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Original Article

A Prospective Study on Evaluation of Antibiotic Usage Pattern in Hospitals

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ABSTRACT

Background: Antibacterials are the most imperative weapons in our hands accounting for majority of ambulatory care prescriptions and one of the most irrationally prescribed drugs. Irrational usage can lead to treatment failure, increase cost burden, lack of availability of drug molecule to treat life-threatening infections and affect patient's quality of life significantly. **Aim:** To study the usage pattern of antibiotics in hospitals. **Objectives:** The primary objective was to assess the prescribing pattern of antibiotics. The secondary objectives of study were to study World Health Organization prescribing indicators for antibiotics, calculate the Defined Daily Dose and to evaluate the cost burden. **Materials and Methods:** A prospective study was conducted for 6 months with 405 patients. Self-designed proforma for data collection was used. Anatomical Therapeutic Chemical Classification System classification and Defined Daily Dose system was used for the quantification of drug utilization. Descriptive statistical analysis was done using Microsoft excel and Statistical Package for Social Sciences. **Results:** Average hospital stay was 5.27±1.93 days. Out of 4934 prescribed drugs, 860 were antibiotics of which 641 were in parenteral formulation. Most of the antibiotics were prescribed by brand name. Cephalosporin/B-lactamase inhibitor (22.97%) was the largely prescribed class. Antibiotics shared 50.04% of the total cost of all drugs. Culture test was performed in 34 patients. **Conclusion:** Performing the culture sensitivity test before prescribing antibiotics should be implemented which can reduce the expense, client frustration with blind antibiotic trials, lower the risk of complications and antibiotic resistance, and improve the chance and speed of patient's recovery.

Keywords: Antibiotics, Usage pattern, Resistance, Cost, DDD.

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INTRODUCTION

Despite the fact that the most leading causes of death and disability in developing countries can be prevented, treated or at least alleviated with cost effective drugs, many people do not have regular access to essential drugs. On the top of that those who have access are using drugs irrationally. Anti-microbials are probably one of the most successful forms of chemotherapy in the history of medicine. Criteria to select an optimal antibiotic for a specific patient include efficacy, risk of adverse events, contraindications, costs of therapy, and details of the clinical condition of the patient. They are the most used therapeutic agents, accounting for the majority of ambulatory care prescriptions. Overuse of drugs (poly pharmacy), inappropriate use of antibiotics (often in inadequate dosage for nonbacterial infections) and overuse of injectable are the common types of irrational drug use which could lead to poor treatment outcomes, drug-drug interactions, high economic burden and to the worst-case loss of the patient's life.[1-6]

Antibiotics are the second leading drugs prescribed according to the national ambulatory medical care. Antibiotic use has been increasing steadily in recent years. Between 2005 and 2009, the units of antibiotics sold increased by about 40%. Increased sales of cephalosporin were particularly striking, with sales (in units sold) increasing by 60% over that five-year period, but some increase was seen in other antibiotic classes also. Factors such as eagerness to provide quick relief to patients have promoted the misuse of antibiotics. It can be also caused by various factors such as health facilities, medication non-adherence, multiple prescribers and dispensers, use of first-generation medications, inappropriate usage of medication, intake of wrong dosage, and incorrect usage of medications, use of counterfeit drugs, over and under usage of medications. During the past two decades, resistance to antibiotics has become a major public health concern due to the rapid spread of multi-resistant bacteria clones. Within seven years of penicillin use, 50% of hospital *Staphylococcus aureus* isolates were resistant.[2,7-10]

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The mass production of antimicrobials gave humanity a temporary advantage in the struggle with microorganisms; however, if the current rate of increase in resistance to antimicrobial agents continues, it is possible we may enter into what some have termed the post-antibiotic era. New methods to optimize antibiotic selection, dose, and duration of therapy are being investigated, and application of some of these strategies has been shown to have a favorable impact on resistance. Much of the classic thinking of how to use antibiotics is changing, and these newer strategies may result in prolongation of the era of the "antibiotic miracle."[4,11]

Bacterial resistance to antimicrobial agents due to the increasing use of antimicrobial agents has become a worldwide concern. Over the past several decades, the increased prevalence of known resistant organisms and the emergence of newly resistant organisms such as penicillin-resistant *Pneumococci*, methicillin resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococci*, extended-spectrum beta-lactamase producing *Escherichia coli, Klebsiella pneumoniae*, and imipenem-resistant gram-negative bacilli, have resulted in delays in effective therapy and the length of hospitalization, and have led to increased costs for patients.[12]

Keeping these facts in mind, the present study was planned mainly because of large number of antibiotics being used now-a-days and secondly the development of antibiotic resistance due to its irrational use which can lead to its ineffectiveness in case of life-threatening infections.

Aim

To evaluate the usage pattern of Antibiotics.

