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Research Article

Comparison of Cumulative Antibiogram Results of Trakya University Hospital for the Years 2015-2016 and 2022-2023

İsmail Davarcı, Hüseyin Güdücüoğlu, Ender Çetinkaya

Department of Medical Microbiology, Trakya University Faculty of Medicine, Edirne, Türkiye

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ORCID IDs of the authors: İ.D. 0000-0002-5835-4237, H.G. 0000-0003-1101-9017, E.Ç. 0000-0002-1705-4828.

ABSTRACT

Objective: A cumulative antibiogram serves as a critical tool in guiding the selection of appropriate empirical therapy, facilitating de-escalation based on susceptibility results, and shaping institutional policies to combat antibiotic resistance effectively. This study aimed to evaluate changes in antimicrobial susceptibility over the years and provide guidance to clinicians in the selection of empirical therapies.

Methods: A retrospective analysis was conducted on the *in vitro* antimicrobial susceptibility test results of bacterial isolates obtained from clinical samples submitted to the Medical Microbiology Laboratory at Trakya University Hospital during the periods of 2015-2016 and 2022-2023. Cumulative antibiogram data were compiled in accordance with the guidelines outlined in the "Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data" (CLSI 2014, M39-A4).

Results: A total of 7524 isolates (5009 Gram-negative, 2515 Gram-positive) were analyzed during the 2015-2016 period, while 5880 isolates (4202 Gram-negative, 1678 Gram-positive) were analyzed during the 2022-2023 period. In both timeframes, the most commonly isolated microorganisms were isolated from urine, blood/catheter, and wound/aspirate/tissue samples. The predominant isolates included *Escherichia coli (E.coli)*, *Klebsiella* spp., and *Enterococcus* spp. Based on the findings, the following antimicrobials were identified as suitable for empirical treatment for *E. coli* infections: carbapenems and amikacin. For *Klebsiella* spp. infections: amikacin. For *Enterococcus* spp. infections: vancomycin, teicoplanin, linezolid, and tigecycline. For *Acinetobacter* spp. infections: combination therapy. Carbapenem susceptibility among *Klebsiella* spp., isolates decreased notably in 2022-2023, ranging between 55% and 62%, in contrast to higher rates observed during 2015-2016.

Conclusion: The regular evaluation of hospital-based antibiogram data and the revision of empirical treatment protocols based on these findings represent a crucial strategy for effectively combating antimicrobial resistance.

Keywords: Antibiogram, cumulative antimicrobial susceptibility testing report, empirical treatment, resistance

INTRODUCTION

According to the World Health Organization (WHO), antimicrobial resistance (AMR) has become one of the most urgent global public health challenges, significantly increasing morbidity and mortality worldwide.[1,2] In 2019, approximately 3.57 million deaths were attributed to antibiotic resistance. Projections by WHO estimate that this number could rise to 10 million annually by 2050.[3,4] The coronavirus disease-2019 pandemic has exacerbated the AMR crisis. During the pandemic, the inappropriate and excessive use of antibiotics, treatments that induce immunosuppression, and prolonged hospital stays have accelerated the development of antibiotic resistance.[5] Additionally, financial constraints in healthcare systems and reductions in healthcare personnel have negatively impacted surveillance and control efforts aimed at combating AMR.[6] The widespread use of hand sanitizers and surface disinfectants

Corresponding author: İsmail Davarcı, **E-mail:** ismaildavarci@trakya.edu.tr

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during the pandemic may further worsen resistance patterns in the coming years.[7] AMR renders first-line antibiotics ineffective, leading to the replacement of these drugs with more expensive alternatives. This situation prolongs disease duration, increases healthcare costs, and imposes significant economic burdens on individuals and societies. According to the World Bank, resistant infections could trigger a global economic crisis. It is estimated that by 2050, AMR could push 28 million people into poverty each year and cost the global economy over $1 trillion annually.[8] Under these circumstances, it is essential to develop effective global strategies to combat AMR, raise public awareness, and promote the judicious use of antibiotics. These measures are critical for mitigating the far-reaching impacts of AMR.

In community -or hospital-acquired infections, the rapid initiation of effective antibiotic therapy targeting the causative microorganisms is critical for improving survival rates.[9-12] However, the isolation and identification of the pathogen in culture, as well as the determination of its antimicrobial susceptibility profile, typically require 24-48 hours. Therefore, particularly in severe infection cases, ensuring an appropriate and broad-spectrum empirical antimicrobial therapy is of vital importance.[13,14]

One of the most essential tools guiding clinicians in the selection of empirical therapy are cumulative antibiogram reports. These reports were standardized for the first time in 2000 with the publication of the M39 guideline by the Clinical and Laboratory Standards Institute (CLSI). CLSI defines a cumulative antibiogram as an analysis and reporting method that reflects the percentage susceptibility of the first isolates per patient to tested antimicrobial agents, collected from a specific institution over a defined time period.[15] Cumulative antibiograms provide clinicians with critical guidance for empirical therapy decisions before the antimicrobial susceptibility results of the patient's isolated pathogen are available. Furthermore, these reports can be compiled at national and international levels, enabling the detection of regional antimicrobial susceptibility patterns and the emergence of new resistance trends.

The aim of this study is to compare the cumulative antibiogram data of bacterial isolates obtained from patient samples submitted to the Medical Microbiology Laboratory at Trakya University Hospital during the periods of 2015-2016 and 2022-2023. The study seeks to evaluate changes in antimicrobial susceptibility over the years and provide guidance to clinicians in the selection of empirical therapies.

MAIN POINTS

- A notable rise in resistance rates was observed among Gram-negative bacteria, including *Klebsiella* spp., *Acinetobacter* spp., and *Pseudomonas* spp. In particular, *Klebsiella* spp. demonstrated a significant decline in carbapenem susceptibility, while *Acinetobacter* spp. exhibited the lowest overall susceptibility rates (S%).
- Recommended empirical therapies include carbapenems, amikacin, tigecycline, vancomycin, and linezolid, depending on the pathogen.
- Given the variations in antimicrobial S% over time, regularly updating and implementing empirical treatment protocols based on antibiogram data is crucial for combating resistance and improving clinical outcomes.

MATERIAL AND METHODS

Ethics Approval and Consent to Participate

The study received ethical approval from the Non-interventional Scientific Research Ethics Committee of the Faculty of Medicine of Trakya University with the protocol code 2024/207 (approval no: 09/35, date: 06.05.2024).

In this study, the *in vitro* antimicrobial susceptibility test results of bacterial strains isolated from clinical samples submitted to the Medical Microbiology Laboratory at Trakya University Hospital during the periods of 2015-2016 and 2022-2023 were evaluated.

