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Antimicrobial Stewardship – An Indispensable Weapon in the Battle Against Drug Resistance

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ABSTRACT

Background: Antimicrobial resistance (AMR) continues to rise globally, largely driven by inappropriate antibiotic use. Antimicrobial Stewardship Programs (ASPs), supported by cumulative antibiograms and antibiotic policies, are essential strategies to optimize antimicrobial use and limit multidrug-resistant organisms (MDROs). This study evaluated the impact of ASP implementation on antimicrobial susceptibility trends, MDRO prevalence, and antibiotic consumption in a tertiary care hospital.

Methods: An ambispective observational cohort study was conducted from January 2022 to December 2024. Clinical isolates from 3092 samples were analysed, of which 1144 were culture-positive. Susceptibility testing followed CLSI guidelines, and annual antibiograms were compared across three surveillance periods: OYB (pre-policy), OYA (one year post-policy), and TYA (two years post-policy). Statistical comparisons were performed using Chi-square or Fisher's exact tests, with $p < 0.05$ considered significant. Antibiotic consumption was assessed using Defined Daily Dose (DDD)/1000 patients.

Results: E. coli and Pseudomonas aeruginosa demonstrated modest improvements in susceptibility following ASP implementation, with significant increases in doxycycline and ciprofloxacin susceptibility, respectively. Klebsiella species showed initial improvement but later decline. Among gram-positive organisms, Staphylococcus aureus exhibited early gains followed by slight reductions, while CoNS showed declining susceptibility, particularly to ciprofloxacin. Streptococci demonstrated progressive susceptibility reduction across years. MDRO prevalence decreased notably: ESBL-producing E. coli (63% → 51%), ESBL-Klebsiella (60% → 52%), and MRSA (24% → 22%). β-lactam/β-lactamase inhibitor consumption significantly declined ($p < 0.05$).

Conclusion: Implementation of a structured ASP, anchored by cumulative antibiogram-guided policy and clinician education, led to favourable trends in antimicrobial susceptibility and a measurable reduction in MDRO burden. Continuous surveillance, reinforced prescriber compliance, and sustained stewardship efforts remain essential to curb AMR.

Keywords: *Antimicrobial resistance, Antimicrobial Stewardship Programs, MDRO, Antibiogram.*

INTRODUCTION

Ever since the discovery of penicillin in 1928, antibiotics have played a pivotal role in reducing morbidity and mortality associated with bacterial infections. However, as Alexander Fleming cautioned, inappropriate antibiotic use facilitates the selection of resistant bacterial strains, a phenomenon now evident in the increasing incidence of infections caused by organisms that are no longer susceptible to many, if not all, broad-spectrum agents.[1] For example, the excessive use of β-lactam antibiotics has contributed to a marked rise in extended-spectrum β-lactamase (ESBL)-producing organisms,

rendering many β-lactam drugs ineffective.[2] The Centers for Disease Control and Prevention (CDC) estimates that nearly 30% of antibiotics used in hospitals are unnecessary or inappropriate, substantially contributing to the development of antimicrobial resistance (AMR).[3]

The global escalation of multidrug-resistant (MDR) pathogens necessitates the implementation of structured interventions such as Antimicrobial Stewardship Programs (ASPs) and institutional infection control policies. Optimizing antimicrobial use through stewardship is crucial to combating AMR, particularly by rationalizing the use of Access, Watch, and Reserve (AWaRe) categories of antimicrobials as delineated in the WHO Essential Medicines List.[4] The cumulative antibiogram—a foundational element of stewardship—plays a central role in guiding empirical therapy, monitoring resistance trends, and shaping institutional antibiotic policies.[5,6]

This study aims to evaluate the impact of ASP implementation, specifically through the development and application of a cumulative antibiogram and antibiotic policy, on antimicrobial susceptibility trends and the incidence of multidrug-resistant organisms in a tertiary care hospital.

