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Microbiology Section

Trend of Antimicrobial Resistance among Bacterial Pathogens using Cumulative Antibiogram in a Tertiary Care Centre in Ahmedabad, Gujarat, India

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ABSTRACT

Introduction: A rising incidence of Multidrug Resistance Organisms (MDRO) have become a major challenge to human health infections due to MDRO results in higher mortality rates, longer durations of hospital stays, and higher healthcare costs. MDRO contribute to over 50% of Healthcare Associated Infections (HAIs).

Aim: To monitor the trends of Antimicrobial Resistance (AMR) among bacterial pathogens over a period of three years by using Cumulative Antibiogram (CA).

Materials and Methods: A retrospective study was done to measure the trends of AMR among gram positive and gram negative organisms over a period of three years. CA capturing the susceptibility data was prepared for Enterobacteriacae, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Acinetobacter* spp. and *Enterococcus* spp. once in every three year (2017, 2018 and 2019) in the month of January.

Results: A total of 1032 isolates, of 10 medically important bacteria were analysed. Total of 21.49%, 30.38% and 54.55% isolates were Extended Spectrum β Lactamase (ESBL) producer in 2017, 2018 and 2019, respectively. There was a rising carbapenem resistance in 2019 (15.5% in *E.coli*, 26% in *Klebsiella pneumonaie* an 21% in *P. aeruginosa).* Among isolates of *S. aureus* identified in 2019, 56% were Methicillin Resistant *Staphylococcus aureus* (MRSA).

Conclusion: CA helps in monitoring resistance trends among clinical isolates which helps in preparation of antibiotic policy. There is rising incidence of ESBL and carbapenem resistance among gram negative bacilli.

Keywords: Antimicrobial resistance, Cumulative antibiogram, Extended spectrum beta lactamase, Methicillin resistant *Staphylococcus aureus*

INTRODUCTION

One of the most serious public health threats of the 21st century is AMR [1]. For survival, microbes are evolving and develops AMR through genetic mutations or acquisition of genetic material through plasmid transfer from a resistant bacterium [2]. AMR commonly develops due to selective pressure applied by antibiotic use, which includes irrational and overuse of antibiotics. India consisting of highest drug resistant pathogens worldwide, including the highest burden of MDR tuberculosis [3].

The nationwide surveillance study documented carbapenem and colistin resistance in *Klebsiella pneumoniae* as 49.3% and 8.8%, respectively [4]. Summarised antimicrobial susceptibility report of commonly isolated microorganisms to usual antibiotics of a particular area in a defined period of time is called CA [5,6].

ESBL are β lactamase enzyme which has the ability to hydrolyze 3rd generation cephalosporin and are inhibited by β lactamase inhibitors. Study for Monitoring Antimicrobial Resistance Trends (SMART) study observed a high prevalence of ESBLs in *E. coli* (79%) and *Klebseilla* spp. (70%) in the year 2006-2007 [7]. *Staphylococcus aureus* is a pathogen associated with both community-acquired as well as HAIs. Soon after introduction of Methicillin in October 1960 MRSA were reported [8]. The incidence of MRSA was higher in Southern part of India [9] (50%) compared to in western part of India (25%) [10].

In this article, authors discuss how to prepare an antibiogram, for the hospital what are the important points to be keep in mind while preparing an antibiogram. Local susceptibility pattern of different organism generated from antibiogram, helps in preparation of empiric antibiotic policy, and monitoring resistance trends of that institute over time. Antibiograms can also be used to compare susceptibility rates among different institutions, geographic area and track the resistance trends.

MATERIALS AND METHODS

This was a retrospective study done to measure the trends of AMR among gram positive and gram negative pathogens isolated from clinical samples over a period of three years (2017 to 2019) and analysis was done in 2020. Antimicrobial susceptibility testing was done on Muller Hinton Agar by Modified Kurby bauer method (Disk diffusion method) [11]. The interpretation of antimicrobial susceptibility was based on the latest Clinical and Laboratory Standards Institute (CLSI) (Performance standards for Antimicrobial susceptibility Testing, CLSI M100 guidelines) [11].