Identification of Bacterial Species and Susceptibility Testing

Bacterial identification and antimicrobial susceptibility testing were performed using both conventional methods and the automated VITEK-2 system (bioMérieux, France). Conventional methods included the evaluation of colony morphology, Gram staining, and basic biochemical tests such as catalase, oxidase, and coagulase when appropriate. Antimicrobial susceptibility test results were interpreted according to the current annual recommendations of the European Committee on Antimicrobial Susceptibility Testing (EUCAST).[16]

Data Collection and Processing

The data used in this study were retrospectively retrieved from the laboratory information system. The collected data were organized according to the guidelines outlined in the Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data (CLSI 2014, M39-A4), based on criteria.[15]

Only verified test results from samples submitted for clinical diagnostic purposes were included in the study; samples submitted for surveillance or screening purposes were excluded.

Susceptibility rates (S%) were calculated exclusively for antimicrobial agents routinely tested in the laboratory.

When multiple isolates of the same bacterial species were identified from the same patient, only the first isolate was included in the study; subsequent isolates were excluded from the analysis.

While calculating S%, data categorized as "intermediate" (I) were included in the percentage of susceptible isolates (S%).

Antimicrobial Agents

The selection of which antimicrobial agents should be tested for each pathogen was determined based on the "Turkish Society of Microbiology Restricted Antimicrobial Notification Table".[17] This table aims to promote rational antimicrobial use and stewardship by recommending targeted antibiotic panels based on organism group, infection site, and clinical relevance. In line with these guidelines, agents were selected to include

first-line, commonly used antibiotics, as well as critical agents for multidrug-resistant pathogens. The antibiotics tested were standardized across isolates of the same species and clinical significance. The susceptibility of the isolates included in the study was evaluated for the following antimicrobial agents:

Beta-lactams: ampicillin (AM), amoxicillin/clavulanic acid (AMC), piperacillin-tazobactam (TZP), cefuroxime (CXM), ceftazidime (CAZ), ceftriaxone (CRO), cefepime (FEP), ertapenem (ETP), imipenem (IPM), meropenem (MEM).

Aminoglycosides: gentamicin (GN), amikacin (AN).

Fluoroquinolones: ciprofloxacin (CIP), levofloxacin (LVX).

Other agents: trimethoprim-sulfamethoxazole (SXT), nitrofurantoin (F), tigecycline (TGC), erythromycin (E), clindamycin (CC), vancomycin (VA), teicoplanin (TEC), linezolid (LZD), tetracycline (TE).

The selection of antimicrobials should be guided by the S% rate based on the severity of the infection. For severe infections such as meningitis or sepsis, the WHO recommends a S% (percent susceptible) rate of ≥90% for penicillin in empirical treatment.[18] In cases where the risk of mortality or severe morbidity is high, antimicrobials with a S% rate of at least 90-95% should be preferred. For milder infections, a S% rate of 80-85% may be acceptable. When no alternatives are available and the S% rate is below 80%, the agent with the highest S% rate or combination therapy should be considered. Local antimicrobial policies and guidelines must also be taken into account when making treatment decisions[19-21]. In this study, we evaluated antimicrobials with a S% rate of ≥90% as suitable options for empirical treatment.

Statistical Analysis

The data were analyzed using IBM SPSS (Statistical Package for Social Sciences) Statistics 21.0. Descriptive statistics were presented as frequencies and percentages. The analyses were performed using descriptive statistics, the chi-square test, and Fisher's Exact test. Results with *P* values < 0.05 were considered statistically significant.

RESULTS

Sample Types and Distribution of Bacteria

This study evaluated isolates from the periods of 2015-2016 and 2022-2023. A total of 7524 isolates (5009 Gram-negative, 2515 Gram-positive) were analyzed during 2015-2016, and 5880 isolates (4202 Gram-negative, 1678 Gram-positive) were analyzed during 2022-2023. In both periods, the most frequently isolated microorganisms were obtained from urine, blood, catheter, and wound, aspirate, and tissue samples. In 2015-2016, microorganisms were most commonly isolated from patients aged 18-65 years, whereas in 2022-2023, isolates were predominantly obtained from patients older than 65 years. For both time periods, the highest number of isolates came from samples submitted by the Internal Medicine department. The most frequently isolated microorganisms during 2015-2016 were *Escherichia coli (E. coli)*, coagulase-negative *Staphylococcus* (CoNS), and *Enterococcus* spp. In 2022-2023, the most common isolates were *E. coli*, *Klebsiella* spp., and *Enterococcus* spp. (Table 1). *E. coli* was the most frequently isolated microorganism from urine samples, while CoNS was predominantly isolated from blood/catheter samples (Table 2). In intensive care units (ICUs), the most frequently isolated microorganisms during 2015-2016 were CoNS, *Acinetobacter* spp., and *Klebsiella* spp. In 2022-2023, the most common ICU isolates were *Acinetobacter* spp., *Klebsiella* spp., and *Enterococcus* spp. Among ICU samples, bacteria were most frequently isolated from blood/catheter samples (48.3%), respiratory samples (tracheal aspirate, sputum, bronchoalveolar lavage) (31.5%), and urine samples (12.8%). The highest bacterial isolation rate in ICUs was observed in Surgical ICUs, with *Acinetobacter* spp. being the most frequently isolated microorganism (Table 3).

Antimicrobial Susceptibility Findings

For *E. coli* isolates, S% exceeding 90% were observed for ETP, IMP, MEM, and AN in both urine and non-urine samples, as well as across outpatient, inpatient, and ICU settings, during both the 2015-2016 and 2022-2023 periods. Additionally, susceptibility to F in urine samples was found to be above 90%.

For *Klebsiella* spp. isolates, S% exceeding 90% were observed only for AN in both study periods. In 2022-2023, susceptibility to carbapenems ranged from 55% to 62%, representing a significant decline compared to the 2015-2016 period.

For *Acinetobacter* spp. isolates, no single antimicrobial agent demonstrated a susceptibility rate exceeding 90% in either study period. Given the limited susceptibility observed across the tested agents, empirical treatment of suspected *Acinetobacter* infections may require the use of combination therapy, especially in settings with high rates of multidrug resistance. For *Pseudomonas* spp. isolates, S% above 90% were observed for FEP and AN during 2015-2016, while in 2022-2023, only AN maintained a susceptibility rate above 90%.

For *Staphylococcus aureus* isolates, S% exceeding 90% were observed for LVX, VA, TEC, LZD, TGC, SXT, and GN. In methicillin-resistant *S. aureus* (MRSA) isolates, a significant decrease in susceptibility to E and CC was detected. Additionally, susceptibility to LVX, SXT, and GN fell below 90% in MRSA isolates. For CoNS, S% above 90% were observed for VA, LZD, and TGC. Similarly, for *Enterococcus* spp., VA, TEC, LZD, and TGC demonstrated S% exceeding 90%. Cumulative antimicrobial susceptibility percentages for Gram-negative and Gram-positive bacteria are presented in Table 4 and Table 5. Notably, the MRSA rate increased from 12.9% to 24.1%, while the vancomycin-resistant *Enterococcus* (VRE) rate rose from 2.5% to 4.2% (Table 6).

DISCUSSION

Cumulative antibiogram reports, regularly and systematically updated, serve as a critical guide for clinicians in selecting empirical antibiotic therapy. Monitoring the S% of commonly used antibiotics through cumulative antibiograms is an essential component of antibiotic stewardship programs.[22,23] This approach allows for the identification of regional resistance patterns and highlights areas requiring targeted interventions.

