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A Cumulative Antibiogram for a Period of one year and its Analysis in a Tertiary Care Hospital

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Abstract
Hospital antibiogram is a periodic summary of antimicrobial susceptibilities of local bacterial strains given to the hospital's clinical microbiology laboratory. It not only helps the clinicians to select the most appropriate empiric therapy, but also in monitoring resistance trends within an institution, thereby optimizing treatment. The current study is mainly designed to know the susceptibility rates and resistance trends of microorganisms isolated from various clinical samples. To monitor antimicrobial resistance trends in this period with emphasis on inpatient and outpatient data.

To prepare a cumulative antibiogram of our institution as a part of antibiotic stewardship program. It is a Tertiary care health institution which delivers its services to the rural and urban population with departments like Medicine, Pulmonary medicine, Surgery, Orthopedics, and Obstetrics and Gynecology. Data was gathered from all outpatient and inpatient specimens received for Culture and sensitivity. The organisms and their susceptibility patterns isolated in the Department of Microbiology were collected and cumulative antibiogram is prepared and from the 6239 specimens received in the Microbiology laboratory during this one year period, most of them from urine followed by sputum, pus and blood. Urine samples (36.5%) from OPD (19.1%) and IPD (80.9%) showed a culture positivity of 46.7% and 42.6% respectively. E.coli (40.4%) was the predominant isolate in urine samples from OPD and Klebsiella species (38.2%) from IPD. Blood samples from OPD (10.4%) showed a culture positivity of 29.2% and IPD (89.6%) about 16%. Blood samples from both OPD and IPD frequently grew Klebsiella species with 45.9% and 45.2% respectively. Sputum (34.2%) samples from OPD (35.2%) showed a culture positivity of 43.2% and IPD (66.8%) with a positivity of 33.2%. Klebsiella species was the predominant isolate in the sputum specimens from both OPD (40%) and IPD (43.3%). Pus samples (16.7%) from OPD (29%) gave a culture positivity of 56.9% and IPD (71%) of 38.1%. Klebsiella species was frequently isolated from both OPD (38.4%) and IPD (42%) pus specimens. Resistance to commonly used antibiotics in institutions is alarmingly high requiring continuous surveillance to assess the sensitivity and resistance pattern at a certain levels. The antibiogram prepared from Hospital diagnostic laboratories are readily accessible and inexpensive tool to monitor antimicrobial resistance patterns in communities and regions.

Keywords: *Antibiogram, Gram-negative organisms, Gram-positive organisms.*

Introduction

Hospital antibiogram is a periodic summary of antimicrobial susceptibilities of local bacterial isolates submitted to the hospital's clinical microbiology laboratory. It not only aids clinicians to select the most appropriate empiric therapy, but also in monitoring resistance trends within an institution, thereby optimizing treatment. The inappropriate use of antimicrobials leads to the emergence of resistant bacteria, an increase in the risk of patient harm from avoidable adverse reactions and interactions with other drugs, infection with multi-resistant bacteria or *Clostridium difficile*, and unnecessary costs. Patients with infections due to resistant bacteria experience delayed recovery, treatment failure and even death. Antimicrobial resistance is defined as decrease in susceptibility of a microorganism to an antimicrobial agent to which it was previously sensitive[1-3]. As a result, standard treatments become ineffective and infections persist and may transmit to others. It is a matter of global concern since it possesses a significant clinical and financial burden. Pan-antibiotic resistant micro-organisms are so extremely limited that clinicians are forced to re-introduce older, previously discarded drugs, such as colistin, that are associated with significant toxicity and for which there is a lack of robust data to guide selection of dosage regimen or duration of therapy. An effective approach to improving antimicrobial use in hospitals is an organized antimicrobial management program known as antimicrobial stewardship (AMS)[4-5]. AMS involves a systematic approach to optimising the use of antimicrobials. It is used by healthcare institutions to reduce inappropriate antimicrobial use, to improve patient outcomes and to reduce the adverse consequences of antimicrobial use (including antimicrobial resistance, toxicity and unnecessary costs). Effective hospital AMS programs have been shown to decrease antimicrobial use and improve patient care. Such programs are essential to local and national efforts to prevent the emergence of antimicrobial resistance and decrease preventable healthcare associated infection. At a local level, regular analyses of antimicrobial resistance should be provided to groups with responsibility for local antimicrobial guidelines (such as an antimicrobial stewardship committee, drug and therapeutics committee) to inform local empirical therapy recommendations and formulary management [6-7].

