patients can require more drugs than as stated by WHO. In such cases polypharmacy can be acceptable. [13]

The percentage of encounters in which antibiotics were prescribed was 96%, which is very high compared to the standard (20.0%-26.8%) derived to be ideal [14] for example 76% were received antibiotics Qatar by Yolande Hanssens [10] & uses 94.4% antibiotics in the study at Sir Takhtsinhji general hospital, Bhavnagar, Gujarat by Mahendra Patel. [15] This finding suggests that antibiotic prescribing needs to be regulated. The high percentage of antibiotics prescribed in our study setting may be due to cultural beliefs about antibiotics, patient expectation to receive antibiotics, or prescribers' belief that the therapeutic efficacy of antibiotics is low. Overuse of antibiotics (96%) is an indication of a problem because it could facilitate emergence of resistance. In addition, empirical treatment is also a problem, where two or more drugs are prescribed but one specific antibiotic is enough after proper diagnosis.

Third Generation Cephalosporin (27.6%) and Beta Lactamase Inhibitors (18%) were the most commonly prescribed groups of AMAs in this study. The commonest AMA prescribed was Ceftriaxone 234 (25%) this is in accordance with similar study done in South India where Ceftriaxone was prescribed most in patients (23%), Ceftriaxone was prescribed in 57% as initial therapy in Qatar by Yolande Hanssens. [10] This may be due to cephaolosporins being safer with a fewer adverse effects & are effective against most common pathogens, they are being prescribed more in this decade for empirical therapy in the Intensive Care Units

The percentage of encounters in which an injection was prescribed that was 100%, which is higher than the standard (13.4%-24.1%) derived to serve as ideal. [14] Similarly percentage of encounters in which an injection was at Hawassa University Hospital was 38.1% higher than the standard, [11] 87.5% in the study of Dharmapuri medical college hospital in South India. [9] Possible reasons for the high use of injections could be (i) beliefs and attitudes of patients and health professionals about the efficacy of injection versus oral medication or (ii) our study setting is a referral hospital where patients with serious conditions are treated, and injectable forms produce faster onset of action. Injections are very expensive compared to other dosage forms and require trained personnel for administration. Moreover, unhygienic use of injections can increase the risk of transmission of potentially serious pathogens, such as hepatitis, HIV/AIDS, and blood-borne diseases.

The percentage of drugs prescribed by generic name was 15.49 % in our study which is less than WHO prescribed value. Which is similar to the study conducted in Western Nepal (15%), [16] only 13.8% prescribed by generic in the study did at Kerala, India [5] & lower compared to study occurred in South Ethiopia. [11] The factor that might have contributed to the low proportion of generic drug prescription is the poor promotion and low production of generic drugs in Gujarat. The use of generic names is recommended by WHO and regarded as an important factor for promoting RUD. The use of generic name contributes to cost reduction and provides more alternatives for drug purchases. [17]

Our study revealed that the percentage of drugs prescribed from national EDL was 53%. Which is comparatively higher than study conducted in Western Nepal (32.8%) [18] & lower than study done in South Ethopia (96.6%). [11] The possible reason for this lower value could be the prescribers lacking the understanding and importance of essential drug concept and formulary. However, it should not be ignored that essential drugs are specially meant for primary health care delivery system, whereas our study was conducted in a tertiary care hospital

IV. Acknowledgment

The authors express their gratitude to Liance general hospital and Astha ICU of mehsana for giving permission for data collection. The authors are thankful to the management of Shri Sarvajanik Pharmacy College, Gujarat for providing the facilities to carry out the research work.

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