Table 1. Characteristics of Samples Included in the Study

	2015-2016		2022-2023		Total	
	n	%	n	%	n	%
Sample Type						
Urine	2901	38.6	2110	35.9	5011	37.4
Blood/catheter	2095	27.8	1538	26.2	3633	27.1
Wound/aspirate/tissue	1363	18.1	1118	19.0	2481	18.5
Respiratory sample	937	12.5	945	16.1	1882	14.0
Sterile body fluid	228	3.0	169	2.9	397	3.0
Age						
>65	3068	40.8	3000	51.0	6068	45.3
18-65	3553	47.2	2356	40.1	5909	44.1
0-18	903	12.0	524	8.9	1427	10.6
Microorganism						
E. coli	2124	28.2	1358	23.1	3482	26.0
Klebsiella spp.	879	11.7	890	15.1	1769	13.2
Enterococcus spp.	969	12.9	748	12.7	1717	12.8
CoNS	1070	14.2	510	8.7	1580	11.8
Pseudomonas spp.	687	9.1	625	10.6	1312	9.8
Acinetobacter spp.	589	7.8	559	9.5	1148	8.6
S. aureus	476	6.3	420	7.1	896	6.7
Proteus spp.	220	2.9	268	4.6	488	3.6
Enterobacter spp.	234	3.1	215	3.7	449	3.3
S. maltophilia	98	1.3	107	1.8	205	1.5
Morganella spp.	97	1.3	83	1.4	180	1.3
Serratia spp.	81	1.1	97	1.6	178	1.3
Department						
Internal medicine	1996	26.5	1405	23.9	3401	25.4
General surgery	1112	14.8	838	14.3	1950	14.5
Emergency medicine	1069	14.2	735	12.5	1804	13.5
Pediatrics	794	10.6	479	8.1	1273	9.5
Urology	405	5.4	499	8.5	904	6.7
Pulmonology	224	3.0	514	8.7	738	5.5
Anesthesiology	296	3.9	245	4.2	541	4.0
Plastic surgery	176	2.3	258	4.4	434	3.2
Orthopedics	242	3.2	189	3.2	431	3.2
Cardiology	256	3.4	146	2.5	402	3.0
Infectious diseases	208	2.8	136	2.3	344	2.6
Neurosurgery	109	1.4	51	0.9	160	1.2
Neurology	111	1.5	46	0.8	157	1.2
Physical therapy and rehabilitation	105	1.4	51	0.9	156	1.2
Cardiovascular surgery	101	1.3	54	0.9	155	1.2
Obstetrics and gynecology	70	0.9	76	1.3	146	1.1
Dermatology	28	0.4	84	1.4	112	0.8
Radiation oncology	111	1.5	1	0.0	112	0.8
Thoracic surgery	44	0.6	26	0.4	70	0.5
Pediatric surgery	25	0.3	15	0.3	40	0.3
Ophthalmology	12	0.2	20	0.3	32	0.2
Otolaryngology	18	0.2	12	0.2	30	0.2
Psychiatry	12	0.2	0	0.0	12	0.1
Total	**7524**	**100.0**	**5880**	100.0	13404	100.0

CoNS, coagulase-negative *Staphylococcus*.

Additionally, cumulative antibiograms facilitate the analysis of resistance trends over successive years, providing valuable insights into the evolution of AMR.[24] However, caution is warranted when interpreting these reports at the patient level. Patient-specific factors play a crucial role in antibiotic selection and in determining whether an isolated microorganism is a true pathogen or a colonizer. A notable limitation of cumulative antibiogram reports in the literature is their qualitative nature, as they typically lack minimum inhibitory concentration (MIC) values, which are critical for more nuanced decision-making, as noted in study.[24] In Türkiye, comprehensive cumulative antibiogram data are scarce. For this reason, the findings of this study have been compared with surveillance data from broad-scale programs. These include the 'National Antimicrobial Resistance Surveillance System (NAMRSS)' by the Ministry of Health Turkish Public Health Institute, the 'Central Asian and European Surveillance of Antimicrobial Resistance (CEASER)', and the 'European Centre for Disease Prevention and Control's 'Antimicrobial Resistance Surveillance in Europe report (ECDC)'. These sources are considered valuable references for reflecting national and regional resistance patterns.

According to the CDC's National Healthcare Safety Network surveillance, the most frequently isolated bacteria in healthcare-associated infections during 2015-2017 were *E. coli* (17.5%), *Enterococcus* spp. (14.8%), *S. aureus* (11.8%), *Klebsiella* spp. (8.8%), and *Pseudomonas* spp. (8.0%).[25] In Türkiye, the NAMRSS surveillance system, established in 2011, included 105 centers from 59 provinces by 2016, forming a nationwide surveillance network. Although the system continues to operate, no data have been published since 2016. The NAMRSS 2016 report, which included only blood and cerebrospinal fluid samples, indicated that the most frequently

Table 2. Distribution of Microorganisms by Sample Type (n)

Sample Type	*E. coli*	*Klebsiella spp.*	*Enterococcus spp.*	CoNS	*Pseudomonas spp.*	*Acinetobacter spp.*	*S. aureus*	*Proteus spp.*	*Enterobacter spp.*	*S. maltophilia*	*Morganella spp.*	*Serratia spp.*	Total
Urine	2507	755	764	100	306	98	62	179	142	15	42	41	**5011**
Blood/Catheter	360	437	547	1165	200	320	278	93	99	64	24	46	**3633**
Wound/Aspirate/Tissue	406	214	328	209	297	164	388	176	126	29	102	42	**2481**
Respiratory Sample	137	319	21	6	475	549	140	32	67	87	6	43	**1882**
Sterile Body Fluid	72	44	57	100	34	17	28	8	15	10	6	6	**397**
Total	**3482**	**1769**	**1717**	**1580**	**1312**	**1148**	**896**	**488**	**449**	**205**	**180**	**178**	**13404**

CoNS, coagulase-negative *Staphylococcus.*

Table 3. Distribution of Microorganisms Isolated from Intensive Care Units (n)

ICU Type	*Acinetobacter spp.*	CoNS	*Klebsiella spp.*	*Enterococcus spp.*	*Pseudomonas spp.*	*E. coli*	*S. aureus*	*Proteus spp.*	*S. maltophilia*	*Enterobacter spp.*	*Serratia spp.*	*Morganella spp.*	Total
Surgical ICU	262	166	216	200	174	69	33	53	27	34	21	19	**1274**
Medical ICU	220	175	181	158	131	96	51	38	34	28	16	10	**1138**
Anesthesia ICU	85	82	86	85	70	37	22	29	19	13	10	3	**541**
Respiratory ICU	71	33	61	43	33	17	12	11	15	7	7	3	**313**
Coronary ICU	33	54	35	47	11	42	21	8	6	14	1	3	**275**
Neonatal ICU	3	104	39	18	10	13	18	0	12	15	9	0	**241**
Pediatric ICU	20	26	10	8	13	8	5	0	4	4	4	0	**102**
Cardiovascular Surgery ICU	0	0	0	1	0	0	0	0	0	0	0	1	**2**
Total	**694**	**640**	**628**	**560**	**442**	**282**	162	139	117	115	68	39	3886

