



Research article

Susceptibility and resistance pattern of bacterial isolates and development of antibiogram in a tertiary care hospital of western India

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ABSTRACT

The main issue in India and at a global level that led to antibiotic resistance is misuse, irrational prescribing of antibiotics, and lack of sufficient data on antibiotic resistance at a local, regional, and national level to develop antibiotic policy that guides all healthcare professional while prescribing antibiotics. The present study was carried out for 12 months in a tertiary care teaching hospital in western India to develop an antibiogram and to check antimicrobial resistance trends in the hospital. Out of 500 patients, 53.6% were male and 46.4% were female patients. A total of 17 bacterial species were identified throughout the study with gram-negative species infections being most common in hospitals. *Escherichia coli* was the most frequently isolated gram-negative species. Ceftriaxone was most prescribed frequently followed by amoxicillin and azithromycin, respectively. In the gram-positive organism, ceftriaxone and amoxicillin resistance rate was 65.35% and 35% respectively. Overall, in the study Ceftriaxone (58%) and amoxicillin-clavulanic acid (38.9%), Azithromycin (56%), and ciprofloxacin (53%) were found most resistant antibiotics, and Amikacin (72%), Clindamycin (18%) were most sensitive. Gram-negative infections were identified mostly and cephalosporine and fluoroquinolones antibiotics were showing high antibiotic resistance. An institutional hospital antibiogram was developed to check local antimicrobial agents for various bacteria.

Keywords: Anti-biogram, Anti-biotics, Anti-microbial stewardship program, Anti-biotic policy, Culture, Sensitivity test

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INTRODUCTION

Antimicrobial resistance (AMR) has emerged as a major risk to the public as a health survey shows 10 million deaths annually by 2050 mainly due to Antibiotic resistance. India carries one of the largest burdens of drug-resistant pathogens all over the world [1, 2]. Antibiotic resistance led to increased healthcare costs, longer hospital stays, and increased mortality rates which affect the quality of healthcare service provided by hospitals. Because this antimicrobial stewardship program was implemented to rationalize antibiotic therapy, as part of it, Antibiogram development is very important to track the antimicrobial resistance pattern in the institution. This antibiogram will be useful to the prescribers to check and prescribe the empirical antibiotics treatment to the patients and also be used to study the epidemiology of resistance and evaluate the efficacy of new antibiotics [2-5]. Antimicrobial resistance (AMR) is a growing public health concern where the microorganism can survive after receiving antibiotic treatment. In hospitals, most of the time standard treatment fails to treat the patients as there is no such data to help the physicians. So, to fill this gap as a part of the antimicrobial stewardship program and make availability of current data on

resistance trends in institution antibiograms are valuable [3]. Various guidelines are developed by the Clinical and Laboratory Standard Institute (CLSI) to standardize methods used to develop Antibiograms. These guidelines can be combined into the WHONET software for the analysis of culture sensitivity data. In Antibiogram, the results are calculated by measuring minimum inhibitory concentrations (MICs) or growth inhibition zone diameters around disks and then converted into susceptibility categories according to the clinical breakpoints, which are defined by various committees [6,7].

Antibiotic susceptibility testing (AST) is used to select effective doses of antibiotics and an empirical therapy is formulated to maintain a patient's health against disease state condition. When any bacterial disease has caused a problem the isolation of suitable culture from the patient, and identification of the microbes is done by using various methods of bacterial identification [5]. The cut-off points are established by the Committees of the Clinical and Laboratory Standards Institute in the United States (CLSI) and by the European Committee on Antimicrobial Susceptibility Testing in Europe (EUCAST) both for inhibition of halo values as in the MICs t o

differentiate the clinical categories of the treatment (EUCAST-2008). These categories have been defined as success or therapeutic failure in the following manner by CLSI and EUCAST: Susceptible, Intermediate, and Resistant^[6-9]. Nowadays antimicrobial stewardship program is a widely accepted tool and includes the selection of an appropriate antimicrobial agent and then optimizing its dose and duration to cure an infection while minimizing the toxicity and conditions for the selection of resistant bacterial strains^[10,11]. Many pharmacists in clinical practice have established roles as experts in multidisciplinary antimicrobial stewardship teams along with microbiologists and infection-specialist physicians who are conventionally responsible for providing advice on the management of infection and developing standard treatment guidelines for antibiotic use in the hospital. Thus, due to the changing scenario and increasing cases of antibiotic resistance various approaches are there in an antimicrobial stewardship program is the first step towards tackling this and reducing antibiotic resistance.