Objective

Primary

- To assess the prescribing pattern of antibiotics in tertiary care hospitals.
- To study the indications for which the antibiotics are being prescribed.
- To assess relationship between patient demographics and prescription pattern.

Secondary

- To study WHO prescribing indicators for antibiotics.
- To identify most prescribed antibiotic.
- To calculate the Defined Daily Dose of antibiotics.
- To assess the cost burden of antibiotics.

MATERIALS AND METHODS

Study Criteria and Population

This was a prospective observational study conducted over a period of 6 months from date of ethics approval; October 2017 to March 2018. The study was conducted in 4 private hospitals of Ahmedabad and Gandhinagar (Gujarat, India) with the approval from the board of management. A total of 405 patients fulfilling the inclusion criteria were recruited for the study. Hospitalized patients on antibiotics with age >18 years of either gender were included in the study. The patients had to be hospitalized for more than 24 hr and had to sign informed consent form for fulfilling the inclusion criteria. This study excluded unconscious or semi-conscious patients and women patients who were pregnant or lactating.

Data Collection Form

Patient Data Collection Form was designed as a mean of data collection tool. All the information and data which was required to study the antibiotic usage pattern were included in Patient Data Collection Form. The form was divided in 9 sections:

Section 1 contains details about patient's demographic information like name, age/sex, diagnosis, date of admission, date of discharge, height, weight and BMI (if measured).

Section 2 contains details about patient's histories-medical/surgical, medication, social, family, and allergy.

Section 3 contains details about the laboratory tests performed and all the abnormal laboratory findings were noted with their reference range and their follow-ups.

Section 4 contains information about the treatment chart and the progress note which includes brand name of drug, generic name, dose, route, frequency, cost/unit, days of treatment and day-wise follow-up report.

Section 5 contains information regarding therapy safety issues related to antibiotics which include Adverse Drug Reaction-suspected antibiotic, indication, and description of reaction, date of onset, management and outcome. Other sub-section includes information related to drug interactions due to antibiotics.

Section 6 contains the Modified Kunin's Criteria.

Section 7 contains details regarding the WHO Drug use indicators like drugs per prescription, antibiotics per prescription, antibiotics by generic name, antibiotics by brand name, Fixed Dose Combinations, antibiotics prescribed from NLEM, switch on therapy from parental to oral route and various formulations of antibiotics used.

Section 8 includes remarks if any-if any other test is performed.

Section 9 includes the list of class of antibiotics used and drugs, total amount of particular drug used and cost of all other drugs and cost of each antibiotic.

Study Procedure

Screening and Enrollment: Screening was done based on the inclusion and exclusion criteria and the patients were recruited for the study after informed consent process.

Patient's data was collected using Data Collection Form.

If any, ADR was reported during study, it was mentioned in the Data Collection Form. ADR reporting practice was not well developed in all the selected sites. So very few ADR were reported.

Drug Interactions related to antibiotics was found using mobile applications-Micromedex Drug Interactions v2.7 and Medscape v4.5.2

The costs of drugs were obtained from hospital pharmacy store and MIMS India.

The ATC code and DDD was obtained from WHO website.

DDD was calculated using formula given below:

$$\text{DDD/100 inhabitants/day} = \frac{\text{Amount of Drug Administered During Study Period (in g)}}{\text{(WHO DDD (in g) x No. of Subjects x Study Period}} \times 100$$

Data collected was kept confidential and analysed statistically.

Data Management

Statistical analysis was performed using MS Office Excel 2016, SPSS Statistics 25 and Graphpad Prism 7. Descriptive analysis was represented as mean with standard deviation, frequency, percentage, range to present preliminary data. Chi square test was performed to test the level of significance of factors like age, gender, duration of hospital stays and no. of antibiotics and cost of antibiotics. Univariate analysis was performed between cost of antibiotics and cost of total drugs to find comparison in groups like sex, age and duration of stay. (CI=95%, α=0.05). Data was said to be statistically significant if $p<0.05$. Linear Regression analysis was performed between related variables.

RESULTS

Response Rate

A total of 405 subjects satisfied the eligibility criteria were enrolled into the study. All the subjects participated and completed the study. Therefore, the response rate was 100%.

Data Interpretation and Distribution

Demographics of study

Out of 405 patients, 180 patients were female, and 225 patients were male. The demographic details are mentioned in Table 1.

Subjects of age group 51-60 yrs (69 subjects) were maximum and of age group >91 yrs (7 subjects) were minimum. The average duration of stay was found to be 5.27±1.93 days.

Drug interactions with antibiotics

Major (67%), moderate (6%) and minor (27%) drug interactions related to antibiotics were found out. The frequency distribution of which is given in Table 2.

WHO prescription analysis

All the 405 prescriptions with antibiotics were analysed using WHO Antibiotic use indicators. The frequency distribution of the same is mentioned in Table 3.