All clinical samples detail were added in Microsoft excel sheet which included patient details like (name, age, sex, registration ID), sample type (e.g., urine, sputum, pus, tissue). Organism was isolated, and it's susceptibility to various antibiotics were checked.

MRSA and ESBL production among clinical isolates were detected as per CLSI guidelines (Performance standards for Antimicrobial susceptibility Testing, CLSI M100) guidelines [11]. In case of *E. coli*, *Klebsiella* spp. and *Proteus mirabilis*, ESBL production was included in susceptibility pattern. Similarly for *S. aureus* MRSA was included in susceptibility pattern of excel sheet.

CA capturing the susceptibility data was prepared as per the CLSI [5] for Enterobacteriacae, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Acinetobacter* spp. and Enterococci once a year every three years (2017, 2018 and 2019).

Inclusion criteria: Only isolates obtained from diagnostic testing (Aerobic culture of clinical samples) were included. Only the first isolate from a patient irrespective of the specimen site was included. Antibiotics which are routinely used were tested by disk diffusion method. Only the percentage susceptible was included in the CA and not those which are intermediate susceptible.

Exclusion criteria: Isolates grown from surveillance cultures or colonisers e.g., MRSA screening were excluded from the study. Repeat isolates from same patient were also excluded.

Number of isolates: Annual analysis was performed if minimum 30 isolates of a particular organism was isolated to ensure a minimum level of precision while doing the calculation.

Frequency of data analysis and reports: Once a year in January (2017, 2018 and 2019).

Data Stratification

Isolate-based approaches was used to calculate percentage susceptible.

Annual resistance was calculated by dividing total number of resistant isolates of a particular organism from total number of isolates of that particular organism. To calculate the trends of ESBL, Carbapenem resistance among Enterobacteriacae and MRSA, annual resistance was used.

For example, the resistant percentage for MRSA was calculated as [12,13]:

$$\frac{\text{Total no. of } S.\ aureus \text{ isolates resistant to oxacillin or cefoxitin}}{\text{Total no. of } S.\ aureus \text{ isolates tested for susceptibility to oxacillin or cefoxitin}} \times 100$$

STATISTICAL ANALYSIS

Data was entered in Microsoft excel and presented as numbers and percentages.

RESULTS

A total of 6821 culture samples were processed over a period of three years. The percentage of received clinical samples in 2017 to 2019 was: Urine (67%, 52%, 44%), Sputum (7%, 34%, 32%), Pus (21%, 11%, 10%), Blood (0, 1%, 20%), Body fluid (4%, 2%, 2%), Endothrecheal secretion and Bronchoalveolar lavage (0, 1%, 2%), and Tissue (1%, 1%, 1%) in year 2017, 2018 and 2019, respectively.

[Table/Fig-1] shows the different type and number of Enterobacteriacae isolated in three years. Antibiogram was prepared for three consecutive years for gram positive and gram negative organisms. Trends of antimicrobial susceptibility of *Staphylococcus aureus*, and *Enterococcus* spp. is demonstrated in [Table/Fig-2-4].

Percentage of ESBL, MRSA and Carbapenem Resistance is shown in [Table/Fig-5] which shows rising trend of ESBL and carbapenem resistance. Antimicrobial susceptibility of *Salmonella* typhi is shown in [Table/Fig-6]. All *Salmonella* typhi isolates were sensitive to Ampicillin, Amoxycillin, Chloramphenicol, Ceftriaxone and Cotrimoxazole.

Organism	2017	2018	2019	Total
E. coli	86	125	159	370
Klebsiella spp.	24	31	53	108
Enterobacter spp.	3	11	18	32
Morgenella spp.	0	0	2	2
Proteus spp.	10	4	13	27
Salmonella spp.	0	7	24	31
S. aureus	38	73	126	237
Enterococcus spp.	5	5	27	37
P. aeruginosa	13	46	118	177
Acinetobacter spp.	0	1	10	11

[Table/Fig-1]: Number of Enterobacteriacae, *S. aureus*, *Enterococcus* spp. and *P. aeruginosa* isolated in 3 years (1032).