The present study is aimed to evaluate the susceptibility rates and resistance trends of microorganisms. To monitor antimicrobial resistance trends in this period with emphasis on inpatient and outpatient data. To prepare a cumulative antibiogram of our institution as a part of antibiotic stewardship program.

Materials and Methods

The present study was conducted in the department of Microbiology over a one year period from January to December 2018. It is a Tertiary care health institution which delivers its services to the rural and urban population with departments like Medicine, Pulmonary medicine, Surgery, Orthopedics, and Obstetrics and Gynecology. Data was gathered from all outpatient and inpatient specimens received for Culture and sensitivity. The organisms and their susceptibility patterns isolated in the Department of Microbiology were collected and cumulative antibiogram is prepared.

Study Population: All the patients attending OPD's and those admitted to the aforementioned departments during the period of the study were included.

Inclusion criteria

1. Susceptibility reports of both outpatient and inpatients were taken into consideration.
2. To prepare the antibiogram, first diagnostic isolate of given species per patient per analysis period was included, (irrespective of body site, antimicrobial susceptibility profile or other phenotypic characters).

3. Blood, urine, sputum and pus cultures were included

Exclusion criteria: While preparing the antibiogram, the following isolates were excluded:

1. Duplicate bacterial isolates
2. Surveillance culture and screening isolates
3. Strains which show intermediate susceptibility

Sample processing: Specimens collected were blood, urine, sputum, wound swabs, pus and body fluids. All samples were inoculated on to Blood and MacConkey agar and urinary specimens onto CLED medium and for all the blood specimens, serial sub-culturing was done onto the same media as mentioned above followed by incubation for 24-48 hrs. Colonies were subjected to Gram staining and were characterized into Gram positive and Gram negative organisms. Biochemical tests were put-up for further identification of the isolates and antibiotic susceptibility testing was performed by Kirby –Bauer disc diffusion method according to CLSI recommendations.

Collection of Data

Antibiogram preparation: Antibiograms were prepared by plotting the number of isolates of a particular micro-organism against the antibiotic to which they were found susceptible.

Antibiogram tables within the specification

Tabulated cumulative antibiograms were prepared for urine isolates, non-urine isolates and if there are more than 30 isolates of a genus, species or other grouping from blood culture for blood isolates as well. Each cumulative antibiogram consists of data for one calendar year and will be published early in the following year.

1. Each cumulative antibiogram table would be annotated with name of the institution that the isolates reported were derived from, the time period over which the isolates were collected and the standard used by the laboratory to determine antibiotic susceptibility like Clinical and Laboratory Standards Institute.
2. Only antibiotic susceptibility data of all first isolates from samples collected for a clinical purpose were included, not isolates from surveillance programs.
3. Only the antibiotic susceptibility data from the first isolate of a bacterial species from each individual each year were included. Multiples were eliminated by including only the initial microbial isolate of a particular species recovered from a patient during the time period analyzed, regardless of antimicrobial susceptibility profile.
4. In general, only "percentage susceptible" data were reported.
5. For each genus, species or other grouping, the number of isolates (the denominator) used in determining the percentage were noted on the antibiogram report.
6. The antibiogram reports antibiotic susceptibilities for the antibiotics in actual clinical use, not the susceptibility to any surrogate antibiotic used in the laboratory.

The antibiogram reports susceptibilities for all the isolates where the number tested is greater than 30.

Results

A total of 6239 specimens were received in the Microbiology laboratory in this study period, and among them urine (36.5%) were the commonly received samples followed by sputum (34.2%), pus (16.7%) and blood (12.6%) (Table 1).