MATERIALS AND METHODS

Study design: This ambispective observational cohort study was conducted in a tertiary care hospital in Raichur, Karnataka, over three years (January 2022–December 2024). Institutional Ethics Committee approval was obtained (certificate number NMC/RCR/IHEC/2025-26/134). Data from the Department of Clinical Microbiology were included. All clinical samples received for aerobic bacterial culture and susceptibility testing were considered, while repeat samples, surveillance cultures, and screening isolates were excluded. Sample processing and organism identification followed standard microbiological protocols.

Blood culture samples were processed using BD BACTEC aerobic and anaerobic bottles. Positive cultures were subcultured on blood, chocolate, and MacConkey agar, and Gram staining was performed. Biochemical reactions appropriate to the organism were used for definitive identification. Only the first isolate per patient was included in the analysis. All laboratory data were entered and stored in a local Laboratory Information Management System (LIMS). Urine cultures were considered significant when growth exceeded 10^5 CFU/mL for a single organism.

Antimicrobial susceptibility testing was performed using the Kirby–Bauer disk diffusion method on Mueller–Hinton agar, and zone diameters were interpreted according to Clinical and Laboratory Standards Institute (CLSI) guidelines.[7] ATCC reference strains—E. coli 25922, P. aeruginosa 29835, S. aureus 25923, and S. pneumoniae 49616—were used as quality controls.

A cumulative antibiogram for the period January–December 2022 was generated according to CLSI M39-A4 guidelines, reporting only the percentage of susceptible isolates. Intermediate categories were excluded. This antibiogram formed the basis of the hospital's updated antibiotic policy, implemented in January 2023 as part of the ASP. A multidisciplinary team comprising microbiologists, physicians, epidemiologists, and infection prevention specialists reviewed data and disseminated the policy to clinical departments. Random prescription audits were performed, and outcome measures were evaluated one year post-implementation (January 2024).

Outcomes measured: Three key outcomes were assessed: changes in antimicrobial susceptibility across the three surveillance periods - OYB (January–December 2022), OYA (January–December 2023), and TYA (January–December 2024)**,** antibiotic consumption expressed as Defined Daily Dose (DDD) per 1000 patients, and incidence of MDR organisms (ESBL-producing E. coli, ESBL-producing Klebsiella, and MRSA). MDR was defined as resistance to at least one antibiotic in three or more antimicrobial classes.

Statistics: Statistical analysis was conducted using SPSS version 26. Susceptibility percentages were converted into absolute numbers of susceptible and non-susceptible isolates. Chi-square tests were used to compare proportions when expected counts were adequate (≥5). When tables contained small or sparse values, Fisher's exact test was used. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 3092 samples were processed over three years, of which 1144 yielded bacterial growth. Six major bacterial groups were analysed across the OYB, OYA, and TYA periods. Tables 1 and 2 present susceptibility patterns.

1. Escherichia coli

Mean susceptibility increased slightly from 65.6% (OYB) to 66.9% (OYA) and 68.5% (TYA). Significant reductions were observed for amoxiclav in OYA (46% → 23%, $p <0.001$), while doxycycline susceptibility significantly increased (37% → 70%, $p <0.001$). Between OYB and TYA, significant differences were found for doxycycline (37% → 53%, $p <0.05$) and nitrofurantoin (95% → 83%, $p <0.05$). Carbapenem susceptibility remained high (93–95%).

2. Klebsiella species
Mean susceptibility improved from 62.1% (OYB) to 74.1% (OYA), then declined to 63.7% (TYA). Significant improvements between OYB and OYA were observed for piperacillin–tazobactam, cotrimoxazole, ciprofloxacin, and ceftriaxone. Between OYB and TYA, susceptibility to cotrimoxazole and nitrofurantoin declined significantly.

3. Pseudomonas aeruginosa
Mean susceptibility increased from 62.3% (OYB) to 67.6% (OYA), with a slight reduction in TYA (64.5%). Significant differences were observed for ciprofloxacin in both comparisons. Carbapenem susceptibility remained consistently high.