860 antibiotics were prescribed from total of 4934 drugs. Average drug prescribed per prescription was 12.18 while the average antibiotic per prescription was 2.12. 64 and 796 drugs were prescribed by generic name and brand name respectively. 262

Table 1: Demographic details.

		Sex		Total
		Female	Male	
Age (Years)	≥20	14	19	33
	21-30	31	32	63
	31-40	26	40	66
	41-50	21	32	53
	51-60	32	37	69
	61-70	27	31	58
	71-80	20	21	41
	81-90	5	10	15
	≥91	4	3	7
Mean±SD		49.32±20.10	48.69±19.66	48.97±19.84
Hospital Stay (days)		5.08±1.56	5.42±2.16	5.27±1.93

Table 2: Drug interactions with antibiotics.

Drug Interaction	Total	Percentage (%)
Major	226	67
Moderate	20	6
Minor	90	27
Total	336	100

Table 3: WHO prescription analysis.

Parameter	Number (%)
Total No. of Prescription	405
Total No. of Drugs	4934 (100%)
Total No. of Antibiotics	860 (17.43%)
Average No. of Drugs/ Prescription	12.18
Average No. of Antibiotics/ Prescription	2.12
Antibiotics by Generic Name	64 (7.44%)
Antibiotics by Brand Name	796 (92.56%)
Antibiotics in Fixed Dose Combination	262 (30.47%)
Antibiotics Prescribed from NLEM	474 (55.12%)
Switch Over therapy	31 (3.60%)

Table 4: Formulations of antibiotics used.

Formulations	Number	Percentage (%)
Parenteral	641	74.53
Tablet	201	23.37
Capsule	9	1.05
Syrup	0	0.00
Eye drop	3	0.35
Ear drop	0	0.00
Others	6	0.70

FDC were used. 474 antibiotics were prescribed from NLEM and 31 i.v. to oral conversion were found.

Formulations of antibiotics used

Various antibiotic formulations were prescribed during the study period. Parenteral antibiotics accounted for a major share of 74.53% followed by tablets and capsules with 23.37% and 1.05% respectively. The frequency distribution of the same is given in Table 4.

Number of antibiotics per prescription

Based on the severity of the infection and culture test reports, the number of antibiotics prescribed per prescription may be more than 1. The frequency distribution of the same is given in Table 5.

It was found that 38% prescription had 2 antibiotics, 31.6% prescriptions had 1 antibiotic and 20% and 10.4% prescriptions had 3 and >4 antibiotics respectively.

Factors affecting the numbers of antibiotics prescribed

The numbers of antibiotics prescribed are based on various factors like gender, age, duration of hospital stay. The hypothesis testing of the same is done in table given in Table 6:

As shown in the table, antibiotics prescribed were compared with age, gender and duration of stay. But only duration of stay (p-value <0.001) was found to be statistically significant. This means that only duration of stay affects the number of antibiotics prescribed.

Table 5: Number of Antibiotics/Prescription.

No. of Antibiotics	Frequency	Percentage (%)
1	128	31.6
2	154	38.0
3	81	20.0
≥4	42	10.4
Total	405	100.0

Table 6: Factors affecting the numbers of antibiotics prescribed.

Factors			No. of Antibiotics				
		N	1	2	3	≥4	*p*-Value
Gender	Male	225	72	83	39	31	0.0535
	Female	180	56	71	42	11	
Age (Years)	≤20	33	9	15	5	4	0.5190
	21-40	129	44	48	19	18	
	41-60	122	38	47	26	11	
	61-80	99	28	36	28	7	
	>80	22	9	8	3	2	
Hospital stay (Days)	≤6	332	117	130	64	21	<0.001*
	7-11	68	11	23	17	17	
	12-16	4	0	1	0	3	
	>17	1	0	0	0	1	

*p-value <0.05 means statistically significant (Univariate Analysis).

Table 7: ADR related to antibiotics.

Suspected Antibiotic	Reaction	Number of Subjects
Ceftriaxone	Diarrhoea	1
Amoxicillin/ Clavulanic Acid	Diarrhoea	2

Adverse Drug Reactions related to antibiotics

Very few ADR were reported in this study and the same is presented in Table 7.

The practice of ADR reporting was poor in our study site. Three patients suffered from ADR due to Ceftriaxone and Amoxicillin/ Clavulanic acid. The reaction observed was diarrhoea. For the management of this ADR, Tab. Racecadotril was given. For prophylactic purpose, non-pharmacological treatment like ORS powder and curds were also recommended.

Antibiotics prescribing frequency

The frequency of the antibiotics prescribed during the study period was classified according to ATC Code. The frequency distribution is depicted in Figure 1.

In our study, it was found that Cephalosporins/B-lactamase inhibitors (23.05%) was largely prescribed class, which was followed by Cephalosporins (17.58%), Fluoroquinolones (15.83%), Nitroimidazoles (13.97%) and B-lactam/B-lactamase Inhibitor (7.57%).

