ANNUAL REPORT

KERALA ANTIMICROBIAL RESISTANCE SURVEILLANCE NETWORK (KARS-Net)

(Reporting period – 01/01/2021 to 31/12/2021)

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ACRONYMS

KARSAP	Kerala Antimicrobial Resistance Strategic Action Plan
KARS-Net	Kerala Antimicrobial Resistance Surveillance Network
WHO	World Health Organisation
AMR	Antimicrobial Resistance
AST	Antimicrobial Susceptibility Testing
BMD	Broth Microdilution
CLSI	Clinical & Laboratory Standards Institute
EQAS	External Quality Assessment Scheme
GLASS	Global Antimicrobial Resistance Surveillance System
IPD	In-patient
ICU	Intensive Care Unit
ID	Identification
IQC	Internal Quality Control
LIMS	Laboratory Information Management System
MRSA	Methicillin-Resistant S. aureus
NFGNB	Non-fermenting Gram-negative bacilli
NCDC	National Centre for Disease Control
OPD	Outpatient
OSBF	Other Sterile Body Fluids
PA	Pus aspirate
R I S	Resistant Intermediate Sensitive
TMP-SMX	Trimethoprim-Sulfamethoxazole

SOP	Standard Operating Procedure
VRE	Vancomycin-Resistant Enterococcus species
WHO	World Health Organization

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1. Executive Summary

This report of 2021 is the first annual report of the Kerala AMR Surveillance Network (KARS-Net) published by Government Medical College, Thiruvananthapuram, the nodal centre for the network. This report includes antimicrobial resistance (AMR) surveillance data pertaining to 7 priority pathogens viz. *Escherichia coli*, *Klebsiella* species, *Pseudomonas* species, *Acinetobacter* species, *Salmonella* enterica serotype *Typhi* and *Paratyphi*, *Staphylococcus aureus* and *Enterococcus* species received from 18 sentinel surveillance laboratories from 9 districts. Antimicrobial susceptibility data of a total of 21,765 priority pathogens isolated from clinical samples of 14,353 unique patients has been reported from 1 January 2021 to 31 December 2021. Out of 14,353 isolates from unique patients, the highest number of isolates (51%) were from urine specimens, followed by 35% from pus aspirate and other sterile body fluids (PA & OSBF), and 13% were from blood specimens. Analysis of the data revealed *Escherichia coli* as the most commonly isolated pathogen (40 %) in the AMR Surveillance data of the year 2021, followed by *Klebsiella* species (24%), *Staphylococcus aureus* (12%), *Pseudomonas* species (11%), *Enterococcus* species (7%) and Acinetobacter species (6%). *Escherichia coli* is the most common pathogen isolated among outpatients and inpatients, while *Klebsiella* species is the commonest pathogen isolated in ICU patients. *Escherichia coli* is the predominant isolate from urine samples (61.4%) ,*Klebsiella* spp is the most common pathogen isolated from blood samples (28.1%) and *S. aureus* is the most common pathogen isolated from PA & OSBF (27.1%). The percentage of Methicillin resistant *S. aureus* (MRSA) isolates is 20%. The resistance to 3rd and 4th generation cephalosporins among *E. coli* is 62% and 48 % respectively, similar to that observed in *Klebsiella* spp. 63% to 3rd generation and 55% to 4th generation cephalosporins. Among the anti-pseudomonal drugs, 40% isolates of *Pseudomonas* spp. isolated from ICU patients are resistant to Ceftazidime whereas Piperacillin/tazobactam resistance is observed in 20% of the isolates. Isolates of *Acinetobacter* spp. show more than 50% resistance to almost all the antibiotics tested except for Minocycline to which 38% of strains are resistant.

2. Kerala Antimicrobial Resistance Surveillance Network (KARS-Net)

Kerala Antimicrobial Resistance Strategic Action Plan (KARSAP) was the first sub national AMR action plan conceptualised in India. It was released by the Honourable Chief Minister of Kerala Sri.Pinarayi Vijayan on 25 October 2018. Kerala Antimicrobial Resistance Surveillance Net Work (KARS-Net) was established in 2018 to estimate the extent, burden and monitoring of AMR in Kerala with the Department of Microbiology, Government Medical College, Thiruvananthapuram as the State nodal Centre. The network had 10 laboratories in the beginning. In 2019, with the technical support from World Health Organisation (WHO) , the network was expanded to 21 laboratories from both public and private sectors .

The Kerala Antimicrobial Resistance Strategic Action Plan (KARSAP) identified AMR surveillance as a strategic priority in line with National and Global AMR action plans. The WHO Country Office for India collaborated with Kerala's AMR surveillance network (KARSNET), with oversight of the State Government and NCDC. The network utilizes WHONET to analyse and share AMR data on a monthly basis. KARS-Net currently includes surveillance of AMR in seven key priority pathogens responsible for the highest antibiotic resistance rates among bacteria that commonly cause human infections. These include *Staphylococcus aureus*, *Enterococcus* species, *Escherichia coli*, *Klebsiella* species, *Pseudomonas* species, *Acinetobacter* species, *Salmonella enterica* serotype *Typhi* and *Para typhi*. KARS-Net plans to generate the State AMR Surveillance report annually and the 2021 data is submitted in WHO's Global Antimicrobial Resistance Surveillance System (GLASS). KARS-Net has included 8 Government Medical College laboratories, 1 government hospital, 1 public health laboratory, 3 semi-autonomous institutions, 4 Private Medical Colleges laboratories, 4 private laboratories and hospitals and Rajiv Gandhi Centre for Biotechnology across 9 districts in Kerala. (Fig. 1) Of these 21 sites, AMR surveillance data was received for the period of one year from 1 January 2021 to 31 December 2021 from 18network centres located in 9 districts.