ICU, intensive care unit; CoNS, coagulase-negative *Staphylococcus.*

Table 4. Comparison of Susceptibility Percentages (%S) for Gram-negative Bacteria

Bacteria	Year	Source	n	AM	AMC	TZP	CXM	CAZ	CRO	FEP	ETP	IMP	MEM	GN	AN	CIP	SXT	F
E. coli	2015-2016	Outpatient clinic	1203	39	69	91	71	83	73	84	100	100	100	83	100	74	61	96
		Ward	773	23	52	82	58	74	59	74	98	100	99	72	100	59	46	96
		ICU	148	14	40	73	53	69	55	69	94	99	98	65	99	54	46	**
		Total	2124	32	61	86	65	79	67	78	99	100	99	78	100	67	54	96
	2022-2023	Outpatient clinic	784	37	65	87	58	64	65	69	98	98	99	88	99	50	62	98
		Ward	440	27	51	78	48	52	55	58	95	99	99	84	99	40	52	100
		ICU	134	26	42	71	58	55	57	69	91	97	99	80	97	51	56	100
		Total	1358	33	58	82	55	59	61	66	96	99	99	87	99	47	58	98
		p§		0.616	0.085	**0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	0.225	**<0.001**	**<0.001**	**<0.001**	**0.015**	**<0.001**
E. coli (urine)	2015-2016	Total	1523	36	67	91	68	80	70	82	100	100	100	80	100	70	58	96
	2022-2023		984	38	68	87	60	65	64	70	98	98	99	88	99	51	62	99
		p§		0.471	0.579	**0.007**	**<0.001**	**<0.001**	**0.004**	**<0.001**	**<0.001**	**<0.001**	0.101*	**<0.001**	**0.004**	**<0.001**	**0.021**	**<0.001**
E. coli (non-urine)	2015-2016	Total	601	21	45	76	58	74	59	72	96	100	99	74	100	60	45	
	2022-2023		374	19	33	72	41	48	53	55	92	99	99	78	98	36	47	
		p§		0.580	**<0.001**	0.207	**<0.001**	**<0.001**	0.050	**<0.001**	**0.003**	0.163	0.970	0.163	**0.032***	**<0.001**	0.579	
Klebsiella spp.	2015-2016	Outpatient clinic	255	0	63	72	55	63	58	69	79	82	85	83	97	67	67	77
		Ward	360	0	48	64	54	66	60	68	76	74	82	81	98	71	71	71
		ICU	264	0	28	34	27	33	30	41	41	35	43	59	98	51	51	**
		Total	879	0	48	59	48	56	52	59	60	66	72	76	98	74	65	74
	2022-2023	Outpatient clinic	247	0	65	66	54	59	65	65	80	88	89	85	98	60	64	75
		Ward	279	0	49	51	45	46	55	49	63	69	73	77	94	52	61	77
		ICU	364	0	24	31	28	32	33	30	35	43	38	59	89	36	44	42
		Total	890	0	43	46	40	43	49	45	55	57	62	75	93	48	55	76
		p§		-	0.063	**<0.001**	**0.002**	**<0.001**	0.160	**<0.001**	**0.029**	**<0.001**	**<0.001**	0.500	**<0.001**	**<0.001**	**<0.001**	0.407

Table 4. Continued

Bacteria	Year	Source	n	AM	AMC	TZP	CXM	CAZ	CRO	FEP	ETP	IMP	MEM	GN	AN	CIP	SXT	F
Acinetobacter spp.	2015-2016	Outpatient clinic	46			17						20	27	48	59	43	43	
		Ward	225			16						17	19	47	42	37	37	
		ICU	318			2						2	2	33	42	17	17	
		Total	589			9						10	12	41	41	13	28	
	2022-2023	Outpatient clinic	32			39						43	45	60	48	52	52	
		Ward	151			13						13	17	36	25	19	28	
		ICU	376			2						3	3	30	12	4	17	
		Total	559			7						8	9	34	17	10	22	
		p§				0.106						0.104	0.112	**0.037**	**<0.001**	0.183	**0.017**	
Pseudomonas spp.	2015-2016	Outpatient clinic	141			90		90		96		86	92		92	90		
		Ward	341			80		87		94		78	85		93	89		
		ICU	205			65		80		95		54	60		89	85		
		Total	687			78		85		95		73	81		92	88		
	2022-2023	Outpatient clinic	145			83		90		89		90	89		100	87		
		Ward	243			83		87		85		85	78		97	83		
		ICU	237			68		81		83		67	67		97	83		
		Total	625			77		85		85		79	76		98	84		
		p§				0.694		0.858		**<0.001**		**0.017**	0.051		**<0.001**	**0.041**		
Enterobacter spp.	2015-2016	Outpatient clinic	65		0	77		71	69	97	97	93	97	95	100	97	94	
		Ward	119		0	76		64	59	91	94	89	96	93	99	93	93	
		ICU	50		0	78		73	66	93	95	94	98	93	100	98	89	
		Total	234		0	77		68	63	93	95	91	96	94	100	92	92	
	2022-2023	Outpatient clinic	54		4	76		79	69	80	81	91	96	95	100	89	85	
		Ward	96		1	73		73	67	77	81	90	91	95	98	92	86	
		ICU	65		0	72		70	69	82	79	91	91	93	95	94	89	
		Total	215		2	73		73	68	79	80	91	92	95	98	92	87	
		p§			0.110*	0.356		0.192	0.288	**<0.001**	**<0.001**	0.917	0.068	0.702	0.199*	0.945	**0.047**	

Table 4. Continued

Bacteria	Year	Source	n	AM	AMC	TZP	CXM	CAZ	CRO	FEP	ETP	IMP	MEM	GN	AN	CIP	SXT	F
Proteus spp.	2015-2016	Outpatient clinic	73	49	85	99	80	95	91	100	99	34	100	84	100	85	59	
		Ward	92	53	88	97	79	96	98	94	99	**	99	80	100	81	55	
		ICU	55	41	74	96	67	88	81	91	98	**	100	57	100	72	48	
		Total	220	49	84	97	77	94	91	95	99	32	100	76	100	80	55	
	2022-2023	Outpatient clinic	97	36	65	90	76	79	68	74	88	80	94	61	97	40	25	
		Ward	87	49	76	95	84	86	83	81	92	80	95	84	98	57	43	
		ICU	84	36	70	84	74	74	75	69	82	85	87	63	93	54	43	
		Total	268	40	70	89	78	79	75	75	87	81	92	68	96	50	37	
		p§		**0.047**	**<0.001**	**<0.001**	0.763	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**0.042**	**0.001**	**<0.001**	**<0.001**	
Morganella spp.	2015-2016		97	0	0	98		61	62	98	99		100	64	100	52	52	
	2022-2023	Total	83	2	0	95		58	87	91	98		98	84	98	63	64	
		p§		0.214*		0.418*		0.726	**<0.001**	**0.046***	1.000*		0.464*	**0.003**	0.464*	0.154	0.112	
Serratia spp.	2015-2016		81	4	5	100		88	86	95	100		100	95	100	95	95	
	2022-2023	Total	97	13	4	95		96	95	96	99		99	100	100	94	98	
		p§		**0.026**	1.000*	0.065*		**0.017**	**0.047**	1.000*	1.000*		1.000*	**0.040***		1.000*	0.412*	
S. maltophilia	2015-2016	Total	98														88	
	2022-2023		107														94	
		p§															0.093	