DDD/1000 inhabitant days

The Defined Daily Dose for each antibiotic was calculated and same is presented in Table 8.

In our study it was found that the DDD/1000 inhabitant day was 11.344 for Cefoperazone/Sulbactam (iv), 10.911 for Ceftriaxone (iv), 7.27 for Metronidazole (iv), 5.96 for Azithromycin (PO) and 3.20 for Azithromycin (iv).

Cost analysis

Cost analysis was performed and presented in Table 9.

In our study, total cost of all drugs was Rs. 2200142.97. The share of antibiotics was about Rs. 1100850.43 (50.04%). The average cost of drugs/prescription was Rs. 5457.15±54976.33. The median

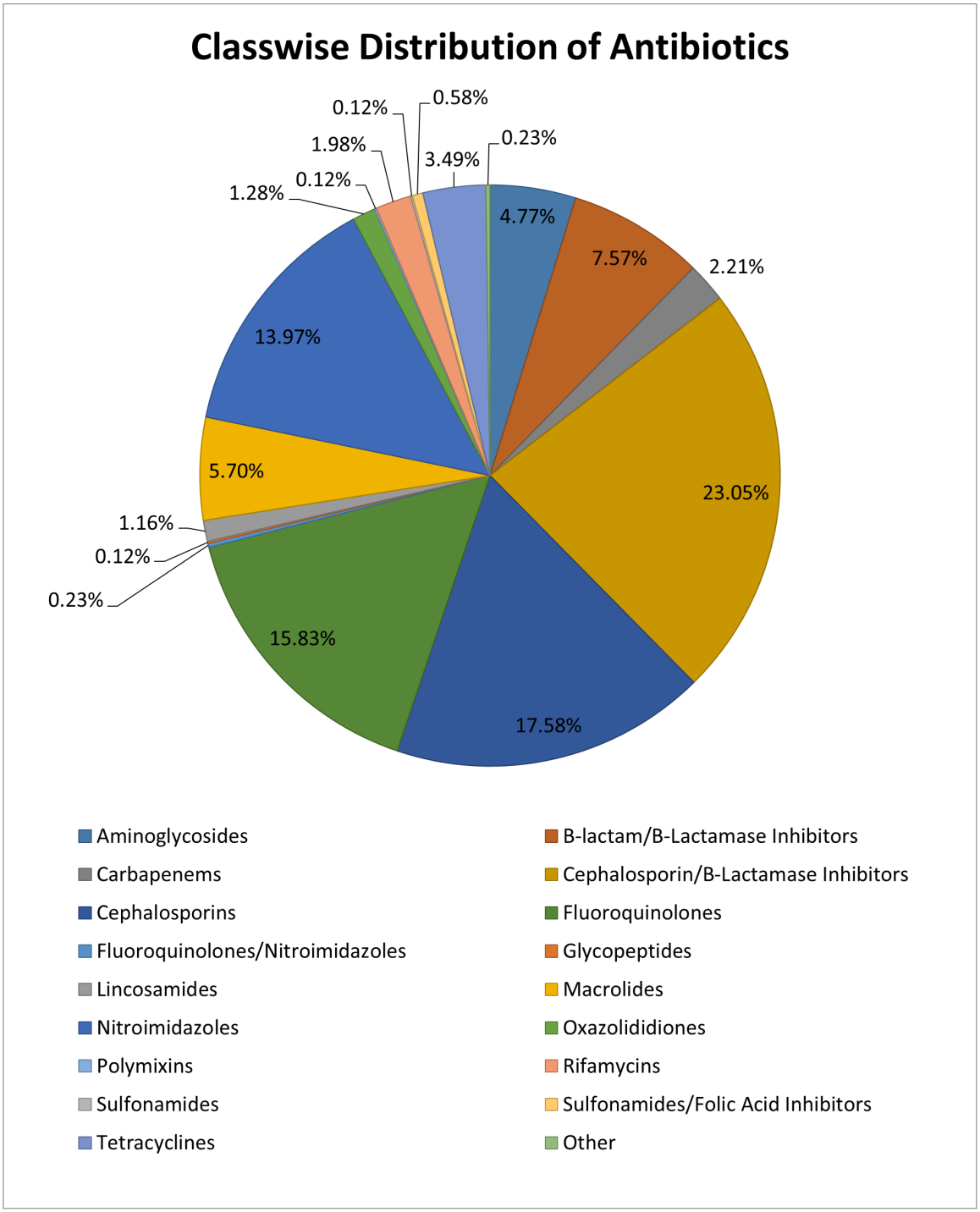

Figure 1: Class wise distribution of antibiotics.

cost of all drugs was Rs. 1726.40. 25th to 75th percentile cost of all drugs was Rs. 874.50-3407.09. In case of antibiotics, the average cost of antibiotics/prescription was Rs. 10872.39±109562.70. The median cost of antibiotics was Rs. 3228.81. The 25th to 75th percentile cost of antibiotics was Rs. 2019.03-6175.70.