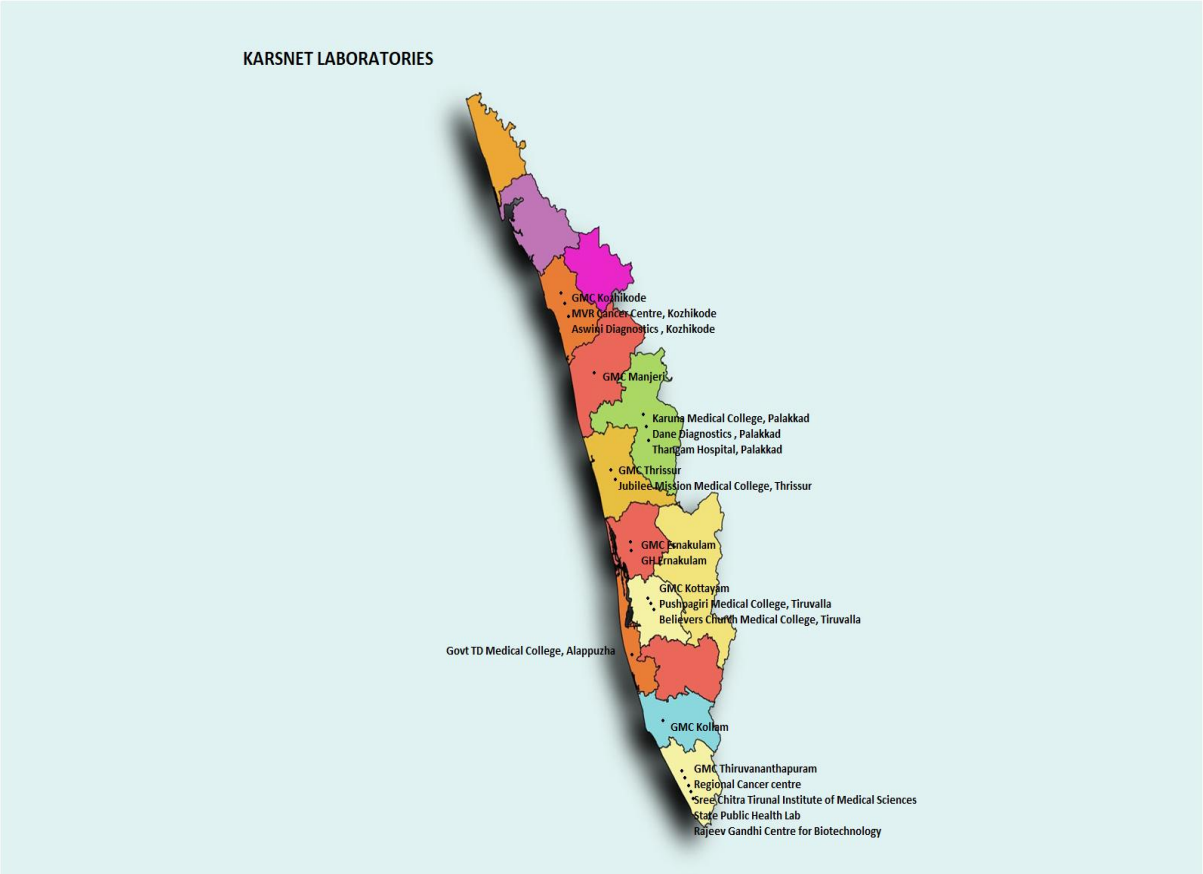

Figure. 1 Kerala AMR Surveillance Network (KARS-Net) Laboratories

List of KARSNET AMR Surveillance Network Sites	
1.	GMC Manjeri
2.	GMC Kozhikode
3.	GMC Thrissur
4.	GMC Ernakulam
5.	GMC Kottayam
6.	GMC Alappuzha
7.	GMC Kollam
8.	GMC Thiruvananthapuram
9.	GH Ernakulam
10.	State Public Health Laboratory, Thiruvananthapuram
11.	Regional Cancer Centre, Thiruvananthapuram
12.	Sree Chitra Tirunal Institute for Medical Sciences &Technology, Thiruvananthapuram

13.	Dane Diagnostics Laboratory, Palakkad
14.	Believers Church Medical College Hospital, Tiruvalla
15.	Jubilee Mission Medical College and Research institute, Thrissur
16.	Thankam Hospital, Palakkad
17.	MVR Cancer Centre & Research Institute, Kozhikode
18.	Aswini Diagnostic Services, Kozhikode

Table 1: List is of sites under KARS-Net that have submitted AMR Surveillance data for the period of January to December 2021

The sentinel surveillance laboratories under KARS-NET follow a standardised approach for AMR data collection, analysis, and reporting of AMR surveillance data using WHONET, an open source microbiology data management software. Trainings are provided on AMR data management using the WHONET software .Online capacity building sessions were also held during 2019 for standardisation of techniques for clinical specimen collection, bacterial culture, identification of pathogens & their antimicrobial susceptibility testing (AST), including frequent trouble shooting sessions for WHONET data management. Onsite support visits were also conducted in 2021 for streamlining AMR surveillance data management and to assess the training needs. Feedback for the data submitted every month is provided using a standardised feedback tool to improve the completeness and quality of AMR data. Under KARS-NET, Standard operating procedures (SOP) and guidance documents have been developed for strengthening the network sites on routine AST techniques and for improving internal quality control for AST testing in laboratories. These SOPs are reviewed on a regular basis.

3. Data Collection

This report includes AMR surveillance data from 18 network laboratories from 1st January 2021 to 31st December 2021 and includes data of 21765 culture-positive clinical samples received at the sentinel surveillance sites during the year 2021 which were processed using conventional/automated culture and identification techniques and AST was done using disk diffusion/ broth micro dilution/automated systems. This data was collected using the WHONET software, an open-source-offline microbiology data entry and analysis application database. WHO provided training to all the KARS-Net laboratories to enter data into WHONET and backlink data from automated ID & AST systems/Laboratory Information Management Systems. All sentinel sites submitted data on monthly basis after validation by the AMR nodal officers of the respective sites. As per programme guidelines, the data is to be submitted by the network sites within 10 days after each month. The data were analysed at Department of Microbiology, GMC Trivandrum and feedback was provided. Sites were also requested to re-submit the revised data if required. The completeness of demographical/clinical data and the antibiotic susceptibility profile are verified. AST profile lists each organism and its AST results in numbers and percentage (%) RIS (Resistance, Intermediate, susceptible) to each antibiotic.

4.Data Analysis

a. Data de-duplication

Data de-duplication was done using the WHONET software to exclude duplicate findings for the same patient where several specimen cultures were collected during patient management so as to include one isolate per specimen per patient. Before starting the de-duplication process, variables containing information about the patient, location, specimen type, pathogen isolated for completeness of records was reviewed. Only the first ID, and AST result of unique patient isolate has been included in this report.

There might be occasions during the in-hospital stay that the same patient had repeated identifications of the same pathogens from repeat sample collection on different dates with different AST profiles. For example, if two blood cultures from the same patient yielded growth of *E. coli*, only the first AST profile has been included in the report; if *E. coli* was detected in one culture and *K. pneumoniae* in the other, both results have been included. Both specimen data are included if *E. coli* is isolated from one blood culture and one urine culture from the same patient.

b. Priority Pathogens under surveillance in KARS- Net

The AMR data collected under the KARS-Net for the year 2021 is from 18 health care facilities in 9 districts; Following are the seven priority pathogens and five clinical samples included under AMR surveillance (Table 2).

Specimen	S. aureus	Enterococcus spp.	Klebsiella spp.	E. coli	Acinetobacter spp.	Pseudomonas spp.	Salmonella Typhi/ Paratyphi
Blood	●	●	●	●	●	●	●
Urine	X	●	●	●	●	●	X
Pus Aspirates	●	●	●	●	●	●	X
Other Sterile Body fluids	●	●	●	●	●	●	X
Stool	X	X	X	X	X	X	●

X- specimen not collected for this pathogen

Table 2. Clinical specimens and priority pathogens included under AMR surveillance

AMR surveillance data of 21,765 isolates submitted under KARS-Net were de-duplicated & analysed. After de-duplication, the number of isolates from unique patients was 14,353(Fig2)