Various studies conducted show that antimicrobial resistance is increasing and need to study the local resistance trends of institutions through constructing an antibiogram. There is a lack of such robust data to guide pathogen-directed therapy and empirical antibiotic therapy^[11]. There is a wide role of clinical pharmacists in identifying and resolving antibiotic resistance and performing various other activities to tackle this overgrowing situation. So, this article aims to describe the resistance and sensitivity patterns and resistance trends in the hospital and the need to develop an antibiogram for developing evidence-based guidelines for prescribing empirical antibiotics in the hospital.

MATERIALS AND METHODS

Study Design and Duration

This was a prospective observational study conducted for 12 months.

Study Site and Inclusion Criteria

This study was conducted in inpatient departments (General surgery, general medicine, pediatrics, orthopedics, and intensive care unit) of Parul Sevashram Hospital, which is a tertiary care teaching hospital of 750-bed strength located in the Western State of Gujarat, Vadodara, India. The inpatients of either gender aged above 12 years, which were diagnosed with infectious conditions and prescribed at least one antibiotic and referred for the culture and sensitivity in the hospital laboratory were included in the study. Pregnant women and terminally ill patients and patients who were not willing to participate in the study were excluded from the study.

Ethical Considerations

The study protocol was submitted to the institutional human ethics committee and the same was approved before the data collection (PUIECHR/PIMSR/00/081734/2310)

Preparation of Data Collection Tool

A suitable data collection tool was developed by referring to a research article from the scientific literature and the same was approved by the doctoral research committee (DRC). The data included in the form was regarding demographic details of patients, culture, and sensitivity test report details including bacterial identification and their susceptibility and resistance pattern towards the prescribed antibiotics.

Study Procedure Including the Culture and Sensitivity Test

The admitted patients were initially screened for the inclusion criteria and the patient satisfying the study criteria were enrolled in the study after obtaining volunteer written informed consent in the predesigned informed consent form. The laboratory technician collected the patients' sample, which was sent to the microbiology laboratory for culture and sensitivity test by laboratory staff for identification of bacteria. Bacterial identification and resistance and susceptibility test were done by the standard criteria of the laboratory as per the clinical laboratory standard institute (CLSI) guideline [9]. The prepared reports were cross-checked and verified by the laboratory in charge and issued to the patients. After receiving the culture sensitivity test report, patient demographic details like age, sex, and socioeconomic status were obtained from the patient profile form and entered in the specially designed data collection forms. All the collected data were entered into WHO NET software used to develop an antibiogram to check the bacterial resistance and susceptibility pattern of all antimicrobials.

Data Analysis

Data analyses were performed using GraphPad Prism software (Version 5.01) and Microsoft Excel (version, 2019). Data were interpreted using descriptive statistics and the results were represented as the percentage of resistance and susceptibility of various bacteria. A p-value less than 0.05 was considered statistically significant at a 95% confidence interval. The quantitative data were calculated in terms of mean and standard deviation. The findings were presented with aids of tables and graphs.

Bio-safety Issues and Risks

Although there were microorganisms involved in the study, the sample collection and microbiological analysis were carried out by trained and registered laboratory technicians, and the risk was limited to the laboratory staff only. There was no risk or harm to the patients.