Antibiotic wise distribution of cost

The cost distribution for each antibiotic is depicted in Figure 2.

In our study, Cephalosporins/B-lactamase Inhibitors shared major proportion of the total cost of antibiotics i.e. 43.55% followed by Carbapenems (13.87%), Penicillins/B-lactamase Inhibitor (11.10%) and Cephalosporins (10.90%).

Table 8: DDD/1000 inhabitant days.

Drug Name	Route	WHO - DDD (in g)	Total Drug used during Study Period (in g)	DDD/1000 inhabitants Days	Drug Name	Route	WHO - DDD (in g)	Total Drug used during Study Period (in g)	DDD/1000 inhabitants Days
Cefoperazone/ Sulbactam	IV	4	2591.3	11.344	Linezolid	PO	1.2	46.8	0.683
Ceftriaxone	IV	2	1246.2	10.911	Clindamycin	IV	1.8	59.1	0.575
Metronidazole	IV	1.5	623.5	7.279	Amoxicillin/ Clavulanic Acid	PO	1	31.375	0.549
Azithromycin	PO	0.3	102.25	5.969	Azithromycin	IV	0.5	15	0.525
Levofloxacin	PO	0.5	162.75	5.700	Moxifloxacin	PO	0.4	11.2	0.490
Levofloxacin	IV	0.5	91.5	3.205	Ofloxacin	PO	0.4	10.8	0.473
Cefixime	PO	0.4	64.4	2.819	Clarithromycin	PO	0.5	11.5	0.403
Doxycycline	IV	0.1	13.8	2.417	Ceftazidime	IV	4	87	0.381
Amikacin	IV	1	128.4	2.248	Linezolid	IV	1.2	24.6	0.359
Meropenem	IV	2	254	2.224	Cefotaxime	IV	4	69	0.302
Doxycycline	PO	0.1	11.1	1.944	Ornidazole	PO	1	10	0.175
Amoxicillin/ Clavulanic Acid	IV	3	331.8	1.937	Clindamycin	PO	1.2	11.7	0.171
Cefuroxime	IV	3	316.5	1.847	Ampicillin/ Sulbactam	IV	6	43.5	0.127
Piperacillin/ Tazobactum	IV	14	1459.5	1.826	Ampicillin/ Clavulanic Acid	IV	6	43	0.125
Rifaximin	PO	0.6	56.8	1.658	Ciprofloxacin	IV	0.5	3.2	0.112
Moxifloxacin	IV	0.4	32	1.401	Ciprofloxacin	PO	1	5	0.088
Ornidazole	IV	1	47.3	0.828	Cefpodoxime	PO	0.4	1.6	0.070
Ofloxacin	IV	0.4	16.7	0.731	Prulifloxacin	PO	0.6	1.8	0.053
Netilmicin	IV	0.35	0.3	0.015	Cefoperazone	IV	4	12	0.053
Cefuroxime	PO	0.5	0.125	0.004	Vancomycin	IV	2	6	0.053
Colistin	IV	3	0.036	0.000	Ampicillin/ Sulbactam	PO	6	12.75	0.037
Gentamicin	IV	0.24	0.36	0.026					

Impact of selected predictors on cost of antibiotics

Cost of antibiotics can depend on various factors like age, duration of stay. Regression analysis was performed to predict the influence of predictors on cost of antibiotics and same is depicted in Tables 10 and 11.

There is no association between age and cost of antibiotics as p-value>0.05. In case of duration of stay (p-value<0.001), p-value<0.05 so there is a strong linear relationship between cost of antibiotics and duration of stay.

The coefficient table shows the equation of the regression line, the slope of the line, the intercept at y-axis ad p-value. The slope of the line (B) is 1472.855., the intercept at y-axis is -392.230 and p-value is <0.001.

Y-axis: Cost of antibiotics.

X-axis: Duration of Stay.

The equation can be given as: y=1472.855x-392.230.

Comparison of the total drug and antibiotic costs with respect to age, gender and duration of hospital stay

The cost of treatment may differ between various age groups, gender and duration of hospital stay. The hypothesis testing of the same is given in Table 12:

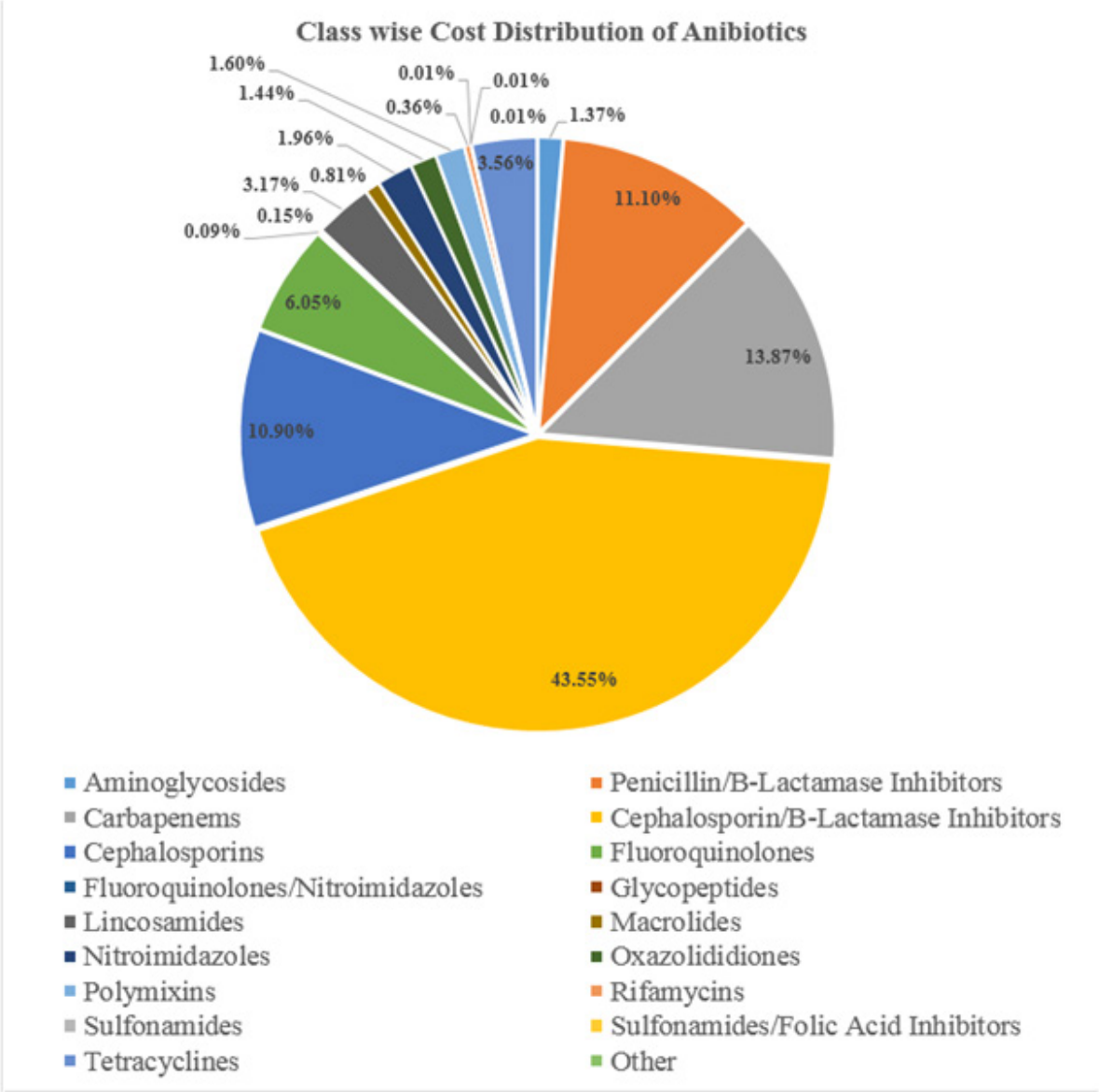

Figure 2: Class wise Cost Distribution of Antibiotics.

Table 9: Cost Analysis.

Parameters	Cost (Rs) (Mean±SD)	
Average cost of drugs/prescription	5457.15±54976.33	
Median cost of all drugs	1726.40	
25th to 75th percentile (all drugs)	874.50 -3407.09	
Average cost of antibiotics/ prescription	10872.39±109562.70	
Median cost of antibiotics	3228.81	
25th to 75th percentile (antibiotics)	2019.03-6175.70	
	Cost (INR)	%
Cost of Antibiotics	1100850.43	50.04
Cost of Other Drugs	1099292.54	49.96
Total	2200142.97	100.00

Table 10: Regression Analysis-Influence of predictor on cost of treatment.

Predictors	Patient's Outcome		
	Outcome = Cost of Antibiotics		
	R value	F	*p*-value
Age	0.72	2.085	0.150
Hospital stays (Days)	0.441	97.221	<0.001*

**p*-value <0.05 means statistically significant (Regression Analysis)

Table 11: Co-efficient Table.

Coefficients[a]						
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	-392.230	393.547		-0.997	0.320
	No. of Antibiotics	1472.855	166.231	0.404	8.860	0.000

Table 12: Comparison of the total drug and antibiotic costs with respect to age, gender and duration of hospital stay.