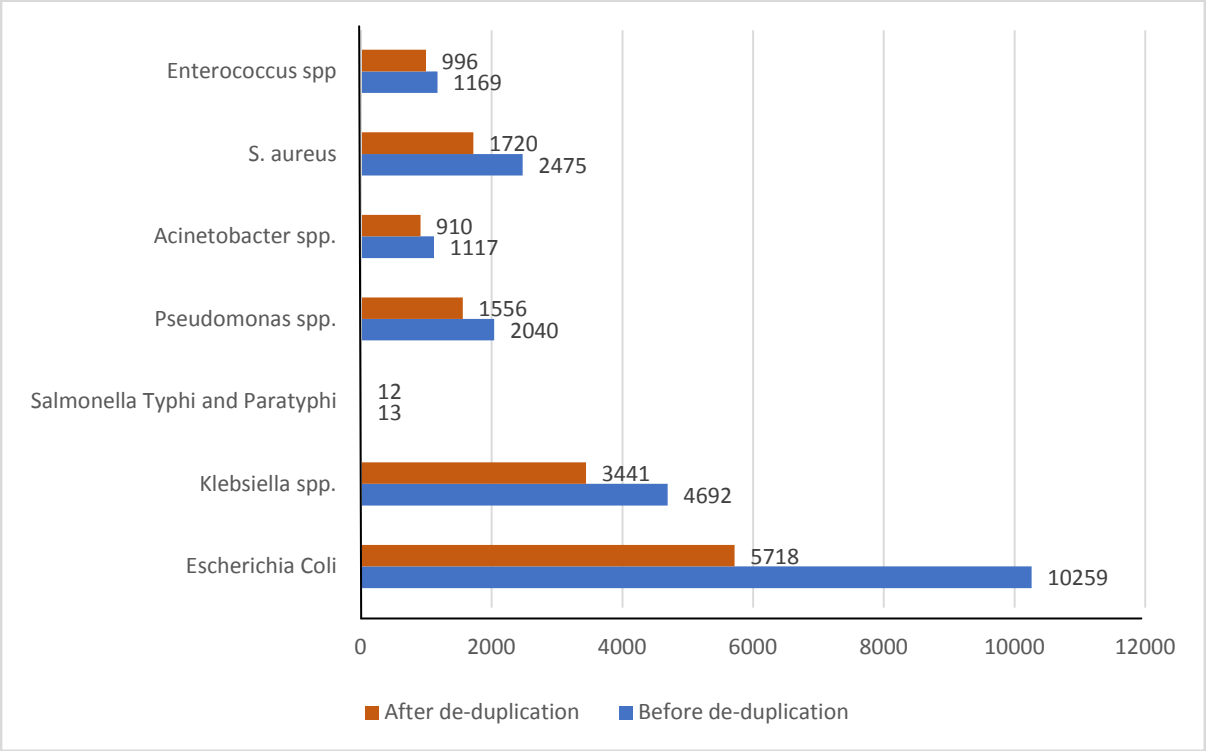

Figure. 2 Priority bacterial pathogens before and after de-duplication

Total number of isolates from unique patients (after de-duplication) = 14,353

- Urine –7,360 (51%)
- Pus Aspirates (PA) and Other Sterile body fluids (OSBF) – 5,090 (35%)
- Blood –1,898 (13%)

Escherichia coli is the predominant isolate in the AMR Surveillance data for the year 2021 (40%) followed by *Klebsiella* spp. (24%), *S. aureus* (12%), *Pseudomonas* spp (11%) , *Enterococcus* spp. (7%), *Acinetobacter* spp. (6%) and *Salmonella Typhi & Paratyphi* (12 isolates) (Fig. 3)

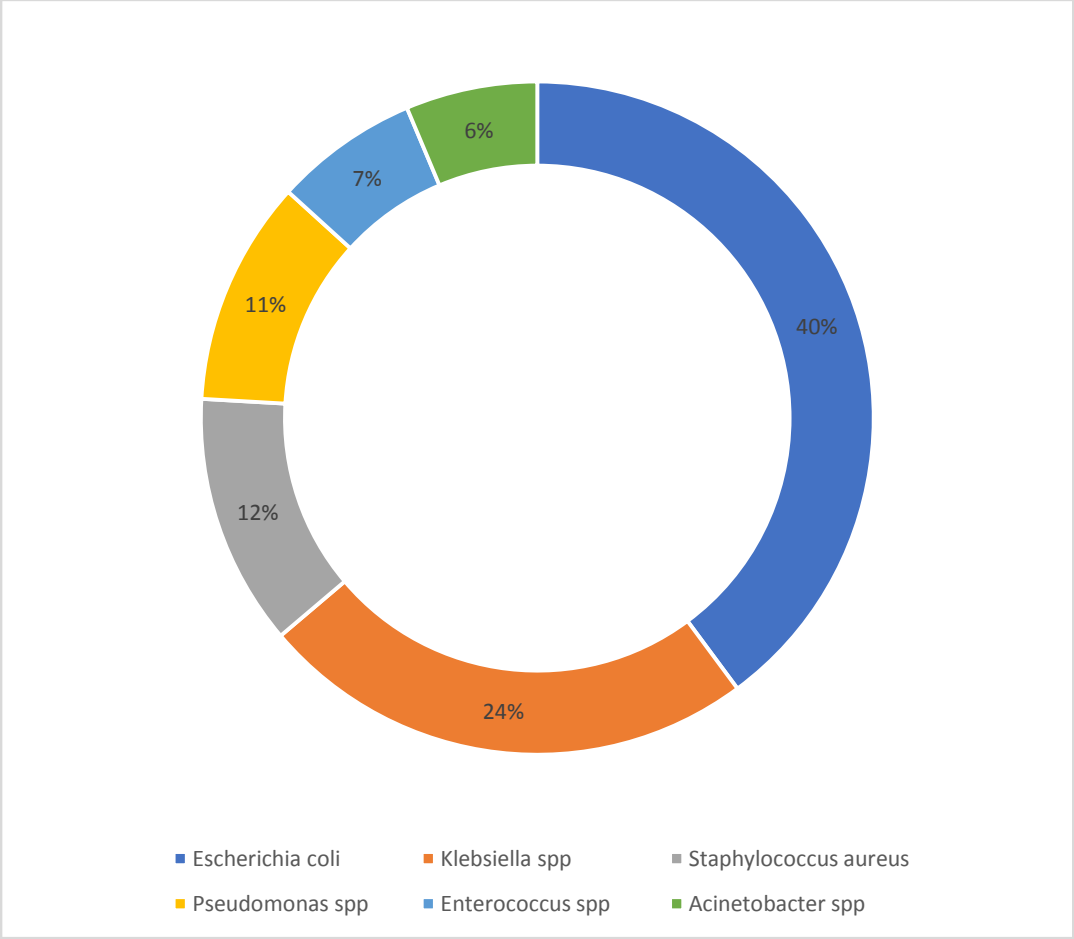

Figure 3 Percentage distribution of isolates in AMR Surveillance data for the year 2021

Pathogens included in this report are predominantly isolated from urine specimens, followed by pus & other sterile body fluids and blood cultures (Fig. 4).

Escherichia coli(61.4%) is the most commonly isolated pathogen from urine, followed by *Klebsiella* spp. (23.7%), *Pseudomonas* spp. (6.2%) , *Enterococcus* spp. (6.1%) and *Acinetobacter* spp. (2.6%)(Fig. 5).

The most commonly isolated pathogen from blood cultures is *Klebsiella* spp. (28.1%) followed by *Acinetobacter* spp. (18.9%), *S. aureus* (18%) , *E. coli* (15.1%), *Pseudomonas spp*. (11.2%) and *Enterococcus* spp.(8.4%) (Fig. 5).

The most frequently reported pathogen from pus & other sterile body fluids is *S. aureus* (27.1%), followed by *Klebsiella spp*. (22.9%) , *E. coli* (17.9%) , *Pseudomonas spp*. (17.4%) , *Enterococcus spp*. (7.6%) and *Acinetobacter spp*. (7%). (Table 3).