Urine samples (36.5%) from OPD (19.1%) and IPD (80.9%) showed a culture positivity of 46.7% and 42.6% respectively (Table 1). *E.coli* (40.4%) was the predominant isolate in urine samples from OPD and *Klebsiella* species (38.2%) from IPD (Figure 1).The antibiogram of urinary isolates which are more than 30 in number were shown in Table 2 and Table 3. Analysis of the antibiotic susceptibility patterns revealed that in community acquired UTI, *E.coli* and *Klebsiella* isolates showed highest susceptibility to Doripenem and least susceptibility to Ampicillin in *E.coli* and Cefoperazone in *Klebsiella* species whereas antibiogram of inpatient urine samples revealed maximum susceptibility to Doripenem in

Klebsiella species, *Pseudomonas* species and *Enterobacter* species, to Colistin in *E.coli* and *Pseudomonas* species and to Vancomycin in *S.aureus* and *Enterococcus* species and least susceptibility to Cotrimoxazole in *Klebsiella* species, Ampicillin in *E.coli*, Cefoperazone in *Pseudomonas* species and *Enterobacter* species and to Penicillin in *S.aureus* and Ciprofloxacin in *Enterococcus* species.

Blood samples from OPD (10.4%) showed a culture positivity of 29.2% and IPD (89.6%) about 16% (Table 1). Blood samples from both OPD and IPD frequently grew *Klebsiella* species with 45.9% and 45.2% respectively (Figure 2). The antibiogram of blood isolates from IPD were shown in Table 4. On analysis of the antibiotic susceptibility patterns, *Klebsiella* isolates showed maximum susceptibility to Doripenem and minimum to Cefotaxime.

Sputum (34.2%) samples from OPD (35.2%) showed a culture positivity of 43.2% and IPD (66.8%) with a positivity of 33.2% (Table 1). *Klebsiella* species was the predominant isolate in the sputum specimens from both OPD (40%) and IPD (43.3%) (Figure 3). The antibiogram of sputum isolates from both OPD & IPD were shown in Table 5. Analysis of antibiogram of sputum from OPD patients showed highest susceptibility to Doripenem and Meropenem in *E.coli* and *Klebsiella* species and least to Levofloxacin in *Klebsiella* species and to Ampicillin in *E.coli* whereas inpatient data revealed *Klebsiella* species and *Proteus* species showed maximum susceptibility to Doripenem and *Citrobacter* species and *Pseudomonas* species to Colistin and least susceptibility to Cotrimoxazole is seen in *Klebsiella* species and *Citrobacter* species and to Cefuroxime in *Proteus* species and to Cefoperazone in *Pseudomonas* species.

Pus samples (16.7%) from OPD (29%) gave a culture positivity of 56.9% and IPD (71%) of 38.1% (Table 1). *Klebsiella* species was frequently isolated from both OPD (38.4%) and IPD (42%) pus specimens (Figure 6).The antibiogram of pus isolates were shown in Table 6. Analysis of the AST patterns of pus from OPD patients showed maximum susceptibility to Colistin and minimum to Ciprofloxacinin *Klebsiella* species whereas IPD patients data showed highest susceptibility to Doripenem in *Kebsiella* species and to Colistin in *Pseudomonas* species, to Vancomycin in *S.aureus* and least to Levofloxacin in *Klebsiella* species and to Ciprofloxacin in *Pseudomonas* species and to Azithromycin in *S.aureus*.

Table 1: Categorical distribution of specimens and culture positives

TYPE OF SPECIMEN												
Type of case	Urine (36.5%)			Blood (12.6%)			Sputum (34.2%)			Pus (16.7%)		
	# No	Sterile	Culture Positives%	# No	Sterile	Culture Positives %	#No	Sterile	Culture Positives %	# No	Sterile	Culture Positives %
OPD	434 (19.1%)	231 (53%)	203 (47%)	82 (10.4%)	58 (71%)	24 (29%)	704 (35.2%)	456 (65%)	248 (35%)	302 (29%)	130 (43%)	172 (57%)
IPD	1842 (80.9%)	1057 (57%)	785 (43%)	706 (89.6%)	593 (84%)	113 (16%)	1428 (66.8%)	810 (57%)	618 (43%)	741 71%)	458 (62%)	283 (38%)
Total: 6239	2276 (37%)			788 (13%)			2132 (34%)			1043 (17%)		