	S. aureus						*Enterococcus* spp.					
	2017		2018		2019		2017		2018		2019	
Antibiotics	Total	%	Total	%	Total	%	Total	%	Total	%	Total	%
	38		73		126		5		5		27	
Penicillin	2	5.2	2	2.7	2	1.5	4	80	1	20	12	44.4
Cefoxitin	18	47.3	37	50.6	55	43.6		-		-		-
Amikacin	15	39.4	65	89	112	88.8		-		-		-
Gentamycin	18	47.3	60	82	96	76.1		-		-		-
Gentamycin HL							2	40	1	0	16	59.2
Netilmycin	24	63.1	70	95	119	94.4		-		-		-
Tobramycin	18	47.3	63	86.3	102	80.9		-		-		-
Ciprofloxacin	6	15.7	13	17.8	46	36.5	1	20	0	0	9	33.3
Levofloxacin	6	15.7	14	19.1	44	34.9	1	20	0	0	9	33.3
Teicoplanin	38	100	73	100	126	100	5	100	5	100	27	100
Vancomycin	38	100	73	100	126	100	5	100	5	100	27	100
Linezolid	38	100	73	100	126	100	5	100	5	100	27	100
Cotrimoxazole	11	28.9	47	64.3	69	54.7		-		-		-
Erythromycin	18	47.3	34	46.5	57	45.2	4	80	0	0	13	48.1
Azithromycin	18	47.3	34	46.5	57	45.2		-		-		-
Clindamycin	26	68.4	53	72.6	98	77.7		-		-		-
D Test	4	10.5	16	21.9	12	9.5		-		-		-
Tetracycline	27	71	65	89	120	95.2	2	40	1	20	5	18.5
Doxycycline	28	73.6	67	91.7	121	96	4	80	1	20	5	18.5
Tigecycline	32	94	73	100	126	100	4	80	1	20	5	18.5
Rifampicin	31	81.5	73	93	124	98.4	4	80	3	60	21	77.7
Chloramphenicol	27	71	69	94.5	117	92.8	4	80	2	40	21	77.7

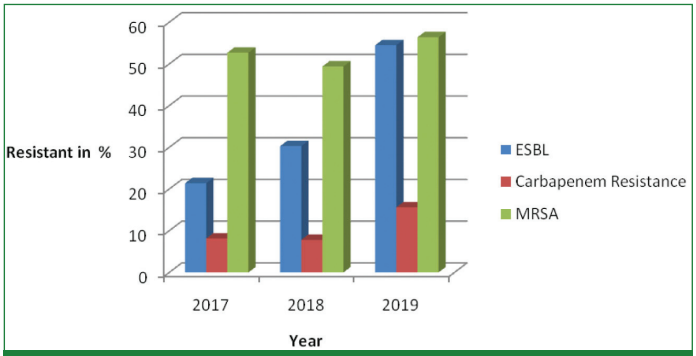
[Table/Fig-2]: Susceptibility pattern of *S. aureus* and *Enterococcus* spp.