Fisher's Exact test
**Insufficient Data
§The 'total' groups were compared.
ICU, intensive care unit, AM, ampicillin, AMC, amoxicillin-clavulanate, TZP, piperacillin-tazobactam, CXM, cefuroxime, CAZ, ceftazidime, CRO, ceftriaxone, FEP, cefepime, ETP, ertapenem, IMP, imipenem, MEM, meropenem, GN, gentamicin, AN, amikacin, CIP, ciprofloxacin, SXT, trimethoprim-sulfamethoxazole, F, nitrofurantoin.

isolated bacteria in Türkiye were *E. coli* (23.8%), *Enterococcus* spp. (18.9%), *Klebsiella spp.* (17.6%), *S. aureus* (15.5%), and *Acinetobacter* spp. (15.1%).[26] In a study conducted in Saudi Arabia, the most frequently isolated Gram-negative bacteria were *E. coli*, *Klebsiella* spp., and *Pseudomonas* spp.[27] Similarly, a U.S.-based study focusing exclusively on Gram-negative bacteria found that *Pseudomonas aeruginosa*, *E. coli*, and *Klebsiella pneumoniae* were the three most frequently isolated microorganisms in both ICU and non-ICU settings. These three bacteria accounted for 56.7% of Gram-negative isolates in ICUs and 70% in non-ICU settings.[28] Our study also identified similar microorganisms, albeit with variations in their rankings across different periods. This underscores the critical importance of regularly and systematically monitoring surveillance data to track trends and inform infection control strategies.

A study conducted under the 'International Network for Optimal Resistance Monitoring' program involving 70 centers from the United States separately evaluated isolates from ICUs and non-ICU settings. In this study, the most frequently isolated bacterium from ICU samples was *Pseudomonas* spp., while *E. coli* was most commonly isolated from non-ICU samples. Furthermore, antimicrobial S% were found to be significantly lower in isolates from ICUs compared to those from non-ICU settings.[28] In a study conducted in Türkiye, the most frequently isolated bacteria from ICU samples were *Acinetobacter* spp. and *Klebsiella* spp.[29] Similarly, in our study, *E. coli* was the most frequently isolated microorganism from outpatient and inpatient ward samples, whereas *Acinetobacter* spp. and *Klebsiella* spp. were predominant in ICU samples. The observed differences in bacterial species between ICU and non-ICU isolates are likely due to the varying infection types common to these patient groups. In ICUs, bacterial growth was most frequently observed in blood/catheter and respiratory samples, whereas non-ICU infections were predominantly associated with urine samples.

Consistent with our findings, a large-scale study also reported that isolates from ICUs exhibited lower antimicrobial susceptibility compared to those from other units, such as outpatient clinics and inpatient wards.[28] In general, it is well-documented that isolates from ICUs tend to have lower S% than those from outpatient or inpatient ward settings. The higher rates of AMR observed in ICUs are attributed to several factors. These include the more intensive use of antimicrobial agents, prolonged hospital stays, and the increased risk of acquiring hospital-associated infections caused by resistant organisms.[23,25] This highlights the critical role of ICUs as hotspots for the development and proliferation of AMR, emphasizing the need for targeted infection control measures in these settings.

In a study conducted by Sader et al. [28] in the United States, S% for *E. coli* isolates from ICUs were reported as follows: TZP 92.1%, CAZ 81.3%, CRO 76.9%, MEM 99.8%, GN 87.6%, and AN 99.4%. For non-ICU *E. coli* isolates, S% were higher: TZP 97.4%, CAZ 90.2%, CRO 88.1%, MEM 99.8%, GN 90.2%, and AN 99.7%. According to the NAMRSS report, S% for *E. coli* in Türkiye were as follows: AM 21.5%, AMC 35.4%, TZP 72.3%, CRO 48.9%, CAZ 45.8%, GN 70.7%, AN 91.3%, CIP 45.5%, IMP/MEM 95%, and ETP 91.8%.[26] Similarly, the CEASER report for Türkiye reported the following rates: AMC 39%, TZP 78%, CAZ 53%, ETP 91%, IMP/MEM 97%, GN 74%, AN 98%, and CIP 48%.[30] The ECDC report indicated that in Türkiye, fluoroquinolone resistance in *E. coli* exceeded 25%, carbapenem resistance ranged between 1-5%, and third-generation cephalosporin resistance exceeded 50%.[31] In another study conducted in Türkiye, *E. coli* isolates from urine samples demonstrated S% exceeding 90% for ETP, MEM and F. For non-urine samples, ETP and MEM also showed S% above 90% 29. In our study, antimicrobial S% were found to be higher than NAMRSS and CEASER reports. However, the S% reported by Sader et al.,[28] even for ICU isolates -particularly for beta-lactam antibiotics- were higher than our findings. While our results were consistent with the ECDC report, third-generation cephalosporin resistance in our study was below 50%. In conclusion, ETP, MEM, IMP, and AN were identified as effective empirical treatment options for *E. coli*-related infections in our study. However, it is important to note the significant decline in S% for ETP, IMP, and AN over time.

According to a study conducted by Sader et al.[28], *Klebsiella* spp. isolates from ICUs exhibited the following S%: TZP 89.1%, CAZ 82.7%, CRO 82.2%, MEM 97.6%, GN 91.5%, and AN 99.2%. For non-ICU Klebsiella spp. isolates, S% were higher: TZP 93.6%, CAZ 88.4%, CRO 87.6%, MEM 98.3%, GN 93.2%, and AN 99.3%. The NAMRSS report indicated that Klebsiella spp. isolates showed S% of 23.2% for AMC, 33.4% for TZP, 31.5% for CRO, 24.7% for CAZ, 50.8% for GN, 70% for AN, 37.3% for CIP, 59.9% for IMP/MEM, and 51.1% for ETP.[26] Similarly, the CEASER report for Türkiye: reported S% of 25% for AMC, 40% for TZP, 30% for CAZ, 49% for ETP, 61% for IMP/MEM, 55% for GN, 73% for AN, and 35% for CIP.[30] The ECDC report highlighted that in Türkiye, third-generation cephalosporin resistance in *Klebsiella* spp. exceeded 50%, while carbapenem resistance ranged between 10-25%.[31] In our study, S% for carbapenems in *Klebsiella* spp. isolates were similar to those reported by NAMRSS and CEASER. However, higher S% were observed for other antibiotics. Sader et al.'s[28] findings demonstrated higher S% overall compared to our results. In our study, carbapenem resistance was found to be between 25% and 50%, which deviates from the range reported in the ECDC report. The high carbapenem resistance observed in *Klebsiella* spp. isolates is particularly concerning and underscores the critical need for stringent antibiotic stewardship strategies to mitigate resistance and improve treatment outcomes.