Figure 1: Distribution of isolates from OPD (n=203) and IPD culture positive urine samples (n=785**)**

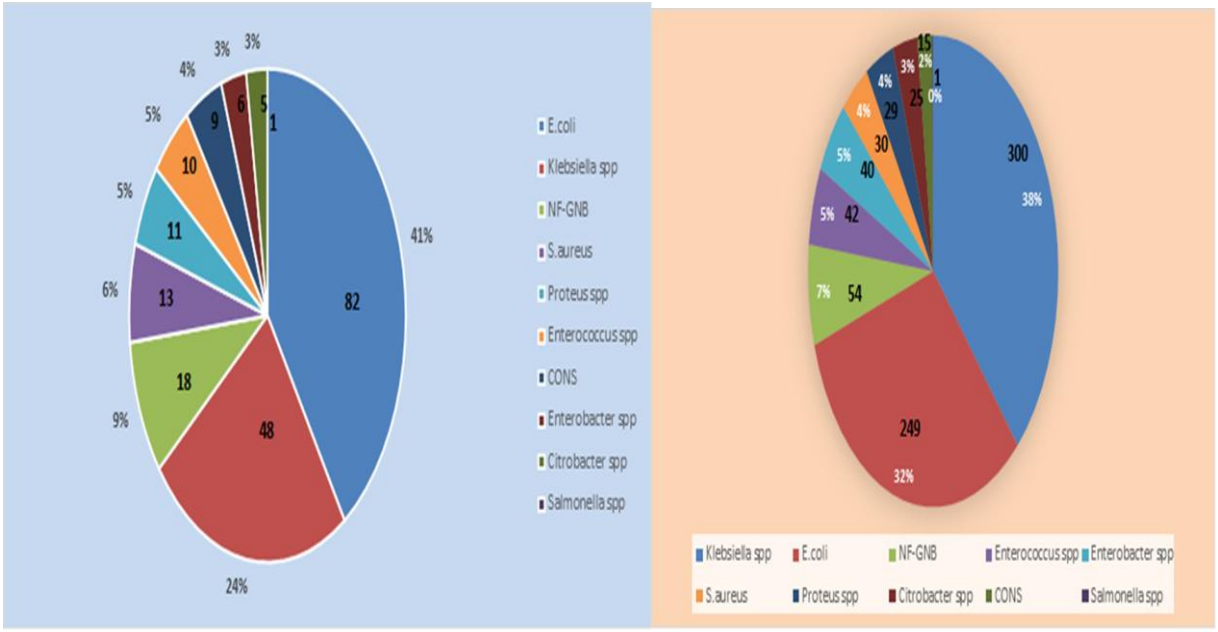


Table 2: Antibiogram of Gram-negative organisms from UTI OPD samples

Gram Negative		E. coli	Klebsiella
Number of isolates		48	82
1st Line antibiotics	Ampicillin	44	IR
	Amoxyclav	95	94
	CTM	70	70
	Nitrofurantoin	92	76
	Norfloxacin	92	93
2nd Line antibiotics	Piparacillin +tazobactum	94	90
	Cefuroxime	79	84
	Cefaperazone	61	66
	Cefotaxime	48	69
	Ceftazidime	61	73
	Cefipime	82	78
	Doripenem	97	96
	Imepenem	92	88
	Meropenem	94	86
	Amikacin	94	86
	Gentamycin	94	91
	Ciprofloxacin	64	75
	Levofloxacin	58	68
OTHER	Colistin	97	93