Variables		N	Cost of Antibiotics Mean±SD	*p*-value	Cost of total drugs Mean±SD	*p*-value
Gender	Male	225	681024.36±4471.05	0.106	1428663.53±10039.55	0.304
	Female	180	426778.01±2781.03		778431.38±4308.97	
Age (Years)	<40	162	411441.67±3978.02	0.032*	777912.96±7063.60	<0.001*
	>41	243	696360.7±3719.03		1429181.95±8663.80	
Hospital stay (Days)	≤6	332	694148.29±2088.16	<0.001*	1470680.75±7231.74	<0.001*
	>7	73	413654.08±7165.53		736414.16±9919.60	

**p*-value <0.05 means statistically significant (Univariate Analysis).

Table 13: Bacteriological examination.

Culture Sensitivity Test	Number (%)
Performed	34 (08.40%)
Not Performed	371 (91.60%)
Total	405

On performing univariate analysis, we found that the average cost of the antibiotics prescribed, and total drugs prescribed were significantly lower in age <40 yr (*p*-value=0.032 and <0.001 respectively). Although the cost of antibiotics and total drugs was lower in female, this was not a statistically significant difference.

Bacteriological examination

Culture sensitivity test is used to identify the susceptibility pattern of antibiotics against various bacteria. Table 13 includes the frequency distribution of culture sensitivity test performed.

DISCUSSION

The current study evaluates the appropriateness of antibiotics prescribed and cost burden due to these prescribed antibiotics. WHO prescribing indicator and DDD was used to access the antibiotic usage pattern. Various policies, guidelines and programs like antibiotic stewardship programs have been developed but still there is non-compliance by the practicing physicians. In order to reduce antibiotic resistance and cost burden, patterns and strategies should be developed to initiate appropriate use of antibiotics.

In our study, subjects of age group 51-60 yrs (69 subjects) were maximum and of age group >91 yrs (7 subjects) were minimum. The average duration of stay was found to be 5.27±1.93 days. In a study performed by Mani S *et al.*,[13] 325 were male and 281 were females. In study performed by Priestly *et al.*,[14] the average hospital stay was similar to our study i.e. 5.5 days.

In our study, major drug interactions accounted 67%, moderate 6% and minor 27%. In a study conducted by Rajalingam *et al.*,[15] 31.75%, 42.56% and 25.67% major, moderate and minor respectively, drug interactions were found.

WHO prescribing indicators were studied as a part of secondary objective of the study. Of the total 4934 drugs prescribed, antibiotics accounted 860 drugs with average of 2.12 antibiotics per prescription. In a study performed by Khan *et al.*,[16] 291 antibiotics were prescribed in 180 prescriptions. Average number of drugs per prescription was 2.74. 1.80% drugs were prescribed by generic name.

Our study findings revealed a high percentage (74.53%) of IV antibiotics prescription since it is the most preferred route of administration in case of hospitalized patients. Tablets and capsules accounted 23.37% and 1.05% respectively. In a study conducted by Feleke *et al.*,[17] 16.9% parentral antibiotics were administered and 83.1% oral antibiotics were administered.

In our study, 38% prescription had 2 antibiotics, 31.6% prescriptions had 1 antibiotic and 20% and 10.4% prescriptions had 3 and >4 antibiotics respectively. In a study conducted by Randad *et al.*,[9] 65% prescriptions had 2 antibiotics, 32% prescriptions had 3 antibiotics and 3 % prescription had 4 antibiotics.

Duration of stay was the only factor that affected the number of antibiotics prescribed in our study. In a study performed by Williams *et al.*,[18] durations of stay and mortality were found to be statistically significant with *p*-values 0.015 and 0.0289 respectively.

ADR was under reported in most of the sites in our study. Just 2 ADR in 3 subjects were reported. In a study performed by Chitra *et al.*,[19] ADR related to antibiotics were observed in 12 patients and the drugs causing ADR were clarithromycin, Piperacillin/Tazobactam, Ceftriaxone, Ofloxacin, Metronidazole and Clindamycin.

Cephalosporins/B-lactamase inhibitors was largely prescribed class in our study, which was followed by Cephalosporins. In a study conducted by Hussain *et al.*,[20] most commonly prescribed classes of antibacterial was various antibacterial FDCs (19.22%), followed by quinolones (18.86%), macrolides (18.15%), β-lactams (11.03%) cephalosporins (6.76%), penicillins (4.27%), aminoglycosides (2.84%), metronidazole (1.78%), clindamycin (1.78%) and tetracycline (0.36%).

In our study, it was found that the DDD/1000 inhabitant day was highest for Cefoperazone/Sulbactam (iv), followed by Ceftriaxone (iv). In a study performed by, Mohanraj *et al.*,[1] DDD of ceftriaxone was found to be 0.00020, Cefixime was 0.0002, ciprofloxacin was 0.0001, Azithromycin was 0.00005 and doxycycline was 0.003.