Antibiotics	Enterobacteriaceae						*Pseudomonas aeruginosa*					
	2017		2018		2019		2017		2018		2019	
	Total	%	Total	%	Total	%	Total	%	Total	%	Total	%
	123		178		269		13		46		118	
Ampicillin	23	18.7	40	22.47	32	11.8		-				-
Piperacillin	34	27.6	49	27.5	55	20.4	9	69.23	32	69.56	80	67.8
Cefuroxime	42	34.15	63	35.3	70	26		-		-		-
Cefexime	42	34.15	64	35.9	71	26.39		-		-		-
Cefazoline	42	34.15	64	35.9	72	26.77		-		-		-
Ceftriaxone	55	44.7	77	43.2	82	30.48		-		-		-
Cefoperazone	55	44.7	77	43.2	82	30.48		-		-		-
Ceftazidime	55	44.7	77	43.2	82	30.48	9	69.23	34	73.91	84	71.1
Cefepime	57	46.3	79	44.38	84	31.23	11	84.62	34	73.91	88	74.5
AMC	92	74.8	133	74.7	158	58.74		-		-		-
AS	92	74.8	133	74.7	158	58.74		-		-		-
PIT	103	83.7	141	79.2	173	64.31	11	84.62	35	76.8	88	74.5
CAC	103	83.7	141	79.2	173	64.31		-		-		-
CFS	103	83.7	141	79.2	173	64.31	11	84.62	36	78.26	88	74.5
Amikacin	87	70.7	147	82.5	201	74.72	8	61.54	32	69.57	86	72.8
Gentamycin	84	68.2	144	80.9	168	62.45	9	69.23	31	67.39	89	75.4
Netilmycin	89	72.3	148	83.1	200	74.35	9	69.23	32	69.57	86	72.8
Tobramycin	80	65	144	80.9	170	63.2	9	69.23	32	69.57	84	71.1
Ciprofloxacin	54	43.9	83	46.6	86	31.97	9	69.23	31	67.39	78	66.1
Levofloxacin	54	43.9	84	47.1	87	32	9	69.23	31	67.39	78	66.1
Imipenem	113	91.8	164	92.1	227	84.39	12	92.3	38	82.6	94	79.6
Meropenem	113	91.8	164	92.1	227	84.39	12	92.3	38	82.6	96	81.3
Ertapenem	113	91.8	164	92.1	227	84.39		-		-		-
Doripenem	113	91.8	164	92.1	227	84.39	12	92.3	38	82.6	98	83
Tetracycline	23/33	69.7	65/109	59.63	50/131	38.17		-		-		-
Doxycycline	23/33	69.7	65/109	59.63	53/131	40.45		-		-		-
Tigecycline	23/33	72.7	103/109	94.4	110/131	83.96		-		-		-
Colistin	112	100	178	100	269	100	13	100	46	100	118	100
Chloramphenicol	22/33	66.7	92/109	84.4	96/131	73.28		-		-		-
Cotrimoxazole	59	47.9	105	59	99	36.8		-		-		-
Aztreonam	53	43	72	40.4	78	29		-		-		-
Nitrofurantoin	82/90	91	65/69	94.2	113/138	81.88		-		-		-
Fosfomycin	87/90	96.6	49/69	71	124/138	89.86		-		-		-

[Table/Fig-3]: Susceptibility pattern of Enterobacteriacae and *Pseudomonas aeruginosa*.
(Amoxicillin- clavulanic acid [AMC], Ampicillin sulbactam [AS], Piperacillin tazobactam [PIT], Cefazidime clavulanic Acid [CAC], Cefoperazone sulbactam [CFS])

Antibiotics	Organism	2017		2018		2019	
		Total	%	Total	%	Total	%
Amoxycillin-clavulanic acid	Enterobacteriacae	31/123	25	45/178	25	111/269	41
	S. aureus	20/38	52	36/73	49	71/126	56
	Enterococcus spp.	1/5	20	4/5	80	15/27	55
Piperacillin-tazobactam	Enterobacteriacae	20/123	16	37/178	20	96/269	35
	P. aeruginosa	2/13	15	11/46	24	30/118	25
Amikacin	Enterobacteriacae	36/123	30	31/178	18	68/269	25
	P. aeruginosa	5/13	38	14/46	30	32/118	27
	S. aureus	23/38	60	8/73	11	14/126	11
Levofloxacin	Enterobacteriacae	69/123	56	94/178	53	182/269	68
	P. aeruginosa	4/13	30	15/46	32	40/118	34
	S. aureus	32/38	84	59/73	80	82/126	65
	Enterococcus spp.	4/5	80	5/5	100	18/27	67
Tigecycline	Enterobacteriacae	10/33	28	6/109	6	21/131	18
	S. aureus	6/38	16	0/73	0	0/126	0
Cotrimoxazole	Enterobacteriacae	59/123	48	73/178	41	170/269	63
	S. aureus	27/38	71	26/73	35	57/126	45