CTM- Cotrimoxazole

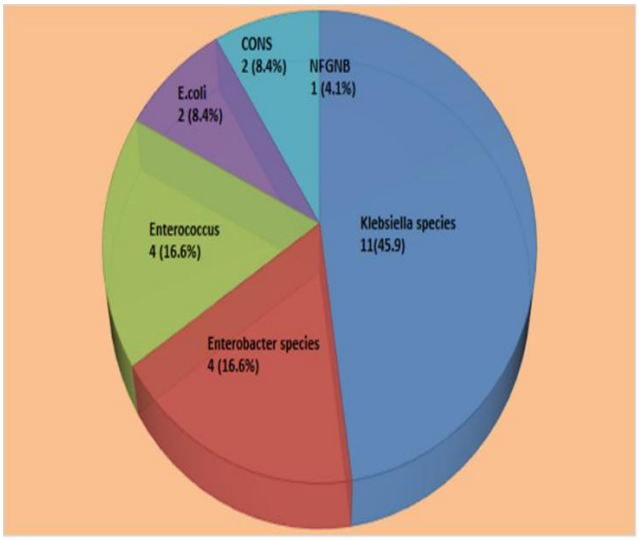
Table 3: Antibiogram of Gram-negative and Gram-positive organisms from UTI IPD samples

Gram Positive		Staph.aureus	Enterococci	Gram Negative	E. coli	Klebsiella spp	Enterobacter spp	Pseudomonas spp
# of Isolates		45	42	# of Isolates	249	300	40	42
1st Line antibiotics	Penicillin	42	76	Ampicillin	32	IR	IR	IR
	Ampicillin	47	70					
	Amoxyclav	54	72	Amoxyclav	86	90	84	IR
	CTM*	63	94	CTM*	57	50	66	IR
	Methicillin	52						
	Nitrofurantoin	86	92	Nitrofurantoin	94	65	62	IR
	Norfloxacin	68	64	Norfloxacin	86	93	67	56
2nd Line antibiotics	Amikacin	74	IR	Cefuroxime	78	80	IR	IR
				Cefaperazone	62	61	47	50
				Cefotaxime	47	51	59	IR
				Ceftazidime	55	51	50	52
				Cefipime	74	63	66	64
	Gentamycin	76	IR	Gentamycin	74	70	62	76
	Ciprofloxacin	74	52	Ciprofloxacin	58	61	44	60
	Levofloxacin	84	79	Levofloxacin	57	60	53	60
	Clindamycin	85	94	Doripenem	96	99	91	94
	Azithromycin	48	73	Imepenem	87	74	66	58
				Meropenem	89	80	72	60
	Teicoplanin	86	93	Amikacin	83	70	66	70
	Vancomycin	90	96					
	Linezolid	67	79	Piparacillin +tazobactum	89	86	69	74
	Ofloxacin	80	73	Ofloxacin	59	66	66	62
OTHER	Colistin			Colistin	98	95	87	94

*CTM :Cotrimoxazole

	Gram Positive Organisms
	Gram negative organisms
	Ist line antibiotics
	Antibiotic not recommended to be used in children without specialist advice
	2nd line antibiotics
	Others
	Intrinsic-resistance is present with this organism
	≥ 90% of isolates susceptible
	70-90% isolates susceptible
	<70% isolates susceptible

Figure 2: Distribution of isolates from culture positive OPD (n=24) and IPD blood samples (n=113)



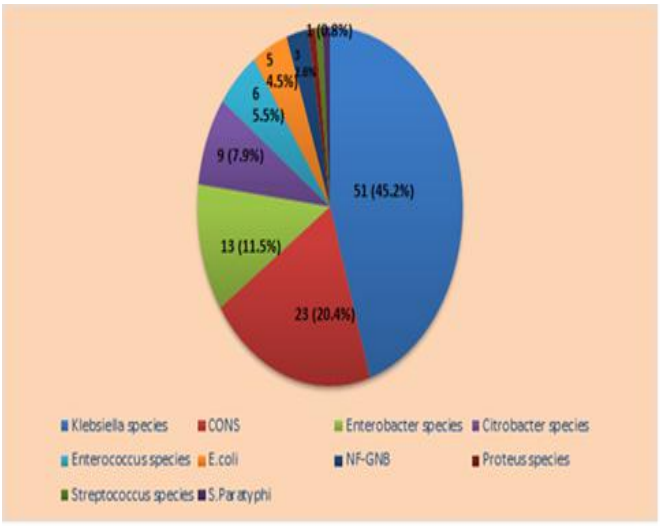
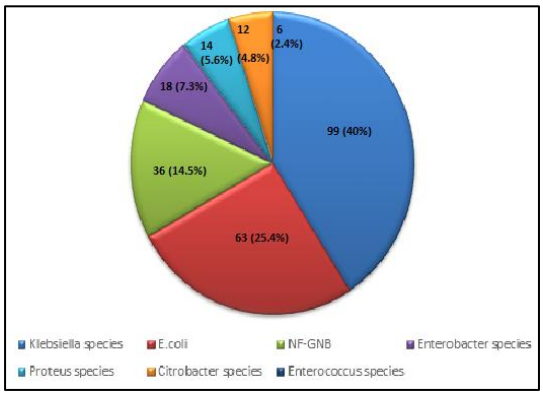