A study reported that antimicrobial S% for *Klebsiella* spp. isolates were lower than *E. coli* isolates. 27. Our findings align with these results. In our study, significant reductions in S% were observed for *Klebsiella* spp. isolates against TZP, CXM, CAZ, FEP, ETP, IMP, MEM, AN, CIP, and SXT. From an empirical therapy perspective, AN was identified as the only effective option for *Klebsiella* spp. infections. Notably, carbapenem S% were approximately 80% in outpatient settings but declined sharply to 30% in ICUs. This highlights the increasing resistance rates in ICUs and underscores the necessity of a more cautious approach when selecting empirical therapies in these settings.

In a study conducted by Sader et al.,[28] *Acinetobacter* spp. isolates from ICUs exhibited S% of 61.0% for TZP, 69.4%

Table 5. Comparison of Susceptibility Percentages (%S) for Gram-Positive Bacteria

Bacteria	Year	Source	n	AM	E	CC	LVX	VA	TEC	LZD	TGC	TE	SXT	GN
S. aureus	2015-2016	Outpatient clinic	148		91	92	96	100	100	100	100	86	99	98
		Ward	256		86	92	97	100	100	100	100	88	98	98
		ICU	72		78	86	95	98	98	100	100	80	98	92
		Total	476		87	91	96	100	100	100	100	86	99	97
	2022-2023	Outpatient clinic	134		71	83	93	100	100	98	100	85	96	100
		Ward	196		69	81	95	100	100	100	99	74	96	98
		ICU	90		82	84	93	100	97	100	100	81	98	93
		Total	420		72	82	94	100	99	99	100	79	96	98
		p§			**<0.001**	**<0.001**	0.109	1.000*	0.195*	0.106*	0.224*	**0.004**	**0.047**	0.542
MSSA	2015-2016	Outpatient clinic	126		93	93	97	100	100	100	100	90	100	99
		Ward	217		91	95	98	100	100	100	100	91	100	99
		ICU	62		83	90	100	98	98	100	100	95	98	98
		Total	405		91	94	98	100	100	100	100	91	99	99
	2022-2023	Outpatient clinic	102		76	88	95	100	100	100	100	96	98	100
		Ward	159		80	87	100	100	100	100	99	89	99	98
		ICU	76		92	94	98	100	100	100	100	93	98	100
		Total	337		81	89	98	100	100	100	100	92	99	98
		p§			**0.001**	**0.028**	0.779*	1.000*	1.000*	-	0.357*	0.705	0.354	0.705
MRSA	2015-2016	Total	71		69	73	84	100	100	100	100	56	92	85
	2022-2023		83		44	46	86	100	97	97	100	43	87	84
		p§			**0.007**	**0.002**	0.877	-	0.500*	0.500*	-	0.139	0.425	0.943
CoNS	2015-2016	Outpatient clinic	178		35	67	73	100	99	99	100	44	83	78
		Ward	482		26	61	68	100	100	99	100	35	81	70
		ICU	410		21	39	48	100	99	97	100	36	72	41
		Total	1070		22	54	62	100	99	98	100	40	77	61
	2022-2023	Outpatient clinic	92		36	74	65	98	**	98	98	51	82	75
		Ward	188		22	57	48	100	92	99	99	53	71	70
		ICU	230		11	28	21	99	68	99	100	71	65	35
		Total	510		19	46	39	99	74	99	99	61	70	53
		p§			**0.144**	**0.002**	**<0.001**	**0.026***	**<0.001**	0.683	**0.026***	**<0.001**	**0.002**	**0.001**

Table 5. Continued

Bacteria	Year	Source	n	AM	E	CC	LVX	VA	TEC	LZD	TGC	TE	SXT	GN
MSCoNS	2015-2016	Outpatient clinic	80		47	79	88	100		100	100	54	94	
		Ward	147		46	84	95	100		99	100	65	93	
		ICU	59		64	91	100	100		100	100	76	98	
		Total	286		50	84	94	100		100	100	64	94	
	2022-2023	Outpatient clinic	40		50	87	90	100		100	100	59	97	
		Ward	51		45	79	91	100		97	100	58	82	
		ICU	33		54	86	81	100		100	100	70	82	
		Total	124		49	83	88	100		99	100	62	86	
		p§			0.894	0.755	0.104	-		0.484*	-	0.675	**0.020**	
MRCoNS	2015-2016	Outpatient clinic	98		25	55	54	100	99	99	100	35	74	
		Ward	335		16	50	54	100	100	99	100	31	73	
		ICU	351		13	30	39	100	99	96	100	30	68	
		Total	784		16	43	48	100	99	98	100	31	71	
	2022-2023	Outpatient clinic	52		25	73	45	97	**	97	97	45	77	
		Ward	137		12	45	35	100	89	100	99	46	72	
		ICU	197		5	21	11	99	66	98	100	69	62	
		Total	386		10	35	23	99	70	99	99	59	67	
		p§			**0.008**	**0.020**	**<0.001**	**0.032***	**<0.001**	0.308	0.101*	**<0.001**	0.210	
Enterococcus spp.	2015-2016	Outpatient clinic	224	79				99	99	100	100			70
		Ward	488	49				97	98	99	100			71
		ICU	257	41				97	97	100	100			64
		Total	969	55				98	98	99	100			69
	2022-2023	Outpatient clinic	146	86				97	96	98	99			71
		Ward	299	56				96	96	100	97			59
		ICU	303	50				95	96	98	90			45
		Total	748	60				96	96	98	94			54
		p§		**0.038**				**0.044**	**0.007**	0.081	**<0.001**			**<0.001**
E. faecalis	2015-2016	Outpatient clinic	174	97				99	100	100	100			69
		Ward	221	100				100	100	100	100			68
		ICU	105	98				100	100	100	100			79
		Total	500	98				100	100	100	100			70
	2022-2023	Outpatient clinic	116	97				99	99	99	100			73
		Ward	163	89				98	98	99	98			78
		ICU	163	88				100	100	98	85			55
		Total	442	91				99	99	98	94			67
		p§		**<0.001**				0.201*	0.053*	**0.032***	**<0.001**			0.323

Table 5. Continued

Bacteria	Year	Source	n	AM	E	CC	LVX	VA	TEC	LZD	TGC	TE	SXT	GN
E. faecium	2015-2016	Outpatient clinic	42	7				96	96	100	100			**
		Ward	259	6				95	96	99	100			73
		ICU	144	1				95	94	100	100			56
		Total	445	4				95	95	99	100			68
	2022-2023	Outpatient clinic	21	**				**	**	**	**			**
		Ward	124	8				94	92	100	96			31
		ICU	136	2				91	90	97	94			31
		Total	281	5				92	91	98	95			31
		p§		0.650				0.120	**0.017**	0.277*	**<0.001**			**<0.001**