RESULTS AND DISCUSSION

A total of 500 patients who were on antibiotics and positive culture tests were included in the study out of 754 culture sensitivity reports collected during the study period, the remaining were excluded from the study as per exclusion criteria. The majority of the patients were from the 18-65 years age category with a total of 278 isolates that were positive for bacterial infection. Most of the patients are from urban areas, and 36% of the patients were from the lower middle class. Most of the patients are from the middle class so the

cost of culture and sensitivity tests is not affordable for the patients. Of 500 patients, 53% (268) patients were male with positive bacterial isolates, and in females, 46% (232) had, a P value= of 0.003. Detailed

demographic characteristics of the patient population are shown in Table 1.

Table 1: Demographic characteristics of the patient population

Variables	Category	Total N (%)	Isolated bacteria		P value
			Gram -ve N (%)	Gram +veN (%)	
Age	≤18 Years	103 (20.6)	46 (44.67)	57 (55.33)	0.003*
	18-65 Years	278 (55.6)	185 (66.54)	93 (33.46)	
	≥65 years	119 (23.8)	78 (65.54)	41 (34.46)	
Gender	Male	268 (53.6)	147 (54.85)	121 (45.150)	0.006*
	Female	232 (46.4)	162 (69.82)	70 (30.180)	
Residence	Rural	199 (39.8)	79 (39.70)	120 (60.30)	0.0001*
	Urban	301 (60.2)	230 (76.41)	71 (23.59)	
Socioeconomic status	Upper (I)	105 (21)	77 (73.30)	28 (26.70)	0.005*
	Upper middle (II)	58 (11.6)	40 (68.97)	18 (31.03)	
	Lower middle (III)	180 (36)	104 (57.78)	76 (42.22)	
	Upper lower (IV)	73 (14.6)	47 (64.39)	26 (35.61)	
	Lower (V)	84 (16.8)	41 (48.80)	43 (51.20)	
Total		2000 (100)	1236 (61.8)	764 (38.2)	

*Indicates statistically significant

A total of 17 bacterial species were isolated, out of which 12 species were from gram-negative bacteria and the remaining were from gram-positive species.

Table 2: Bacterial species identified in the study

Organism	Male		Female		Total	
	N	%	N	%	N	%
E. Coli	47	35.33	86	64.66	133	26.6
Klebsiella Spps.	37	47.43	41	52.56	78	15.6
S Aureus	22	34.92	41	65.80	63	12.6
Pseudomonas	35	57.37	26	42.62	61	12.2
Enterococcus	05	41.66	07	58.33	12	2.4
Acinetobacter	27	58.69	19	41.30	46	9.2
Staphylococci	10	47.61	11	52.38	21	4.2
Salmonellaspps.	7	70	3	30	10	2
MRSA	15	40.54	22	59.45	37	7.4
Salmonella Typhi	16	41.02	23	58.97	39	7.8

(Abbreviation: E coli - Escherichia coli, MRSA - Methicillin-resistant Staphylococcus aureus)

Out of 500 patients, 309 (62%) gram-negative species were obtained. E. coli, Klebsiella, and S Aureus were most frequently in our study. In the gender-wise distribution of isolates E coli and Klebsiella were mostly isolated and E coli isolation rate was high in

female patients and klebsiella was almost the same in both males and females. This variation is due to the region-wise difference of various bacterial infections from one place to another. In our study, gram-negative infections are predominant as compared to gram-positive infections and E coli is the most isolated bacteria. In many studies, E coli was predominantly isolated. No. of isolates found in male and female patients were given in Table 2.

In gram-positive organism infections, amoxicillin was widely used in the treatment of staphylococcus bacterial infections. 35% of cases were found to be resistant to amoxicillin which is a widely used antibiotic and high resistance was found in Staphylococcus epidermis to amoxicillin. Various antibiotics were tested for different isolates in which staphylococcus (209), staphylococcus epidermis (197), and Enterococcus faecium (87) were most frequently tested for different antibiotics respectively and a high resistance rate was found in staphylococcus aureus species. The overall resistance and susceptibility pattern of gram-positive organisms are shown in Table 3.