Table 4: Antibiogram of Gram-negative organisms from Blood IPD samples

Gram Negative		Klebsiella spp
# of Isolates		51
1st Line antibiotics	Ampicillin	IR
	Amoxyclav	99
	CTM	71
2nd Line antibiotics	Piparacillin +tazobactum	73
	Cefuroxime	57
	Cefaperazone	52
	Cefotaxime	43
	Ceftazidime	94
	Cefipime	69
	Doripenem	100
	Imepenem	89
	Meropenem	92
	Amikacin	82
	Gentamycin	77
	Ciprofloxacin	71
	Levofloxacin	67
	Ofloxacin	79
OTHER	Colistin	93

CTM-Cotrimoxazole

Figure 3: Distribution of isolates from culture positive OPD (n=248) and IPD sputum samples (n=618)



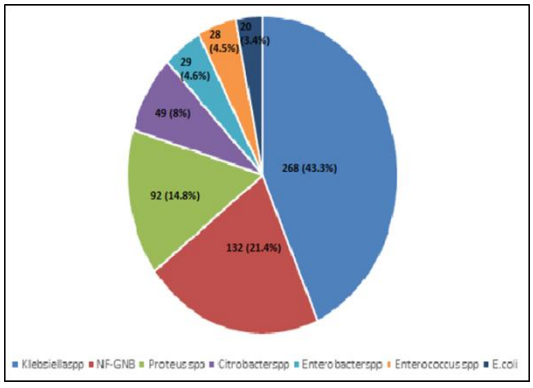


Table 5: Antibiogram of Gram-negative and Gram-positive organisms from Sputum OPD and IPD samples

Gram Negative		E. coli	Klebsiella spp	Gram Negative	Klebsiella spp	Proteus spp	Citrobacter spp	Pseudomonas
# of OPD Isolates		63	99	# of IPD Isolates	268	92	49	45
1st Line antibiotics	Ampicillin	64	IR	1st Line antibiotics	IR	54	IR	IR
	Amoxyclav	84	82		78	79	IR	IR
	CTM	76	60		63	64	54	IR
2nd Line antibiotics	Piparacillin +tazobactum	88	83	2nd Line antibiotics	87	86	88	85
	Cefuroxime	72	75		86	52	IR	IR
	Cefaperazone	86	80		75	68	70	72
	Cefotaxime	86	74		73	66	64	IR
	Ceftazidime	88	86		67	74	72	88
	Cefipime	92	97		76	72	74	87
	Doripenem	98	100		99	96	92	94
	Imepenem	88	89		76	84	82	81
	Meropenem	98	100		81	94	88	90
	Amikacin	86	89		79	80	85	86
	Gentamycin	84	89		80	82	86	84
	Ciprofloxacin	86	86		77	62	56	75
	Levofloxacin	96	74		74	76	64	79
	Ofloxacin	88	89		85	64	64	85
OTHER	Colistin	96	98	OTHER	95	IR	98	98

CTM- Cotrimoxazole

Figure 6: Distribution of isolates from culture positive OPD (n=172) and IPD Pus samples (n=283)