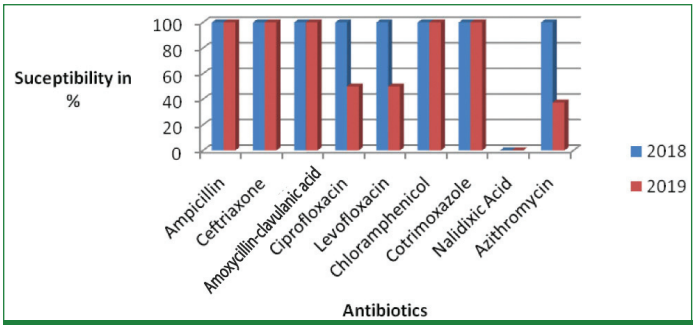
[Table/Fig-4]: Trends of Antibiotic resistance among Enterobacteriacae, P. aeruginosa, *S. aureus* and *Enterococcus* spp.



[Table/Fig-5]: Trends of ESBL, Carbapenem resistance among Enterobacteriacae and MRSA.

Among Enterobacteriacae compared to 2017 and 2018, there was a high rate of resistance to amoxycillin-clavulanic acid, amikacin, tigecycline, levofloxacin and cotrimoxazole in 2019. levofloxacin resistance among *P. aeruginosa* was around 30% (2017-30% 2018-32%, 2019-34%). All *S. aureus* isolated in 2018 and 2019 were sensitive to Tigecycline [Table/Fig-4].

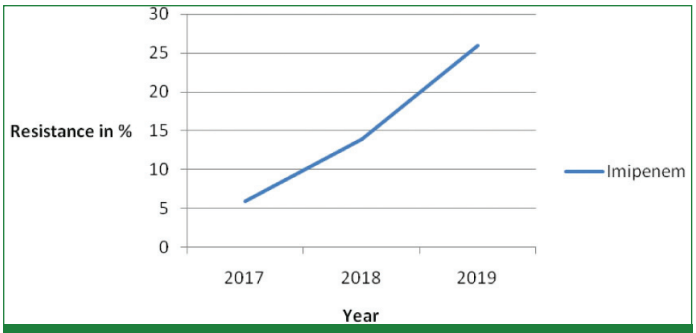
There was a rising rate of carbapenem resistance among *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *E.coli* is shown in



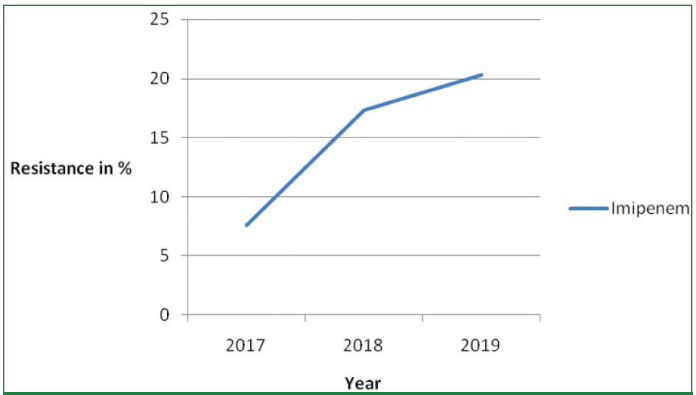
[Table/Fig-6]: Trends of Susceptibility patterns of *Salmonella* typhi.
In 2017, Salmonella typhi was not isolated from any clinical specimen

[Table/Fig-7-9]. In this study, many clinical isolates of *Acinetobacter* spp. were not found. Hence, it's trends of antibiotic resistance was not prepared. In 2019, 90% of clinical isolates of *Acinetobacter* spp. were resistance to carbepenem however, all these isolates were sensitive to tigecycline and colistin.