4. Staphylococcus aureus
Mean susceptibility improved initially (69.1% → 79.7%) but declined in TYA (73.1%). Significant changes were noted for erythromycin (increase) between OYB and OYA, and decreases in amoxiclav, azithromycin, and ciprofloxacin between OYB and TYA.

5. Coagulase-Negative Staphylococci (CoNS)
Mean susceptibility exhibited a gradual decline. Significant reductions were observed for ciprofloxacin in both OYA and TYA comparisons, and for amoxiclav between OYB and TYA. Linezolid and vancomycin remained highly effective.

6. Streptococci
Mean susceptibility remained high but showed a progressive decline (92.7% → 83.8% → 74.0%). Significant decreases were observed for erythromycin, amoxiclav, azithromycin, and ciprofloxacin.

Table 3 shows change in mean susceptibility of isolates across the years of study. There was a gradual decline noticed in the rate of multi drug resistant organisms which included Methicillin Resistant Staphylococci (MRSA), Extended Spectrum Beta Lactamase (ESBL) producing E. coli and Klebsiella on a comparative analysis of three years data (Graph 1). MRSA prevalence which was 24% one year before implementation of antibiotic policy decreased to 22% after two years of implementation. ESBL producing E. coli prevalence was 63% one year before which declined to 62% one year after and then further decreased to 51% two years after duration. Similarly, ESBL producing Klebsiella also showed a decline from 60% in one year before period to 52% in two years after period.

The antibiotics consumption and Daily Defined Dose (DDD)/1000 patients is shown in Table 4. No significant change was observed in Fluoroquinoles, Carbapenems, Vancomycin and 3rd generation cephalosporins, while a significant change ($p<0.05$) was seen in consumption of Beta lactam and Beta lactamase Inhibitors antibiotics.

Table 1: Comparison of antibiotic susceptibility patterns before and after implementation of antibiotic policy. (Gram negative bacilli)

Bacteria	No		% susceptibility of each antibiotic											
			Ak	Gen	Amc	Ptz	Cot	Dox	Mrp	Imp	Cip	Ctr	Caz	Nit
E.coli	95	OYB	72	66	46	71	46	37	90	93	39	37	-	95
	128	OYA	82	55	23	70	40	70	94	95	52	38	-	96
	92	TYA	82	82	50	81	49	53	88	88	38	49	-	83
p value to compare between OYB and OYA			0.091	0.107	**0.0003**	1	0.407	**0.0001**	0.521	0.578	0.064	0.937		0.875
p value to compare between OYB and TYA			0.153	**0.028**	0.721	0.112	0.834	**0.035**	0.755	0.415	1	0.128		**0.016**
Klebsiella species	53	OYB	76	57	48	62	25	48	93	92	36	40	-	93
	40	OYA	85	60	35	85	55	68	96	95	60	65	-	94
	71	TYA	75	75	46	78	44	47	79	79	43	48	-	78
p value to compare			0.385	0.907	0.334	**0.028**	**0.005**	0.081	0.945	0.945	**0.035**	**0.026**		0.945

between OYB and OYA														
p value to compare between OYB and TYA			1	0.054	1	0.1	**0.044**	1	0.068	0.068	0.488	0.463		**0.045**
Pseudomonas aeruginosa	22	OYB	79	70	16	77	21	47	97	100	47	19	79	88
	44	OYA	90	84	16	92	26	30	95	94	84	10	40	86
	63	TYA	86	86	20	91	36	30	92	92	73	10	68	71
p value to compare between OYB and OYA			0.253	0.241	1	0.253	1	0.315	1	0.53	**0.002**	0.504	**0.011**	1
p value to compare between OYB and TYA			0.558	0.135	1	0.222	0.357	0.297	0.959	0.403	**0.036**	0.483	0.597	0.266