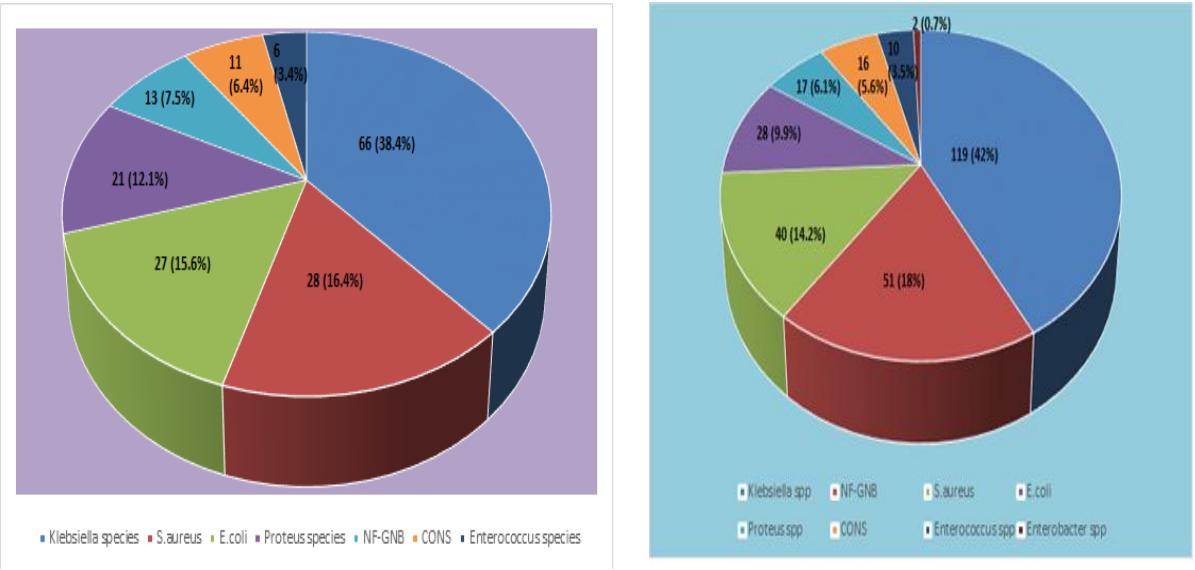


Table 6: Antibiogram of Gram negative and Gram positive organisms from Pus OPD and IPD samples

Gram Negative		Klebsiella spp	Gram Negative	Klebsiella spp	Pseudomonas spp	Gram Positive	Staph. aureus
# of OPD isolates		66	# of IPD isolates	119	35	# of IPD isolates	40
1st Line antibiotics	Ampicillin	IR	1st Line antibiotics	IR	IR	Penicillin	74
	Amoxyclav	84		76	IR	Methicillin	86
	CTM	85		46	IR	Amoxyclav	78
						CTM	53
2nd Line antibiotics	Piparacillin +tazobactum	88	2nd Line antibiotics	85	88	Linezolid	72
	Cefuroxime	76		77	IR		
	Cefaperazone	85		81	84		
	Cefotaxime	86		61	IR		
	Ceftazidime	85		56	86		
	Cefipime	85		69	92		
	Doripenem	96		98	94		
	Imepenem	88		65	88	Azuthromycin	41
	Meropenem	86		69	92	Clindamycin	71
	Amikacin	78		67	68	Amikacin	84
	Gentamycin	80		65	72	Teicoplanin	86
	Ciprofloxacin	74		64	64	Ciprofloxacin	72
	Levofloxacin	76		59	66	Ofloxacin	70
	Ofloxacin	76		83	75	Vancomycin	88
OTHER	Colistin	98	OTHER	98	98		

CTM- Cotrimoxazole

Discussion

Antibiotics are one of the pillars of modern medicine and play a vital role both as the prophylaxis and management of infectious diseases. Successful treatment of patients with bacterial infection relies on the identification of bacterial pathogens and on the selection of an antibiotic effective against that particular organism. Antibiogram is a versatile document which, besides exhibiting the antibiotic susceptibility pattern across the institution, presents a clear picture of the most common disease-causing organisms in various units of the hospital. Antibiotic stewardship refers to the implementation of coordinated efforts to promote the appropriate use of antibiotics in order to improve patient outcomes, reduce antibiotic resistance, and prevent the spread of multidrug-