[Table/Fig-7]: Trends of carbapenem resistant in *E.coli*.



[Table/Fig-8]: Trends of carbapenem resistant in *Klebsiella penumoniae*.



[Table/Fig-9]: Trends of carbapenem resistant in *Pseudomonas aeruginosa*.

DISCUSSION

This study showed a rising rate of ESBL and carbapenem resistance among Enterobacteriaceae. Similarly in *Pseudomonas aeruginosa* increasing rate of resistance was found to piperacillin-tazobactam and fluroquinolones over a period of three years. *Escherichia coli, Klebsiella* spp., *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Enterobacter* spp., are related with the HAI and there have been increasing rates of resistance [14-16], and MDR within these bacteria [17,18].

Antibiogram helps in monitoring trends of AMR by which it helps us planning empiric antibiotic policy for that particular Institute. This will allow choosing presumptive antibiotic for particular pathogen based on local susceptibility data. It also helps in antimicrobial stewardship and infection control practices.

The AMR among India has been significantly increased due to several factors and one of them is unwarranted use of antibiotics [19]. There is limited data available regarding trends of antibiotic consumption from India which suggest that consumption of antibiotics is higher in India compared to other developing countries [20,21] and it is much lower in developed countries [22].

Increase rate of MDRO also affects economy of healthcare centre due to heavy expenditure on antibiotics procured. One of the best methods to prolong the shelf-life of existing and newer future Antimicrobial agents is Antimicrobial Stewardship Programme (AMSP). Study by Mauldin PD et al., shows HAI due to antibiotic resistant gram negative pathogens is associated with higher total hospital cost (29.3%) and increased length of stay (23.8%) as compared to the susceptible gram positive pathogens [23].

Implementation of AMSP on priority will help rationalise antimicrobial usage in our country. The ultimate goal of antimicrobial stewardship is to reduce the adverse consequences of antibiotics and increase in emergence of resistant organisms [24,25]. To prevent AMR, Centers for Disease Control and Prevention suggested to "use antimicrobials wisely," and recommended healthcare providers to "Use local data; know your antibiogram" [6].

Third-generation cephalosporins and fluroquinolones resistance was 75-80% in *E. coli*, 65-77% in *K. pneumoniae*, 73-87% in *A. baumannii* and around 40% in *P. aeruginosa* [4]. This study showed raising fluroquinolones resistance among Enterobacteriacae (57-69%).

ICMR-AMRSN data 2016-2018 also showed that majority of the gram negative isolates were MDR [4]. The proportion of carbapenem resistance was high in gram negative bacteria during the 2019 in present study. As per ICMR-AMRSN data, higher non susceptibility to meropenem was observed in *A. baumannii* (69.8, 81.3, 80.1%) followed by *K. pneumoniae* (48.6, 51.8, 50.4%), *P. aeruginosa* (32.9, 31.3, 30.9%) and *E. coli* (13, 21 and 23%) in 2016, 2017 and 2018, respectively [4]. Present study shows maximum resistance to imipenrm among *Acinetobacter* spp. (2019-90%) followed by *K. Pneumoniae* (6,14,26%), *E. coli* (8, 6.5, 15.5%) and *P. aeruginosa* (7, 17, 21%) in 2017, 2018, and 2019, respectively.

Infections due to MDRO is challenging and difficult to treat. Colistin is a last resort antibiotic used for treating severe gram negative infections. In this study, no colistin resistant isolate was found however, carbapenems and colistin resistant was 13% in *K. pneumoniae* isolates (ICMR-AMRSN data 2016-2018) [4]. *Burkholderia* and *Stenotrophomonas* are usually misidentified as *Pseudomonas* by most of the laboratories [26]. Carbapenems have no effect on *Stenotrophomonas* and *Burkholderia* is intrinsically resistant to colistin [11]. Correct identification of above mentioned pathogens helps in treatment with appropriate antibiotics and also gives correct resistance pattern of *Pseudomonas* spp.