OYB= One year before implementation of policy, OYA= One year after implementation of policy, TYA= Two years after implementation,
Ak= Amikacin, Gen= gentamicin, Amc= Amoxicillin clavulanate, Ptz= Piperacillin tazobactam, Cot= Cotrimoxazole, Dox= Doxycyclin, Mrp= Meropenem, Imp= Imipenem, Cip= Ciprofloxacin, Ctr= Ceftriaxone, Caz= Ceftazidime, Nit= Nitrofurantoin

Table 2: Comparison of antibiotic susceptibility patterns before and after implementation of antibiotic policy. (Gram positive cocci)

Bacteria	No		% susceptibility of each antibiotic												
			Ak	Gen	Amc	Ptz	Cot	Dox	Azm	E	Cip	Ctr	Van	Lz	Cx
S.aureus	72	OYB	72	60	79	87	52	72	62	46	41	69	93	89	76
	64	OYA	94	90	86	96	75	80	78	65	30	65	88	84	70
	65	TYA	92	88	68	90	74	79	56	54	19	63	83	75	78
p value to compare between OYB and OYA			**0.002**	**0.00008**	0.418	0.193	**0.007**	0.416	0.072	**0.032**	0.202	0.77	0.419	0.601	0.543
p value to compare between OYB and TYA			**0.004**	**0.0004**	0.183	0.961	**0.011**	0.518	0.501	0.443	**0.005**	0.543	0.121	0.064	0.932
CoNS	83	OYB	94	73	89	88	49	90	51	60	88	59	88	86	
	48	OYA	90	80	85	95	60	92	65	45	40	70	86	70	
	94	TYA	92	82	67	91	60	79	37	52	34	62	90	85	
p value to compare between			0.568	0.605	0.724	0.233	0.299	1	0.17	0.157	1.748	0.245	0.883	0.07	

OYB and OYA															
p value to compare between OYB and TYA			0.73	0.243	**0.0008**	0.597	0.227	0.056	0.101	0.35	9.839	0.835	0.773	1	
Streptococci	14	OYB	92	90	97	100	77	88	83	96	100	81	100	100	
	28	OYA	88	85	92	96	69	94	55	42	80	82	96	95	
	68	TYA	90	88	68	94	49	75	46	70	36	70	81	95	
p value to compare between OYB and OYA			1	0.866	0.797	1	0.717	0.852	0.087	**0.005**	0.16	1	1	1	
p value to compare between OYB and TYA			1	0.972	**0.031**	0.803	0.078	0.604	**0.014**	0.16	**0.00003**	0.78	0.167	0.984	

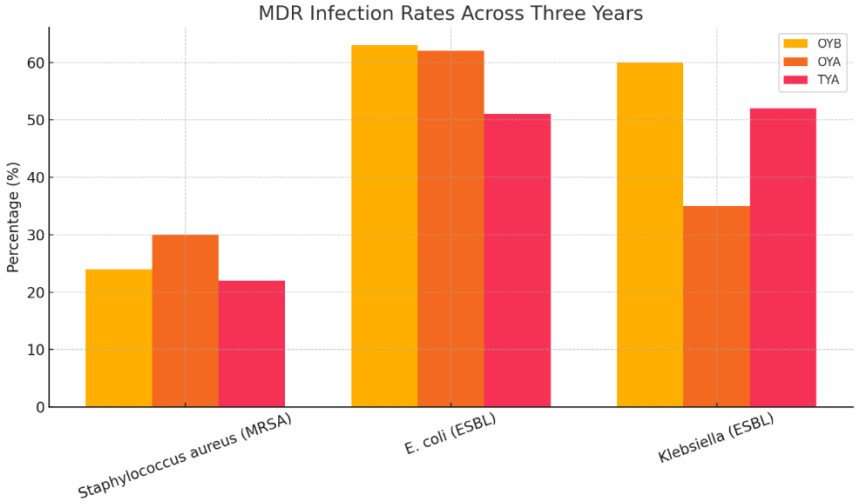
Dox= Doxycyclin, Azm= Azithromicin, E= Erythromycin, Lz= Linezolid, Cx= Cefoxitin