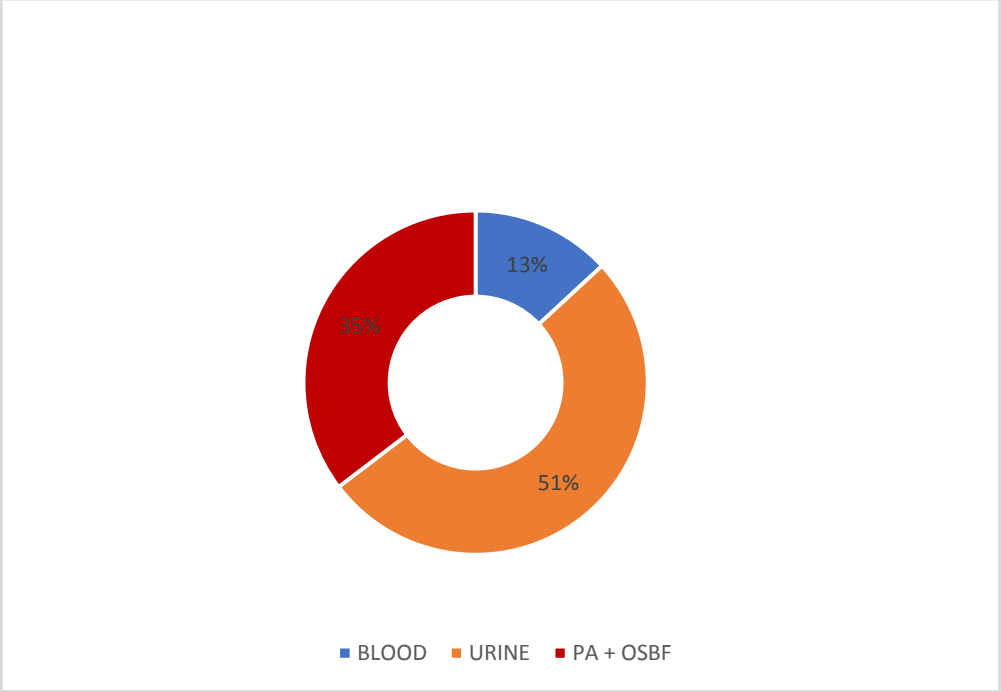

Figure 4 Distribution of isolates by specimen type

Priority Pathogen	Blood (N=1898)	Pus Aspirate &OSBF (N=5090)	Urine (N=7360)	Stool (N=5)	Total (N=14353)
	No of isolates (%)	No of isolates (%)	No of isolates (%)		No of isolates (N)
Escherichia Coli	287(15.1%)	913(17.9%)	4518(61.4%)		5718
Klebsiella spp.	533(28.1%)	1167(22.9%)	1741(23.7%)		3441
Salmonella Typhi and Paratyphi	7(0.4%)			5	12
Pseudomonas spp.	212(11.2%)	887(17.4%)	457(6.2%)		1556
Acinetobacter spp.	358(18.9%)	357(7.0%)	195(2.%)		910
S. aureus	342(18.0%)	1378(27.1%)			1720
Enterococcus spp	159(8.4%)	388(7.6%)	449(6.1%)		996
Total	**1898**	**5090**	**7360**	**5**	**14353**

Table 3 Specimen wise isolation of Priority Pathogens

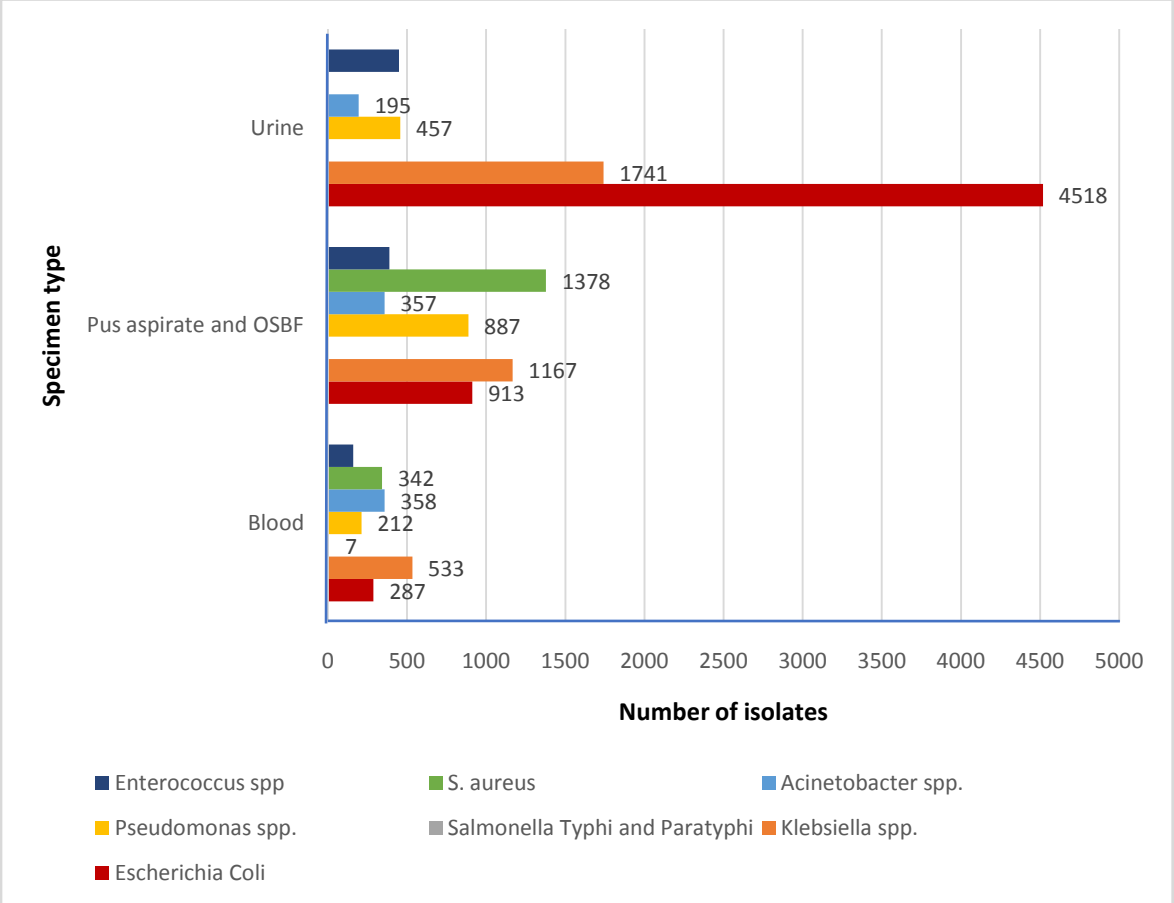

Figure 5 Specimen wise distribution of AMR surveillance Priority Pathogen

Number of isolates included in this report are more from female patients 52% (7371) compared to male patients 48% (6831) (Fig. 6). Gender data is missing in 151 results. Among males, highest number of isolates are from patients in 60 & above years age group (2,403) and in females also, the highest number of isolates are from patients in 60& above years age group (2,585) (Table 4). Data regarding age is also missing in151 entries.