Table 3: Antimicrobial sensitivity and resistance pattern of the gram-positive organism

Name of antibiotics	Staphylococcus aureus		Enterococcus faecium		Staphylococcus Epidermis		Coagulase Negative Staphylococci		MRSA	
	R	S	R	S	R	S	R	S	R	S
Azithromycin	29	31	6	7	25	39	07	19	3	0
Amoxicillin	17	36	0	4	40	56	09	8	6	29
Ceftriaxone	35	25	2	8	0	8	2	10	0	0
Cefixime	1	5	4	12	0	0	0	0	3	3
Clindamycin	0	0	0	3	2	7	0	3	0	0
Cefotaxime	0	3	2	3	1	1	0	1	1	0
Cefperazone	2	13	5	07	0	4	1	2	0	0
Ampicillin	4	6	0	0	0	0	1	1	0	0
Piperacillin	0	2	9	15	6	8	0	0	5	7

(Abbreviation: R – Resistant S - Sensitive)

In our study, gram-negative isolates were found most and E coli was isolated more frequently. Ceftriaxone was widely prescribed as an antibiotic and was found to be highly resistant antibiotic gram-

negative isolates as 65.55% of cases were found resistant. Now a day's gram-negative infections were more and increasing trends towards the use of cephalosporin and fluoroquinolone type of

antibiotics which is responsible for increasing resistance to these antibiotics. Amikacin and clindamycin were the most sensitive antibiotics in gram-negative infections. Various antibiotics were tested for different gram-negative isolates in which staphylococcus (209), staphylococcus epidermis (197), and Enterococcus faecium (87) were most frequently tested for different antibiotics respectively

and a high resistance rate was found in staphylococcus aureus species. This variation in the resistance is due to region-wise resistance trends of antibiotics to the bacteria that's why every hospital needs to develop an antibiogram to check local resistance trends. The overall resistance and susceptibility pattern of gram-negative isolates was shown in Table 4.

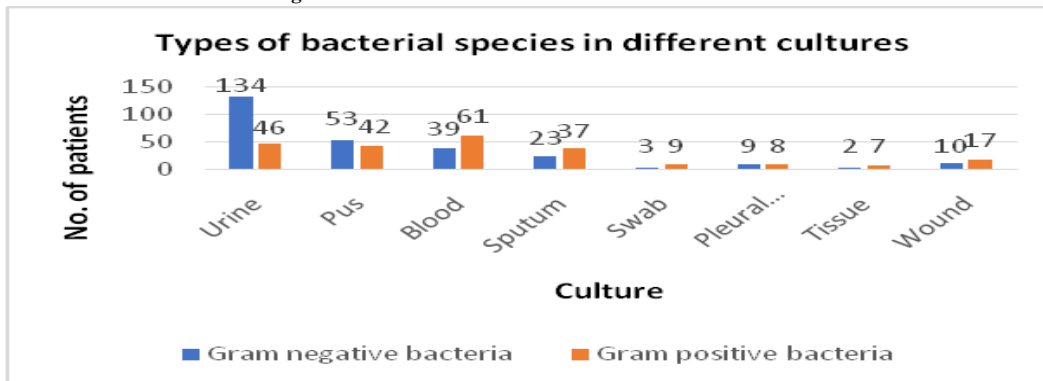
Table 4: Antimicrobial resistance pattern of the gram-negative organism

Name of antibiotics	E. Coli		Klebsiella		Pseudomonas Aeruginosa		Acinetobacter spss.		Salmonella	
	R	S	R	S	R	S	R	S	R	S
Amikacin	9	30	7	18	18	41	0	0	0	0
Ceftriaxone	47	17	13	8	44	17	0	0	14	20
Ciprofloxacin	34	29	0	3	10	5	0	2	7	5
Levofloxacin	15	20	7	10	13	7	0	0	2	3
Linezolid	0	7	0	0	4	15	3	2	1	0
Cefixime	5	12	9	20	4	3	0	1	5	1
Cefotetan	0	2	3	5	4	6	0	0	0	0
Clindamycin	2	8	0	5	3	9	1	0	0	0
Ofloxacin	9	17	0	0	0	0	2	2	12	25
Meropenem	0	3	4	10	2	1	6	9	0	10
Gentamycin	1	13	7	27	18	30	7	4	0	0
Metronidazole	0	10	8	31	13	24	2	8	2	2
Nitrofurantoin	11	18	0	0	0	0	0	0	0	0