Increasing MIC to ceftriaxone and increased susceptibility to co-trimoxazole, ampicillin and chloramphenicol were found with typhoid data from the ICMR network. All *Salmonella* isolates from our institute show 100% susceptibility to ceftriaxone, co-trimoxazole, ampicillin amoxycillin-clavulanic acid and chloramphenicol. However, the susceptibility to fluroquinolones was 100% and 50% in 2018, and 2019, respectively. However, all of the isolates were resistance to Nalidix acid. The recent outbreak of ceftriaxone-resistant *Salmonella* typhi in Hyderabad, Pakistan, was identified through AMR surveillance, which led to the implementation of appropriate control measures to contain the outbreak [27].

The overall MRSA prevalence in this study was 53% in 2017, 50% in 2018 and 57% in 2019. The prevalence of MRSA in a study from Chennai [9] was reported as 40-50%. *S. aureus* constituted 17% of Catheter Related Blood Stream Infections (CRBSIs) in that centre. A study in Delhi high shows high prevalence of MRSA (35% in ward and 43% in ICU) from blood culture [22].

There was a rising rate of carbapenem resistance in *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* over a period of three years (2017-2019). There was no significant change in the incidence of MRSA over a period of three years (2017-2019). The data from this study suggest to avoid use of fluroquinioloes in case of enteric fever as all isolates of *Salmonella* typhi are resistant to Nalidix acid (Nalidix acid resistant *Salmonella* typhi has poor response to fluroquinolones [11]).

Limitation(s)

This study had limited number of *Acinetobacter* spp. isolates over a period three years hence, the trend of antibiotic resistance of *Acinetobacter* spp. was not done. Similarly, five isolates of *Enterococcus* spp. were isolated in each year (2017 and 2018). Such small numbers are not suitable to determine the antimicrobial susceptibility pattern.

CONCLUSION(S)

The trends of antibiotic resistance from pathogens generated by antibiogram helps in decreasing mortality and expenditure by providing in depth knowledge about antibiotic policy, AMSP and this helps the physician to start the appropriate therapy in the beginning.