* Fisher's exact test
**Insufficient Data
§The "total"groups were compared.
MSSA, Methicillin-Susceptible *Staphylococcus aureus*; MRSA, Methicillin-Resistant *Staphylococcus aureus*; MSCoNS, Methicillin-Susceptible Coagulase-Negative *Staphylococcus*; MRCoNS, Methicillin-Resistant Coagulase-Negative Staphylococcus; ICU, ıntensive care unit; AM, ampicillin; E, erythromycin; CC, clindamycin; LVX, levofloxacin; VA, vancomycin; TEC, teicoplanin; LZD, linezolid; TGC, tigecycline; TE, tetracycline, SXT,trimethoprim-sulfamethoxazole; GN, gentamicin.

for CAZ, 70.1% for MEM, 70.8% for LEV, and 74.3% for GN. For non-ICU *Acinetobacter* spp. isolates, S% were slightly different: TZP 61.9%, CAZ 62.4%, MEM 72.2%, LEV 69.8%, and GN 79.4%.[28] According to the NAMRSS report, *Acinetobacter* spp. isolates showed S% of 22.7% for GN, 27.6% for AN, 8.8% for CIP, and 7.7% for IMP/MEM.[26] Similarly, the CEASER report indicated S% of 10% for IMP/MEM, 20% for GN, 30% for AN, and 9% for CIP in Türkiye.[30] The ECDC report highlighted carbapenem resistance exceeding 50% in *Acinetobacter* spp. isolates in Türkiye.[31] The findings of our study were consistent with the NAMRSS, CEASER, and ECDC reports. However, the S% reported by Sader et al.[28] were notably higher than our results. Among Gram-negative bacteria, *Acinetobacter* spp. isolates exhibited the lowest antimicrobial S%. In our study, a significant decrease in S% was observed for GN, AN, and SXT over time. Notably, no single antimicrobial agent demonstrated sufficiently high susceptibility to be recommended alone for empirical treatment of *Acinetobacter* spp. infections. Given the overall low susceptibility profile, particularly in the context of multidrug resistance, the use of combination therapy may be considered a more appropriate empirical treatment strategy until definitive culture and susceptibility results are available.

In a study by Sader et al.[28], *Pseudomonas* spp. isolates from ICUs demonstrated S% of 76.9% for TZP, 81.7% for CAZ, 76.1% for MEM, 69.5% for LEV, and 88.1% for GN. For non-ICU isolates, S% were higher: TZP 83.4%, CAZ 87%, MEM 83.7%, LEV 68.4%, and GN 87.4%. According to the NAMRSS report, *Pseudomonas* spp. isolates showed S% of 69.9% for TZP, 76.5% for CAZ, 69.5% for FEP, 73.9% for GN, 62.3% for CIP, and 53.9% for IMP/MEM. Similarly: the CEASER report indicated S% of 66% for TZP, 72% for CAZ, 69% for FEP, 62% for IMP/MEM, 79% for GN, and 65% for CIP in Türkiye 30. The ECDC report noted that carbapenem resistance in *Pseudomonas* spp. isolates in Türkiye ranged between 10-25%.[31] The findings of our study showed that S% were higher compared to the NAMRSS and CEASER reports and were consistent with the ECDC report. Among antimicrobials, AN was identified as the most effective option for empirical therapy in *Pseudomonas* spp. infections. While S% for other antimicrobials were below 90%, rates for CAZ, FEP, and CIP were above 80%. A significant decrease in susceptibility to FEP was observed, alongside a notable increase in susceptibility to IMP. However, it is crucial to consider that S% are even lower in ICU settings, which should be carefully accounted for when planning empirical therapy for critically ill patients.

According to the NAMRSS report, *S. aureus* isolates exhibited S% of 85.5% to CIP and 94% to LZD, with no resistance detected to VA or an unspecified agent, TEC.[26] Similarly, the CEASER report from Türkiye also reported no resistance to VA and LZD in *S. aureus* isolates.[30] Our study findings are consistent with these reports, indicating high S% for most antimicrobials in *S. aureus* isolates. However, a significant reduction in susceptibility was observed for E, CC, and TE. From an empirical therapy perspective, LVX, VA, TEC, LZD, TGC, SXT, and GN are viable options. Notably, susceptibility differences between methicillin-susceptible *S. aureus* (MSSA) and MRSA isolates are significant. For MSSA isolates, all antimicrobials except E and CC are appropriate for empirical therapy. In contrast, for MRSA isolates, empirical therapy should be limited to VA, TEC, LZD, and TGC. These findings underscore the importance of carefully tailored treatment strategies to ensure the effective management of *S. aureus* infections.

CoNS isolates were found to have lower S% than *S. aureus*. Significant reductions in susceptibility were observed for all antimicrobials except LZD and TE. From an empirical therapy perspective, only VA, LZD, and TGC were identified as effective treatment options. Methicillin-susceptible CoNS (isolates demonstrated higher S% than methicillin-resistant CoNS (MRCoNS) isolates. However, SXT, which was a viable empirical therapy option in 2015-2016, showed a significant decline in S% by 2022-2023, rendering it unsuitable for empirical use. In MRCoNS isolates, notable reductions in susceptibility were

Table 6. Distribution of MRSA and VRE Rates Across Outpatient clinic, Ward, and ICU (%)

MRSA	**2015-2016**	Outpatient clinic	14.2
		Ward	9.6
		ICU	20.6
		Total	12.9
	2022-2023	Outpatient clinic	19.2
		Ward	25.7
		ICU	26.1
		Total	24.1
VRE	**2015-2016**	Outpatient clinic	1.4
		Ward	2.8
		ICU	2.9
		Total	2.5
	2022-2023	Outpatient clinic	2.9
		Ward	4.3
		ICU	4.6
		Total	4.2

MRSA, methicillin-resistant *Staphylococcus aureus;* VRE, vancomycin-resistant *Enterococcus* rate; ICU, intensive care unit.

observed for E, CC, LVX, and TEC. Conversely, a significant increase in susceptibility to TE was recorded. Despite this, only VA, LZD, and TGC were deemed suitable for empirical therapy in MRCoNS infections. These findings highlight the importance of carefully assessing resistance patterns when planning treatment strategies for CoNS infections, ensuring that therapeutic choices are guided by the most current susceptibility data.