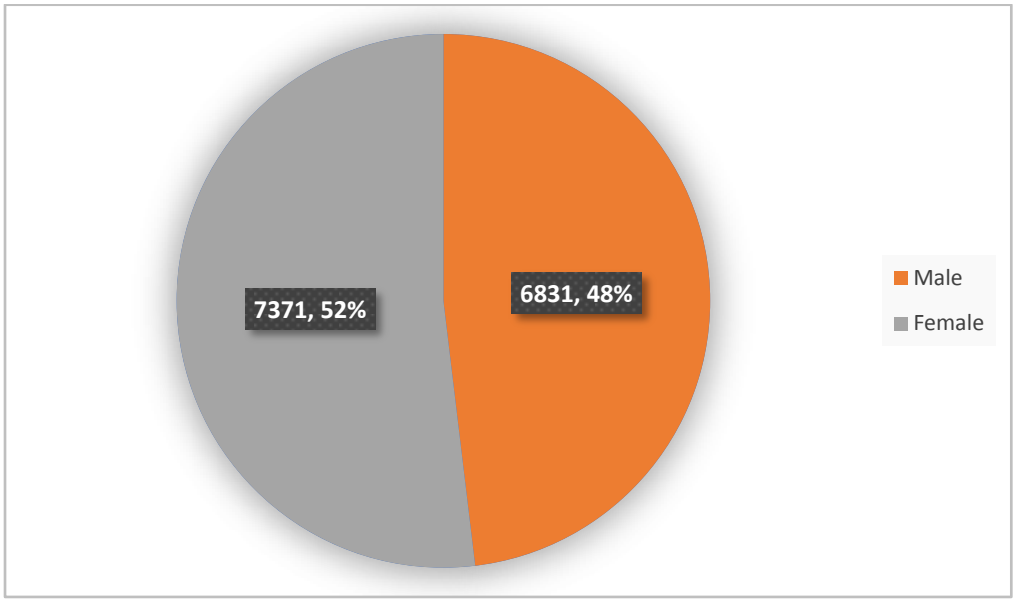

Figure 6 Overall distribution of isolates on the basis of gender

Age	Male	Female
0 to 9	944	968
10 to 19	312	271
20 to 29	1091	403
30 to 39	796	507
40 to 49	752	792
50 to 59	1041	1289
60 & above	2403	2585
Unknown	32	16
Total	**7371**	**6831**

Table 4 Gender and age-wise distribution of isolates

In the year 2021, the highest number of isolates are from IPD 6,128 (43%), followed by OPD 5,854 (41%), followed by ICU 1,494 (10%) (Fig. 7).

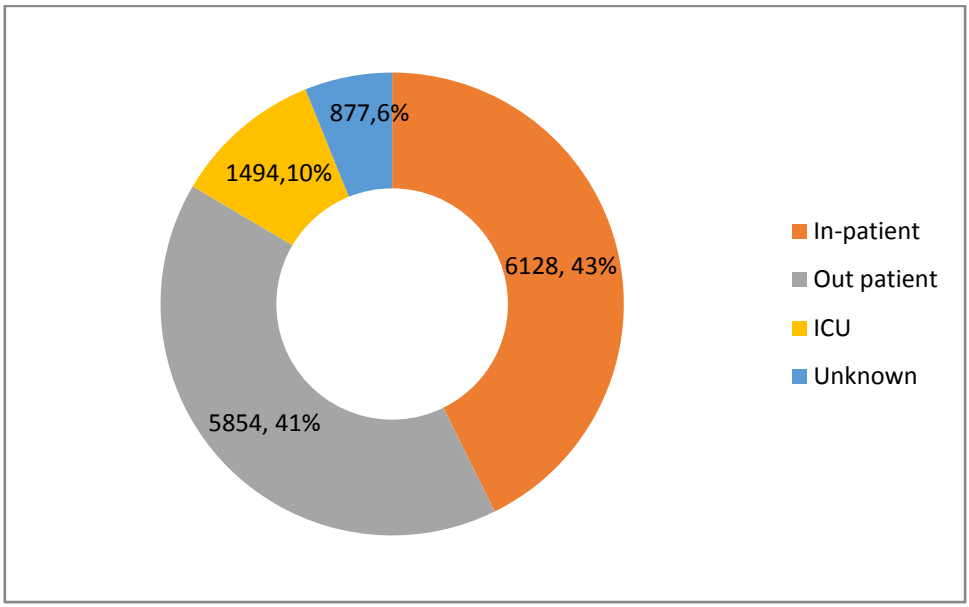

Figure 7 Location-wise distribution of isolates

Priority Pathogens	ICU (%)	IPD(%)	OPD(%)
Escherichia Coli	315 (21)	2116 (35)	2944 (50)
Klebsiella spp.	476 (32)	1614 (26)	1172 (20)
Salmonella Typhi and Paratyphi	1 (0.06)	7 (0.11)	1 (0.02)
Pseudomonas spp.	171 (11)	757 (12)	560 (10)
Acinetobacter spp.	272 (18)	416 (7)	157 (3)
S. aureus	103 (7)	719 (12)	719 (12)
Enterococcus spp	156 (10)	499 (8)	301 (5)
Total(13476)	**1494 (11)**	**6128 (45)**	**5854 (43)**

Table 5. Location-wise distribution of Priority Pathogens

Among IPD patients, highest number of isolates are of *E coli (*35%) followed by *Klebsiella* spp.(26%), *S. aureus* (12%), *Pseudomonas* spp. (12%), *Enterococcus* spp.(8%), *Acinetobacter* spp. (7%) and *Salmonella Typhi* and *Paratyphi (7* Nos) (Table 5, Fig 8). Predominantly isolated pathogen from OPD patients is *E. coli* (50%), followed by *Klebsiella* spp. (20%), *S. aureus* (12%), *Pseudomonas* spp. (10%), *Enterococcus* spp. (5%), *Acinetobacter* spp. (3%) and *Salmonella Typhi* and *Paratyphi (*1 Nos). (Table 5; Fig. 8).

Highest number of isolates from ICU patients are of *Klebsiella* spp. (32%) , followed by *E. coli (*21%), *Acinetobacter* spp. (18%) ,*Pseudomonas* spp. (11%), *Enterococcus* spp. (10%), *S. aureus* (7%) and *SalmonellaTyphi* and *Paratyph i(*1 Nos).(Table 5; Fig. 8)