Table 3: Change in mean susceptibility of isolates across the years of study

Organism	Mean Susceptibility OYB	OYA	TYA	Overall Trend	Significant Change (OYB vs OYA)	Significant Change (OYB vs TYA)
E. coli	65.6%	66.9%	68.5%	Mild improvement	Amoxiclav ↓, Doxycycline ↑	Doxycycline ↑, Nitrofurantoin ↓
Klebsiella	62.1%	74.1%	63.7%	Improved then declined	Ptz ↑, Cot ↑, Cip ↑, Ctr ↑	Cot ↑, Nitrofurantoin ↓
Pseudomonas	62.3%	67.6%	64.5%	Improvement then mild drop	Ciprofloxacin ↑	Ciprofloxacin ↑, Ceftazidime ↓, Nitrofurantoin ↓
Staphylococcus aureus	69.1%	79.7%	73.1%	Improvement then decline	Erythromycin ↑	Amoxiclav ↓, Azithromycin ↓, Ciprofloxacin ↓
CoNS	73.6%	70.3%	69.3%	Gradual decline	Ciprofloxacin ↓	Ciprofloxacin ↓, Amoxiclav ↓
Streptococci	92.7%	83.8%	74.0%	Progressive decline	Erythromycin ↓	Amoxiclav ↓, Azithromycin ↓, Ciprofloxacin ↓

Table 4: The consumption of antibiotics according to Defined Daily dose [DDD] /1000 patients

Class of antibiotics	OYB	OYA	P value
Beta lactam- beta lactamase inhibitors	77.3	65.9	**0.001249**
3rd generation cephalosporins	37.4	30.3	0.0599
Carbapenems	64.5	60.8	0.3394
Fluoroquinolones	33.4	30.1	0.4079
Vancomycin	51.2	44.6	0.0905



Graph 1: MDR infection rates

DISCUSSION

The appropriate usage of right antibiotic has been instrumental in reducing the morbidity and mortality in patients suffering from bacterial infections. But rampant use, misuse and abuse of antibiotics due to ignorance, has not only contributed to unnecessary economic burden on patients but also development of resistance strains in the hospital set up as well as community. This study demonstrates that a structured ASP—centred on cumulative antibiogram development and policy implementation—can positively influence susceptibility trends and reduce MDR burden.

A modest improvement in susceptibility among major gram-negative organisms—particularly *Escherichia coli* and *Pseudomonas aeruginosa*—was observed following ASP implementation. *E. coli* showed a gradual increase in mean susceptibility from 65.6% (OYB) to 68.5% (TYA), with statistically significant increases in doxycycline susceptibility and stable efficacy of carbapenems. A study conducted by Ziv-On, E.; Friger et.al proved that similar trends have been reported in institutions where ASP initiatives improved adherence to empirical therapy guidelines and reduced inappropriate broad-spectrum use.[8] The sustained high susceptibility of carbapenems against *E. coli* and *Klebsiella* species underscores the preserved efficacy of these agents, likely reflecting restricted usage policies—an important AMS goal.

Klebsiella species demonstrated an initial improvement in mean susceptibility in the first year after policy implementation (74.1% in OYA) but a decline in the following year (63.7% in TYA). This pattern suggests early gains after stewardship introduction, followed by possible lapses in adherence or external selection pressures. Similar fluctuating trends have been documented in other Indian tertiary centres, emphasizing the need for continuous monitoring and quarterly reinforcement of antibiotic policy compliance.[9,10] The declining susceptibility to nitrofurantoin and cotrimoxazole among *Klebsiella* species aligns with global concerns regarding rising resistance among urinary isolates.[11,12]

In *P. aeruginosa*, the pronounced improvement in ciprofloxacin susceptibility—from 47% in OYB to 84% in OYA and 73% in TYA—signals a meaningful impact of reduced fluoroquinolone misuse. This aligns with evidence that *Pseudomonas* exhibits rapid inducible resistance to fluoroquinolones and can show significant reversibility when selective pressure decreases.