All the study drugs costed Rs. 2200142.97 of which antibiotics accounted 50% of this cost. The median cost of antibiotics was Rs. 3228.81. In a study conducted by Williams *et al.*,[18] The total cost of antibiotics prescribed in all patients was Rs 3, 99,016, an average of Rs 1995.08/patient (±SD 2099.99). The median cost was Rs 1489 and the 25th to 75th percentile was Rs 500-2016. The total cost of all drugs was Rs 5,45,177, with an average of Rs 2725.88/patient (± SD 2242.38). The median cost of drugs prescribed was Rs 2100 and 25th to 75th percentile was Rs 1500-2950. Thus, the total cost incurred by antibiotics was nearly 73.2% of the total drug costs in these patients.

Strong relationship was observed between cost of antibiotics and duration of stay. In a study conducted by Yusof *et al.*,[21] it was found that there was no association between age, average days of treatment and cost of treatment. There was a positive relation between no. of days in hospital and cost of treatment.

Univariate analysis was performed to compare the total drug cost and antibiotic cost with respect to age, gender and duration of hospital stay. In a study performed by Williams *et al.*,[18] it was found that the average cost of the total drugs prescribed and antibiotics prescribed were significantly lower in younger patients (<45 years) (*p*-value=0.005 and 0.006, respectively). Although the total cost of antibiotics and drugs was lower in surgical patients and in patients with APACHE scores <15, this was not a statistically significant difference.

Other important finding was initiating the empirical antibiotic therapy regardless of the culture sensitivity testing. Culture sensitivity test was done in only 8.40% patients. Such low rate of testing was due to duration for test results, expectation of speedy recovery by the patients and health care providers, incomplete information regarding nosocomial infection. These serious lapses not only make patient's further treatment plan difficult but also leads to unavailability of susceptible antibiotic in case of life-threatening infections in future. In our study, culture test was performed only in 34 subjects out of 405. In the study performed by Benjamin *et al.*,[22] culture test was performed in 106 out of 209 subjects.

Some of the limitations of this study includes non-inclusion of out-patients and non-collection of post discharge data. Further, due to latest combinations available in the market and past publication of National List of Essential Medicines, Modified Kunin's Criteria was not implemented. Cost of other medical procedures and indirect cost was not included in cost analysis.

CONCLUSION

About 45 different, narrow and broad-spectrum antibiotics from various classes were used in our study. Most of the prescriptions included 2 or more antibiotics. Most of the prescriptions contained Fixed Dose Combination. The dosage regimen (dose, duration, schedule) of antibiotics were accurate according to guidelines. The antimicrobial treatment was started on the basis of clinical examination and not the susceptibility testing. The frequency for getting culture sensitivity test done is very less. In most of the patients with culture sensitivity test done, it was found that about 90% were resistant to cephalosporin class. On contrary, cephalosporins were used as empirical therapy. ADR reporting system was very poor. There is a need to initiate the ADR reporting habit. There is a need to collect proper medication history regarding the antibiotic usage and immunization. A shift from brand names to generic names is required to be done. Cheaper alternative antibiotic can be opted instead of costly brands. Hospital specific antibiotic treatment guidelines should be formed on the basis of various studies conducted in the hospitals. Presence of common micro-organisms in hospital environment should be detected regularly. Cost of antibiotics comprised of the larger share in the total cost of all drug. Generic products should be opted. Drug Utilization Studies for various classes of antibiotics should be carried out on regular basis.

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CONFLICT OF INTEREST

The authors declare no competing interest.

ABBREVIATIONS

ADR: Adverse Drug Reaction; **APACHE:** Acute Physiology and Chronic Health Evaluation; **ATC:** Anatomical Therapeutic Chemical Classification System; **DDD:** Defined Daily Dose; **NLEM:** National List of Essential Medicines; **SPSS:** Statistical Package for Social Sciences; **WHO:** World Health Organization.

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STATEMENT OF ETHICS

The study was approved by Institutional Ethics Committee of K.B. Institute of Pharmaceutical Education and Research, Gandhinagar (KBIEC-ECR/144/Indt/GJ/2014) with Approval No. KBIEC/2017/98. Informed consent was obtained from all the patients prior to their enrollment in the study.

SUMMARY

Antibiotics are the second leading prescribed drugs which has resulted in their irrational use. The study included 405 eligible subjects. Out of the 4934 drugs prescribed, antibiotics accounted for 860 (17.43%) drugs. 74.53% of the antibiotics were prescribed in parenteral form. Statistically significant relation was observed between the duration of stay and the number of antibiotics prescribed. Cephalosporins/B-lactamase inhibitors was the largely prescribed class of antibiotics, which was followed by Cephalosporins. Culture sensitivity test was performed only in 34 out of 405 subjects. The present study concluded that antibiotics need to be used rationally to avoid unavailability of these antibiotics during life threatening conditions due to culture sensitivity issues.

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