According to the NAMRSS report, *Enterococcus faecalis* isolates demonstrated S% of 94% for AM, 42.8% for GN, and 98.7% for VA. For *Enterococcus faecium*, S% were 8.4% for AM, 38.3% for GN, 84% for VA, and 99% for LZD 26. Similarly, the CEASER report indicated S% of 95% for AM, 66% for GN, 100% for VA, and 100% for LZD in *E. faecalis* isolates in Türkiye. For *E. faecium* isolates, S% were 11% for AM, 45% for GN, 87% for VA, and 100% for LZD. In our study, the findings were consistent with the NAMRSS and CEASER reports, except for VA susceptibility, which was slightly lower. In addition to VA, TEC, LZD, and TGC were identified as effective empirical therapy options. A significant decrease in susceptibility was observed for AM, LZD, and TGC in *E. faecalis* isolates. Despite this decline, AM, in addition to VA, TEC, LZD, and TGC, remains a viable option for empirical treatment of *E. faecalis* infections. However, AM susceptibility in *E. faecium* isolates is substantially lower than in E. faecalis. Furthermore, significant reductions in susceptibility to TEC, TGC, and GN were noted for *E. faecium* isolates. For *E. faecium* infections, only VA, TEC, LZD, and TGC were deemed suitable for empirical therapy. These findings underscore the critical importance of carefully evaluating resistance patterns in the management of *Enterococcus* infections to optimize therapeutic outcomes.

According to the NAMRSS report, the MRSA rate was reported as 23.6%. The CEASER report for Türkiye indicated a slightly higher rate of 31%,[30] while the ECDC report stated that MRSA rates in Türkiye range between 25 and 50%.[31] In our study, MRSA rates were found to be consistent with the NAMRSS report but lower than the rates reported in the CEASER and ECDC reports. The observed increase in MRSA rates was primarily attributed to samples originating from inpatient wards. This highlights the need for enhanced infection control measures specifically targeting ward-based infections to mitigate the spread of MRSA.

According to the CEASER report, the VRE rate in Türkiye was reported as 1%. In contrast, the ECDC report indicated a higher VRE rate, ranging between 10-25%.[31] In our study, the observed VRE rate was higher than the CEASER report, but lower than the range reported in the ECDC data. This increase in VRE rates was largely attributed to samples collected from outpatient clinics and ICU patients. These findings emphasize the critical importance of strengthening infection control measures, particularly in these settings, to effectively manage and reduce the spread of VRE.

According to ECDC reports, AMR rates are lower in Northern and Western Europe, while significantly higher rates are observed in Eastern and Southern Europe, as well as in Türkiye.[31] In our study, the resistance rates at our hospital were found to be lower compared to the NAMRSS and CEASER reports, indicating the implementation of an effective antimicrobial stewardship program within our institution. However, the persistence of high resistance rates underscores that AMR cannot be fully mitigated through measures at the level of a single hospital or region alone. Addressing this global challenge requires comprehensive nationwide strategies and enhanced international collaboration and coordination to effectively combat AMR on a broader scale.

When comparing our findings with national and international surveillance data, we observed some differences in S%. These variations may be attributed to several factors, including differences in patient populations, hospital-specific antimicrobial stewardship strategies, local infection control practices, diagnostic methodologies, and sample selection criteria. As this study was conducted in a single tertiary care center, the observed resistance patterns may reflect the unique characteristics of the institution. These findings underscore the importance of cumulative antibiogram data tailored to specific regions or healthcare settings, because they provide more clinically relevant guidance for empirical therapy decisions than generalized national estimates.

In accordance with current WHO recommendations, antimicrobials with a susceptibility rate of ≥90% are considered appropriate for empirical treatment in severe infections.[18] In this study, some antimicrobial agents demonstrated S% below this threshold. These findings suggest that such agents may be less reliable for empirical use in serious infections, such as bloodstream infections or meningitis, and should be used with caution. However, in cases of mild or moderate infections-especially when supported by local antibiogram data or when alternative agents are limited-agents with S% between 80-90% may still be considered, provided that close clinical monitoring and follow-up microbiological testing are ensured. In instances where no suitable alternatives are available,

combination therapy or the agent with the highest S% rate may be considered, as reflected in local antimicrobial stewardship strategies. This underscores the importance of continually updating cumulative antibiograms and integrating them into institutional treatment guidelines.

Although empirical therapy suggestions in this study were based on antimicrobial agents with ≥90% S%, it is important to emphasize that such recommendations should not be generalized across all clinical contexts. The choice of empirical treatment must be guided not only by local susceptibility trends, but also by the specific clinical setting, infection site, severity of illness, and patient-related factors such as renal function, immune status, and comorbidities. Moreover, the pharmacokinetic and pharmacodynamic properties and toxicity profiles of antimicrobial agents should be carefully considered before empirical use. Therefore, the findings of this study should be viewed as a microbiological foundation to support, but not replace, individualized clinical decision-making and alignment with institutional treatment protocols.[18,32,33]

One of the limitations of this study is the absence of MIC distribution data. Only categorical susceptibility data (i.e., susceptible or resistant) were presented. In addition, molecular characterization of resistance mechanisms - such as the detection of extended-spectrum β-lactamase, *Klebsiella pneumoniae* carbapenemase, or oxacillinase-48 type carbapenemase genes- was not routinely performed in our laboratory and was, therefore, not available for analysis in this study. Furthermore, interpretive breakpoints defined by EUCAST were not uniform across the two study periods. Specifically, isolates from 2015-2016 were interpreted using EUCAST versions 5.0 to 6.0, while data from 2022-2023 were evaluated based on versions 12.0 to 13.0. Updates in clinical breakpoints for certain antimicrobial agents -particularly aminoglycosides and fluoroquinolones- may have led to reclassification of isolates with MIC values near the susceptibility thresholds. Although overall trends remained consistent, this methodological variation should be taken into account when comparing the two time periods.

In conclusion, the cumulative antibiogram data from our region demonstrate higher S% compared to those of the national average, in Türkiye. However, the growing resistance problem, particularly among Gram-negative bacteria, is a significant concern. This emphasizes the critical importance of accurately selecting empirical treatment options to effectively manage infections.

The recommended antimicrobials for empirical therapy are as follows:

For *E. coli* infections: carbapenems, and AN.

For *Klebsiella* spp. and *Pseudomonas* spp. infections: AN.

For *Acinetobacter* spp. infections: combination therapy.

For *S. aureus* infections: LVX, VA, TEC, LZD, TGC, SXT, and GN.

For CoNS infections: VA, LZD, and TGC.

For *Enterococcus* spp. infections: VA, TEC, LZD, and TGC.

These findings highlight the necessity of regularly assessing regional antibiogram data and updating empirical therapy protocols based on these data. Such an approach is essential for improving the effectiveness of infection management and combating AMR.

Ethics

Ethics Committee Approval: The study received ethical approval from the Non-interventional Scientific Research Ethics Committee of the Faculty of Medicine of Trakya University with the protocol code TÜTF-GOBAEK-2024/207(approval no: 09/35, date: 06.05.2024).

Informed Consent: Retrospective study, and permission was obtained from the hospital administration to collect the data used in the study.

Footnotes

Author Contributions

Concept - İ.D.; Design - İ.D., H.G.; Supervision - İ.D., H.G.; Materials - İ.D., H.G., E.Ç.; Data Collection and/or Processing - İ.D., H.G., E.Ç.; Analysis and/or Interpretation - İ.D., E.Ç.; Literature Search - İ.D., H.G., E.Ç.; Writing - İ.D., H.G., E.Ç.; Critical Review - İ.D., H.G.

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