Various cultures were obtained from the patients for culture and sensitivity tests in which urine was the most frequently collected sample. Maximum no. of bacterial species was identified in the urine

sample and E coli was the most isolated bacteria in the urine sample. Detailed culture wise no. types of bacterial species identified in the study were shown in Figure 1.

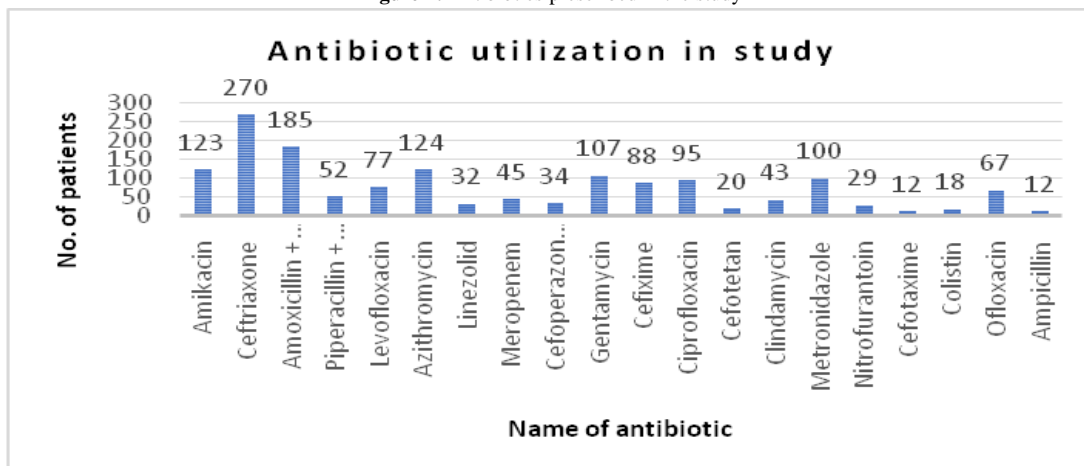
Figure 1: Total no. of isolates identified in different cultures



During the study 20 different types of antibiotics were prescribed in different departments in the hospital. cephalosporine class of antibiotics was widely utilized throughout the study (424) in

which ceftriaxone was highly prescribed antibiotics in this category and colistin and ampicillin were the least utilized antibiotics. The total no. of antibiotics prescribed in a study is shown in Figure 2.

Figure 2: Antibiotics prescribed in the study



During the study period in most of the patients, at least one of the antibiotics was found to be resistant to isolated bacteria, which ceftriaxone (58%) and amoxicillin-clavulanic acid (38.9%), Azithromycin (56%), and ciprofloxacin (53%) were found most resistant, and Clindamycin (18%), Amikacin (72%) were most sensitive antibiotic. It is found that almost half of the antibiotics were

found be resistant. Cephalosporin group antibiotics were found most resistant in our study and resistance to third-generation cephalosporin and fluoroquinolone antibiotics increased very rapidly. Detailed resistance and susceptibility patterns of all antibiotics was shown in Figure 3 and Figure 4.