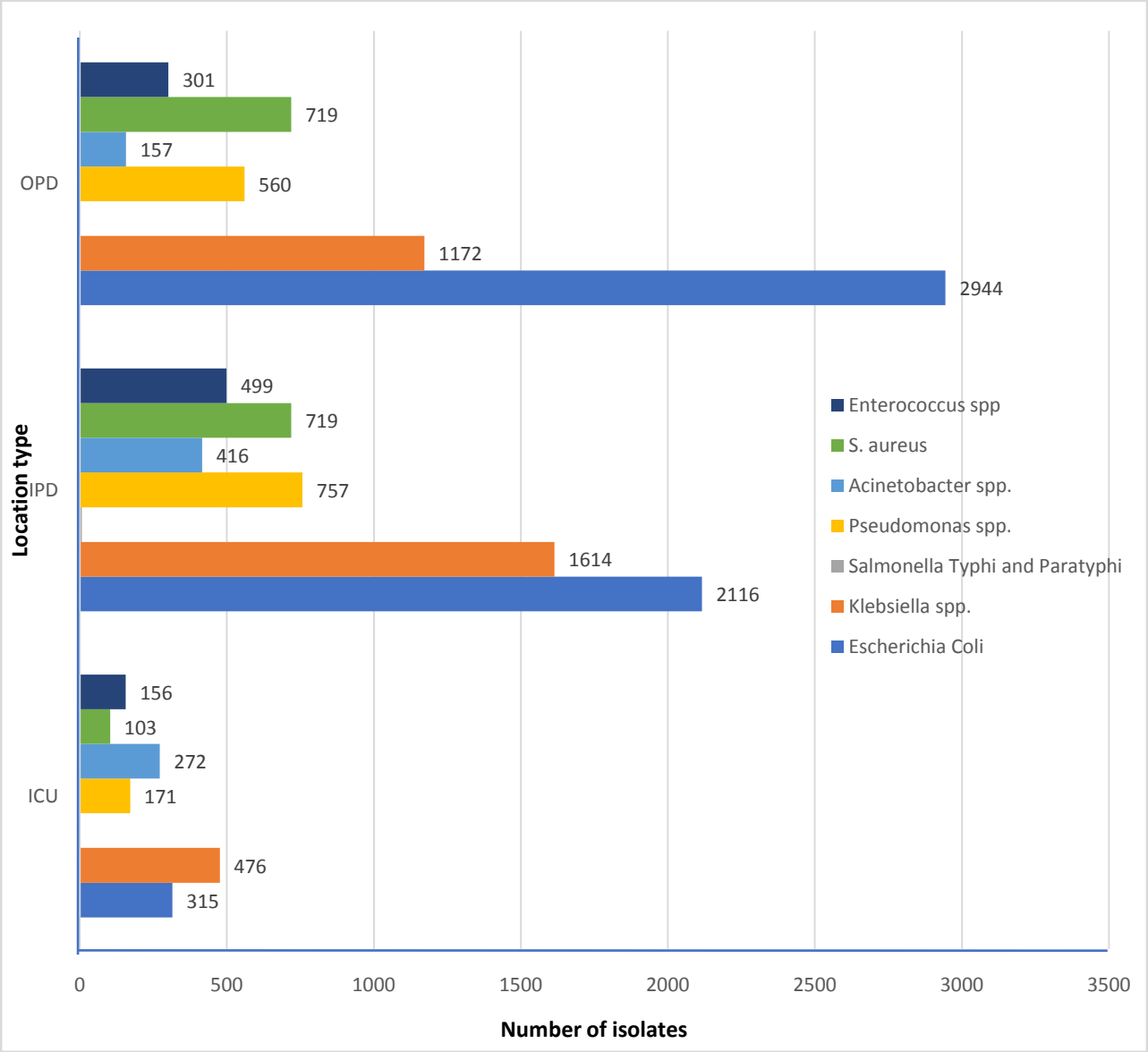

Figure 8 Location wise isolation of different Priority Pathogens

5. AMR profile of priority pathogens

The data collected under Kerala AMR Surveillance Network (KARS-Net) is for antibiotics as per the NCDC AMR surveillance data management Standard Operating procedure (SOP). This AMR surveillance data is from patients visiting out-patient departments (OPD) of the hospitals, from patients admitted to the in-patient departments (IPD) and intensive care units (ICU).

a. Gram Positive Cocci

Antimicrobial susceptibility data of a total 3644 gram-positive isolates was reported from 2716 unique patients during 2021.

Staphylococcus aureus

Staphylococcus aureus constituted 12% of all the isolates reported by network sites to GMC Thiruvananthapuram. (Fig. 3). The 2,475 *S. aureus* isolates have been reported from 1,720 unique patients (Fig. 2). During 2021, *S. aureus* has been predominantly isolated from out-patients and in patients and most commonly from the Pus aspirate and OSBF specimens (Table 2 and Fig. 5). It is observed that the MRSA among *Staphylococcus aureus* was 20%.

MRSA rates differ based on the source of isolation. Methicillin resistance is highest among *S. aureus* isolated from blood cultures that is 22%, followed by 19% in isolates from PA+OSBF (Table 6). Ciprofloxacin resistance is seen in 40% of *S. aureus* isolates from blood culture specimens and in 44% of *S. aureus* isolates from PA & OSBF (Table 6). Resistance to Erythromycin is 64% in blood culture isolates and 53% in isolates from PA & OSBF. Gentamicin resistance is observed in 18% of isolates from blood culture specimens and in 19% isolates from PA & OSBF specimens. Location type wise resistance profile of *Staphylococcus aureus* isolated from blood culture specimens is shown in Fig.9. A few centres have reported Linezolid resistant *S.aureus* isolates, but none were confirmed by MBD.

Antibiotic tested	Blood + PA+OSBF (N=1720)			Blood (N=342)			PA+OSBF (N=1378)		
	Number tested	Number Resistant	% R	Number tested	Number Resistant	%R	Number tested	Number Resistant	% R
Cefoxitin	1176	236	20	258	58	22	918	178	19
Amikacin	789	96	12	93	4	4	696	92	13
Gentamicin	1435	269	19	282	52	18	1153	217	19
Ciprofloxacin	1162	501	43	184	74	40	978	427	44
TMP/SMX	1514	259	17	234	50	21	1280	209	16
Clindamycin	1300	251	19	233	61	26	1067	190	18
Erythromycin	1550	843	54	251	161	64	1299	682	53
Linezolid	1346	5	0	284	1	0	1062	4	0
Doxycycline	617	26	4	67	2	3	550	24	4

Table 6. Resistance profile of Staphylococcus aureus (N= 1720)

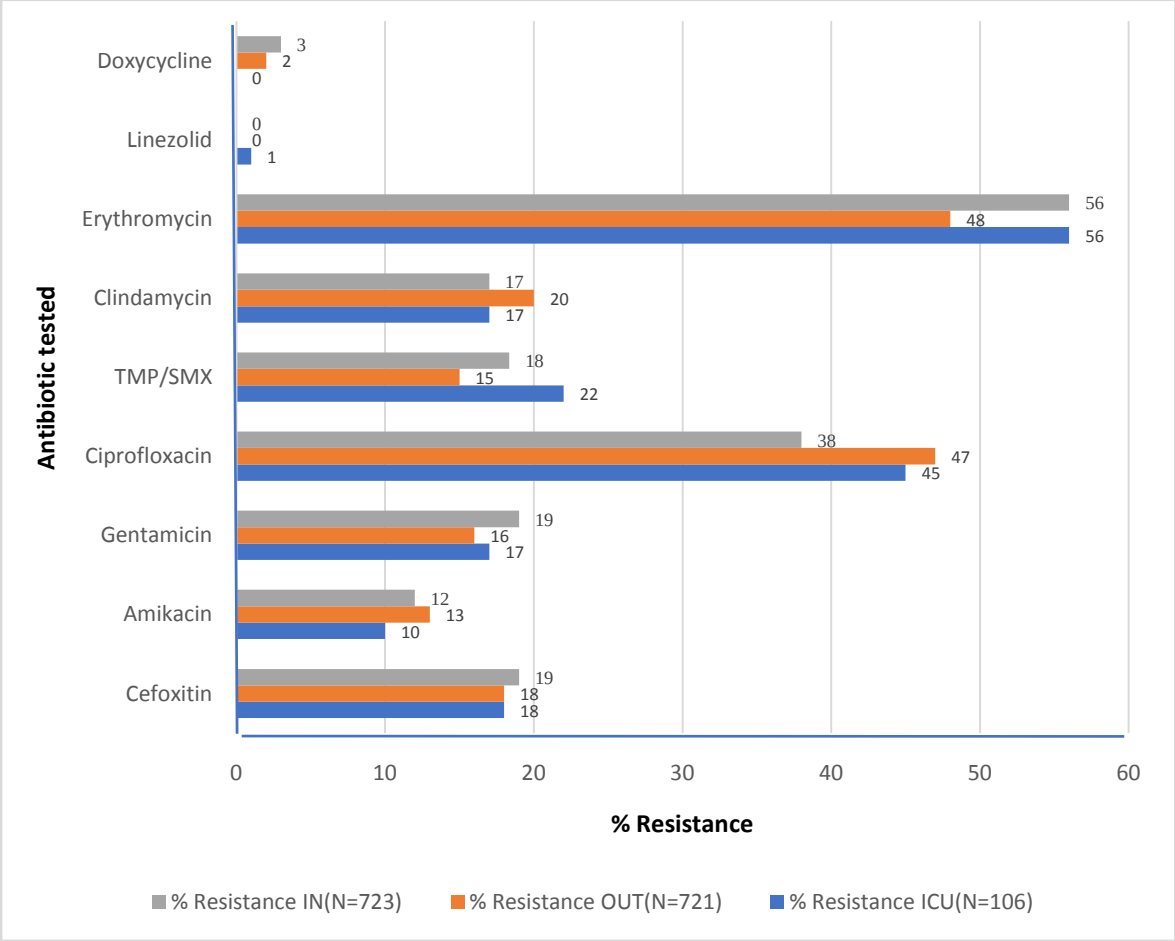

Figure 9 Location type wise resistance profile of *Staphylococcus aureus* isolated from blood culture specimens