Among gram-positive organisms, *Staphylococcus aureus* showed initial improvement in mean susceptibility followed by a mild decline in TYA, with significant reductions in ciprofloxacin, azithromycin, and amoxiclav susceptibility. These findings may reflect the persistent community-acquired MRSA burden in South India and the need for stricter gatekeeping of macrolides and β-lactams. Despite this, glycopeptide susceptibility remained consistently high, reinforcing their continued role as reliable agents against resistant *S. aureus*. Coagulase-negative staphylococci (CoNS) exhibited a gradual decline in mean susceptibility, driven primarily by substantial reductions in ciprofloxacin and amoxiclav effectiveness. This mirrors broader trends of increasing resistance among CoNS, particularly in device-associated infections, and underscores the necessity for robust infection control measures alongside stewardship.[13] A study conducted by Alone R.D., et al concluded that the high prevalence of MRCoNS and biofilm producers necessitates strict infection control and antibiotic stewardship.[14]

A key finding of this study was the sustained reduction in MDRO rates after implementation of the antibiotic policy. The prevalence of MRSA, ESBL *E. coli*, and ESBL *Klebsiella* decreased progressively over the two-year follow-up period. The decline in ESBL-producing organisms—from 63% to 51% in *E. coli* and 60% to 52% in *Klebsiella*—is particularly notable, as ESBL infections contribute significantly to morbidity, mortality, and healthcare cost.[15] These results indicate that routine dissemination of antibiograms, physician education, and structured prescription audits can translate into

measurable reductions in MDRO burden, a finding corroborated by multiple AMS interventions worldwide. The study by Rajendran R et al concluded that AMS programs (including guideline use, education, and feedback) are associated with reduced prevalence of MDROs and bacterial resistance and decreased unnecessary antibiotic use.[16] In accordance to our study, Darwish Rm et al compared pre- and post-ASP periods and showed that implementation of a structured stewardship program led **to** improvements in susceptibility patterns and reduced resistance in several key pathogens.[17]

Antibiotic consumption analysis showed a significant reduction in the use of β-lactam/β-lactamase inhibitors ($p<0.05$), suggesting improved prescribing discipline, possibly driven by tighter controls on empirical therapy following antibiogram release. No significant changes were observed in cephalosporin, carbapenem, fluoroquinolone, or vancomycin use, indicating that further stewardship reinforcement—such as prospective audit-and-feedback or formulary restriction—may be needed to influence these classes. Taken together, the study demonstrates that an ASP centred around cumulative antibiogram development, education, and policy enforcement can produce favourable trends in susceptibility and MDRO rates. However, certain organisms showed variable or declining susceptibility patterns, highlighting that stewardship must be continuous, dynamic, and integrated with robust infection prevention programs to achieve sustained benefit.

CONCLUSION

A structured and institutionally supported Antimicrobial Stewardship Program—anchored by cumulative antibiogram development, clinician education, and an evidence-based antibiotic policy—can meaningfully influence antimicrobial resistance trends in a tertiary care setting. Improvements in susceptibility among key gram-negative and gram-positive organisms, alongside the notable decline in MRSA, ESBL-producing *E. coli* and *Klebsiella*, demonstrate that stewardship interventions can curb the emergence and spread of multidrug-resistant pathogens. Although fluctuations in susceptibility for certain organisms underscore the dynamic nature of resistance, the overall reduction in MDRO burden reflects the positive impact of coordinated stewardship and infection-control efforts. Sustained success will require continuous surveillance, regular updating of antibiograms, reinforcement of prescriber compliance, and integration of stewardship principles across all clinical departments. Strengthening these measures is essential to preserving antimicrobial efficacy and safeguarding patient outcomes in the face of rising global antimicrobial resistance.

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