Figure 3: Antibiotic resistance and susceptibility pattern of antibiotics

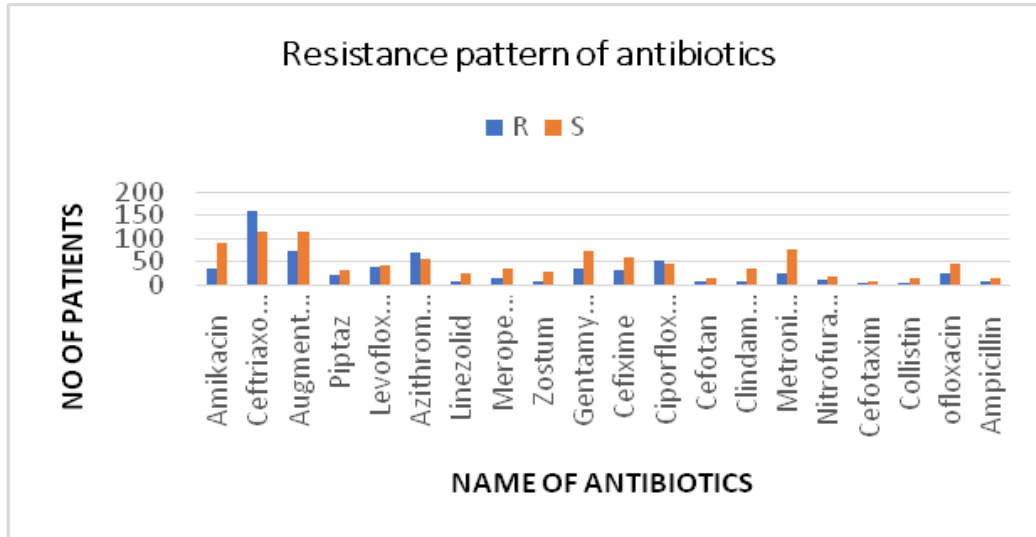
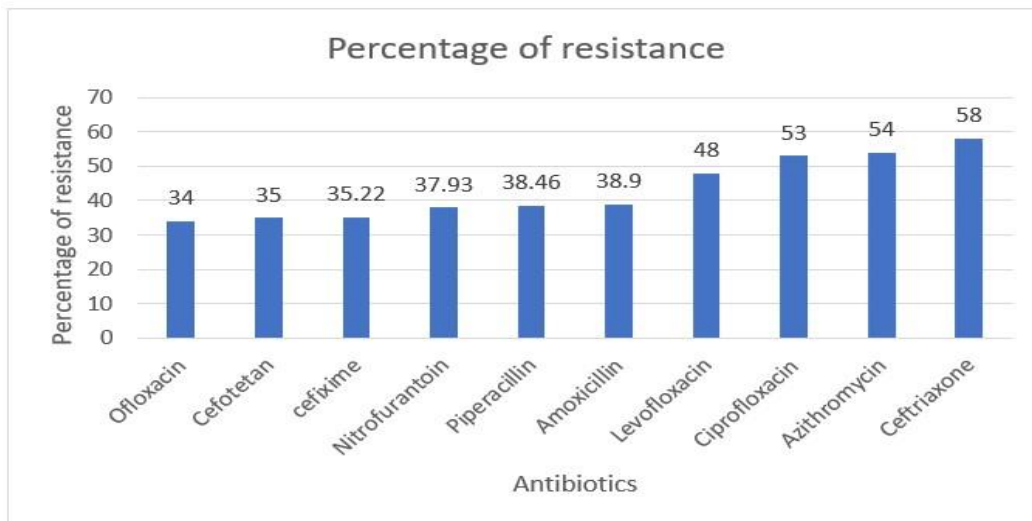


Figure 4: Antibiogram and percentage resistance of most used antibiotics in the study



CONCLUSION

This descriptive observational study concluded that most of the antibiotics were resistant to various bacterial species *E. coli* was the predominant bacteria among all, and cephalosporin and fluoroquinolone were found most resistant antibiotics. Therefore, it is concluded that there is a need for a system like an antimicrobial stewardship program in the hospital to track antibiotic resistance. These programs need strict implementation in every hospital to evaluate and prevent antibiotic resistance. This research also highlights the need for culture and sensitivity tests and the immediate need for the involvement of clinical pharmacists and the microbiology department in the development of institutional

antibiograms to tackle antibiotic resistance.

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Conflict of interest:

None

Financial support:

None

Ethics statement:

This study was approved by the Institutional Ethics Committee of the hospital with approval no. (PUIECHR/PIMSR/00/081734/2310)

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