Enterococcus species

Enterococcus spp. constitutes 7% of all the isolates in the 2021 data (Fig. 3). Data of 996 isolates is reported from 1,169 unique patients, and the resistance profile details are given in Table 8. More than 60 % resistance is observed in blood culture isolates of *Enterococcus* spp. to Ampicillin and Erythromycin (Table 7). Of the 996 *Enterococci* analysed, highest rate of resistance is observed in Erythromycin (75%), followed by Tetracycline(69%), Ciprofloxacin (63%), Doxycycline (57%) , high-level Gentamicin (35%) and Ampicillin (33%).(Fig. 10)

Five percent of the *Enterococcus* spp. tested for antimicrobial susceptibility are resistant to Vancomycin and 2% of the isolates are resistant to Linezolid. In urine, blood and PA & OSBF high resistance is found for Erythromycin (73%, 82% & 72% respectively) and Ciprofloxacin (69%, 58% &42% respectively). In urine, blood and PA & OSBF lower resistance is found for Vancomycin (6%, 6% &3% respectively) (Table 7). Among ICU patients, higher percentage of VREs are found in urine specimens than in blood and OSBF specimens (Fig. 11; Fig. 12) While higher percentage of Linezolid resistant *Enterococci* are isolated from urine specimens (7%)ofOPD patients than that from blood and PA+OSBF (3%)(Fig. 11; Fig. 12) The overall Linezolid resistance was found to be 2.4%.

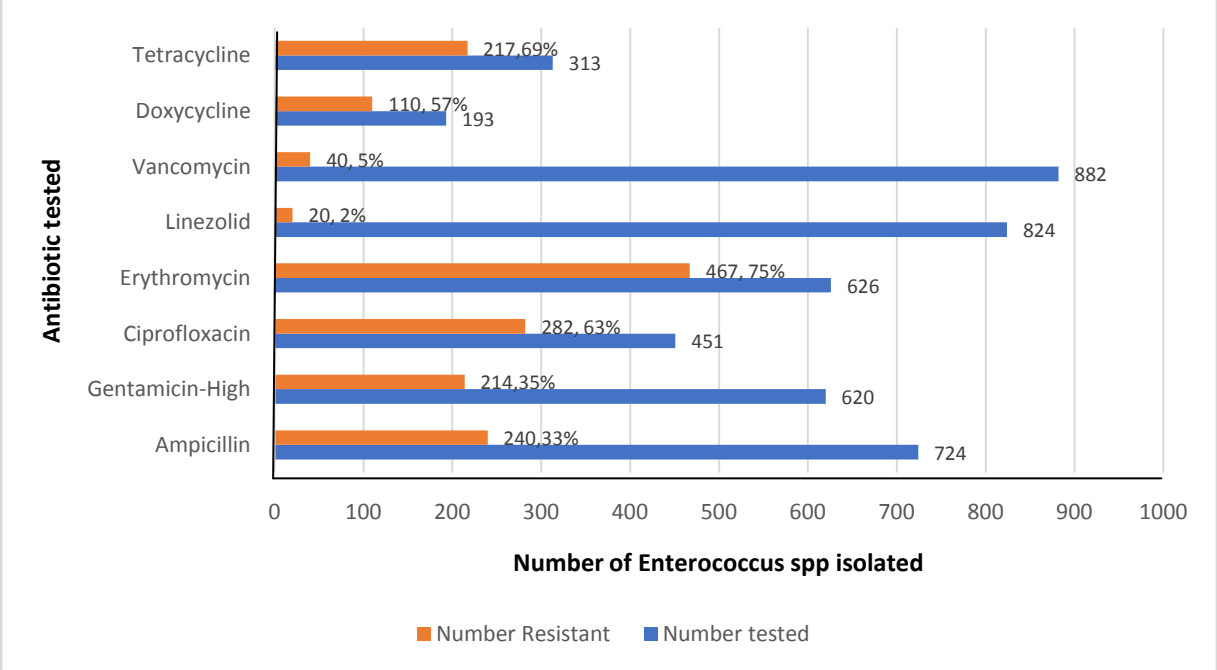

Figure 10 Resistance profile of *Enterococcus* species (N=996)

Antibiotic tested	PA+OSBF(N=388)			Blood{N=159)			Urine(N=449)		
	Number tested	Number Resistant	%R	Number tested	Number Resistant	%R	Number tested	Number Resistant	%R
Ampicillin	322	72	22	122	73	60	280	95	34
Gentamicin-High	303	71	23	115	60	52	202	83	41
Ciprofloxacin	84	35	42	50	29	58	317	218	69
Erythromycin	338	244	72	137	113	82	151	110	73
Linezolid	352	6	2	135	3	2	337	11	3
Vancomycin	346	9	3	140	8	6	396	23	6
Doxycycline	112	64	57	57	37	65	24	9	38
Tetracycline	44	26	59	27	22	81	242	169	70