resistant organisms[8-12]. Our study aimed at isolation, identification of the causative agents and analysis of their antibiotic susceptibility patterns followed by preparation of a cumulative antibiogram for the most common isolates which are more than 30 in number during this study period. In our study, out of the total bacterial isolates, gram-negative bacteria were more prevalent than were gram-positive bacteria. This predominance of gram-negative bacteria is in concordance with the findings of the similar conducted by Al-Jawady, et al. 2012[15].For most patients hospitalized for a complicated UTI or acute pyelonephritis, empiric initial treatment with Ceftriaxone while awaiting culture results is appropriate, if there is no history of a UTI with a Ceftriaxone resistant bacteria. Ceftriaxone maintains very good activity against the most common Gram-negative bacteria in the urine[13-14].The results of the present study agreed with the findings of previous studies of Eswarappa et al. (2011)[16] Aswani et al. (2014)[17], Syed et al. (2012)[18] and Lathika et al., (2015)[19] reported *E.coli* and Klebsiella as predominant Uropathogens. One of the most important reasons for development of anti-microbial resistance is indiscriminate use of antibiotics. Other commonest organisms isolated in our study are Pseudomonas species, *Staphylococcus aureus*, Enterobacter species, Enterococci species. Patients who are hospitalized for CAP with concern for MDROs or patients being treated for HAP should have sputum obtained for culture, ideally before antibiotic administration, to help guide and narrow antibiotic therapy. Most SSTIs are due to either *Streptococcal* infection or *Staphylococcus aureus*. Meropenem remains active against almost all Enterobacteriaceae. Najeeb et al.[20] reported majority of Gram negative bacteria were foundfrom pus infections. Other than that the *Acinetobacter* species, *Staphylococcus epidermidis, Klebsiella, Streptococci, Enterobacter cloacae* and *Moraxella* species were also isolated. Mostly these organisms were resistant to commonly used antibiotics like Ampicillin, Amoxicillin, Cefotaxime. They were comparatively less resistance to Ceftazidime and Gentamicin, while Amikacin, Tobramycin, Quinolones and Imipenem were relatively less resistant. Vancomycin was effective in 100% cases of *Staphylococcus* group.In the present study, analysis of the AST patterns of pus from OPD patients showed maximum susceptibility to Colistin and minimum to Ciprofloxacin in *Klebsiella* species whereas IPD patients data showed highest susceptibility to Doripenem in *Klebsiella* species and to Colistin in *Pseudomonas* species, to Vancomycin in S.aureus and least to Levofloxacin in Klebsiella species and to Ciprofloxacin in *Pseudomonas* species and to Azithromycin in *S.aureus*. *Klebsiella* was the most reported organism isolated in the respiratory tract in studies done by Rajan, et al. and Patel, et al.[21-22] accordance to the results of current study. Resistance to commonly used antibiotics in institutions is alarmingly high requiring continuous surveillance to assess the sensitivity and resistance pattern at a certain levels. The antibiogram prepared from Hospital diagnostic laboratories are readily accessible and inexpensive tool to monitor antimicrobial resistance patterns in communities and regions. Resistance to important antibiotic groups, including Quinolones and Carbapenems has increased substantially over the past few years. It is suggested that empiric antibiotics should be used according to the local antibiograms. A constant evaluation of current practices on the basis of trends in multidrug resistance and antibiotic consumption patterns isessential.

Conclusion

The present study has concluded that presentation of a cumulative antibiogram for a period of one year and its antibiogram analysis helps in formulating the guidelines for the treatment of different infectious diseases. Resistance to important antibiotic groups, including Quinolones and Carbapenems has increased substantially over the past few years. It is suggested that empiric

antibiotics should be used according to the local antibiograms. A constant evaluation of current practices on the basis of trends in multidrug resistance and antibiotic consumption patterns is essential. Antibiograms should be prepared regularly and made readily available to the clinicians to guide them in therapy. There is a need for a central database in India where various laboratories can upload their antibiogram regularly and this data can be very useful in formulating guidelines for treatment of various infectious diseases.

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