REFERENCES

[1] Crowther-Gibson P, Govender N, Lewis DA, Bamford C, Brink A, von Gottberg A, et al. Part IV. Human infections and antibiotic resistance. SAMJ: South African Medical Journal. 2011;101(8):567-78.
[2] Lipsitch M, Samore MH. Antimicrobial use and antimicrobial resistance: A population perspective. Emerging Infectious Diseases. 2002;8(4):347.
[3] India TB. Revised National Tuberculosis Program Annual Status Report. New Delhi, India: Directorate General of Health Services, Ministry of Health and Family Welfare. 2017.
[4] Walia K, Madhumathi J, Veeraraghavan B, Chakrabarti A, Kapil A, Ray P, et al. Establishing antimicrobial resistance surveillance & research network in India: Journey so far. The Indian J Med Res. 2019;149(2):164-79.
[5] Clinical and Laboratory Standards Institute (CLSI). Analysis and presentation of cumulative antimicrobial susceptibility test data. 3rd ed. Approved guideline M39-A3. Wayne PA. CLSI, 2014.
[6] Hindler JF, Stelling J. Analysis and presentation of cumulative antibiograms: A new consensus guideline from the Clinical and Laboratory Standards Institute. Clin Infect Dis. 2007;44(6):867-73.
[7] Hawser SP, Bouchillon SK, Hoban DJ, Badal RE, Hsueh PR, Paterson DL. Emergence of high levels of extended-spectrum-β-lactamase-producing gram-negative bacilli in the Asia-Pacific region: Data from the Study for Monitoring Antimicrobial Resistance Trends (SMART) program, 2007. Antimicrob Agents Chemother. 2009;53(8):3280-84.
[8] Jevons MP. "Celbenin"-resistant staphylococci. British Med J. 1961;1(5219):124.
[9] Gopalakrishnan R, Sureshkumar D. Changing trends in antimicrobial susceptibility and hospital acquired infections over an 8 year period in a tertiary care hospital in relation to introduction of an infection control programme. J Assoc Physicians India. 2010;58(Suppl):25-31.
[10] Patel AK, Patel KK, Patel KR, Shah S, Dileep P. Time trends in the epidemiology of microbial infections at a tertiary care center in west India over last 5 years. J Assoc Physicians India. 2010;58(58):37-40.
[11] Clinical and Laboratory Standards Institute (CLSI). Performance standard for Antimicrobial susceptibility Testing 29th edition M 100 Wayne PA. CLSI, 2019.
[12] Antimicrobial-Resistant Phenotype Definitions Analysis of Antimicrobial-Resistant Organisms in NHSN n.d. https://www.cdc.gov/nhsn/pdfs/ps-analysis-resources/phenotype_definitions.pdf.
[13] Antimicrobial Resistance rate table n.d. https://www.cdc.gov/nhsn/pdfs/ps-analysis-resources/aur/ar-qrg-ratetable-508.pdf.
[14] Weinstein RA, Gaynes R, Edwards JR, National Nosocomial Infections Surveillance System. Overview of nosocomial infections caused by gram-negative bacilli. Clin Infect Dis. 2005;41(6):848-54.
[15] National Nosocomial Infections Surveillance System Report. Data summary from January 1992 through June, issued October 2004. Am J Infect Control. 2004;32(8):470-85.
[16] Rhomberg PR, Jones RN. Contemporary activity of meropenem and comparator broad-spectrum agents: MYSTIC program report from the United States component (2005). Diagnostic Microbiology and Infectious Disease. 2007;57(2):207-15.
[17] Paterson DL. Resistance in gram-negative bacteria: Enterobacteriaceae. American J Infect Con. 2006;34(5):S20-28.
[18] Slama TG. Gram-negative antibiotic resistance: There is a price to pay. Crit Care. 2008;12(4):01-07.
[19] Kotwani A, Holloway K, Chaudhury RR. Methodology for surveillance of antimicrobials use among out-patients in Delhi. Indian J Med Res. 2009;129(5):555-60.
[20] Shankar RP, Partha P, Shenoy NK, Easow JM, Brahmadathan KN. Prescribing patterns of antibiotics and sensitivity patterns of common microorganisms in the Internal Medicine ward of a teaching hospital in Western Nepal: A prospective study. Ann Clin Microbiol Antimicrob. 2003;2(1):01-09.
[21] De Castro MS, Pilger D, Ferreira MB, Kopittke L. Trends in antimicrobial utilization in a university hospital, 1990-1996. Revista de Saude Publica. 2002;36(5):553-58.
[22] Wattal C, Joshi S, Sharma A, Oberoi JK, Prasad KJ. Prescription auditing and antimicrobial resistance at a tertiary care hospital in New Delhi, India. J Hosp Infect. 2005;59(2):156-58.
[23] Mauldin PD, Salgado CD, Hansen IS, Durup DT, Bosso JA. Attributable hospital cost and length of stay associated with health care-associated infections caused by antibiotic-resistant gram-negative bacteria. Antimicrob Agents Chemother. 2010;54(1):109-15.
[24] Antimicrobial Stewardship Program Guideline. November 15 2011. http://iamrsn.icmr.org.in/images/pdf/AMSP_Guidelines_final.pdf.
[25] Walia K, Ohri VC, Mathai D. Antimicrobial Stewardship Programme (AMSP) practices in India. The Indian J Med Res. 2015;142(2):130-38.
[26] Gautam V, Singhal L, Ray P. Burkholderia cepacia complex: Beyond pseudomonas and acinetobacter. Indian J Med Microbiol. 2011;29(1):04-12.
[27] Yousafzai MT, Qamar FN, Shakoor S, Saleem K, Lohana H, Karim S, et al. Ceftriaxone-resistant Salmonella Typhi outbreak in Hyderabad City of Sindh, Pakistan: high time for the introduction of typhoid conjugate vaccine. Clin Infect Dis. 2019;68(Supplement_1):S16-21.

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