Table 7. Specimen wise resistance profile of *Enterococcus* species

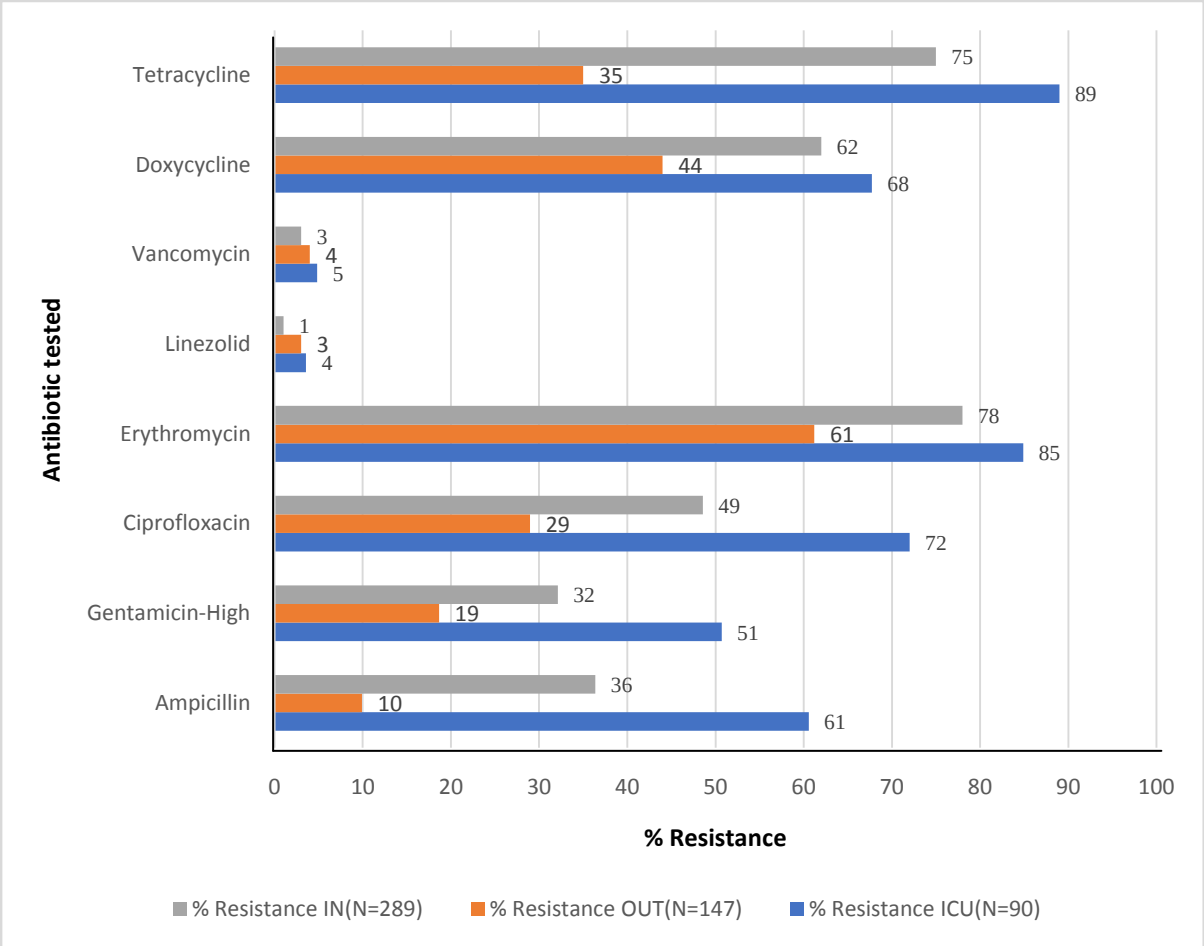

Figure 11 Resistance profile of *Enterococcus* species isolated from blood and PA & OSBF from different location types in healthcare facilities

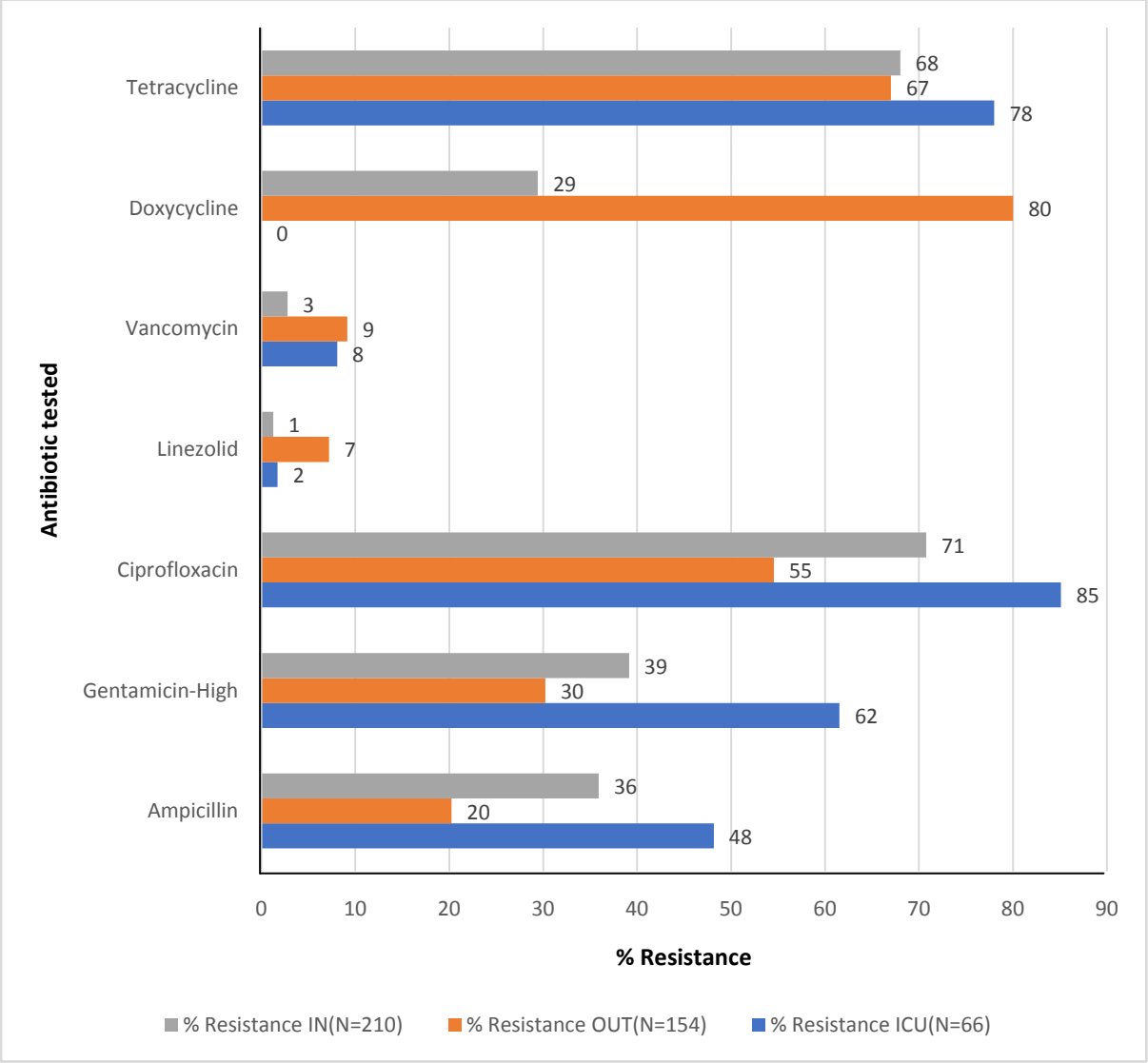

Figure 12 Resistance profile of *Enterococcus* species isolated from urine specimens from different location types in healthcare facilities

b.Gram negative bacilli

Gram-negative pathogens included for AMR surveillance under KARS-Net are among the commonest cause of bacterial infections in patients attending the healthcare facilities. The gram-negative priority pathogens included under the KARS-Net are *E. coli*, *Klebsiella* spp., *Pseudomonas* spp., *Acinetobacter* spp., *Salmonella enterica serotype Typhi* and *Paratyphi*. In the year 2021, total 18,121 gram-negative pathogens are isolated from 11,637 unique patients from 18 network sites.

i. *Enterobacteriaceae*

Enterobacterales i.e. *E. coli*, *Klebsiella* spp. and *Salmonella Typhi and Paratyphi*, constitute the majority 9,171 (64%) (Fig. 3) of the overall priority pathogens in this annual AMR surveillance report.

Escherichia coli

A total of 10,259 *E. coli* isolates were reported from 5,718 unique patients. The highest number of *E coli* was reported from urine samples, followed by PA & OSBF and blood (Table 8) and the overall resistance profile is given in Figure 13. In urinary tract infection patient's beta-lactam antibiotic resistance is high, it is 82% to Ampicillin followed by 62% to Cefotaxime, 48% to Cefepime, 8% to Meropenem and 10% to Imipenem . Among non-beta-lactam antibiotics, 61% resistance was observed to Ciprofloxacin, 53% to Trimethoprim-Sulfamethoxazole (TMP/SMX) and 11% to Nitrofurantoin (Table 8). Similarly, in E. coli isolates from blood, percentage resistance to beta-lactam antibiotics, i.e. 84% to Ampicillin, 66% to Cefotaxime, 48% to Cefepime, , 10% to Meropenem and 10% to Imipenem. Among non-beta-lactam antibiotics, 64% resistance to Ciprofloxacin and 56% to TMP/SMX is observed (Table 8). In PA & OSBF isolates of *E. coli*, resistance reported is 84% to Ampicillin followed by 58% to Cefotaxime, 46% to Cefepime, , 9% to Imipenem, 10% to Meropenem, 62% to Ciprofloxacin and 52% to TMP/SMX (Table 8)

Resistance profile of E. coli isolates from blood, urine, PA & OSBF from different location types is shown in Fig. 14

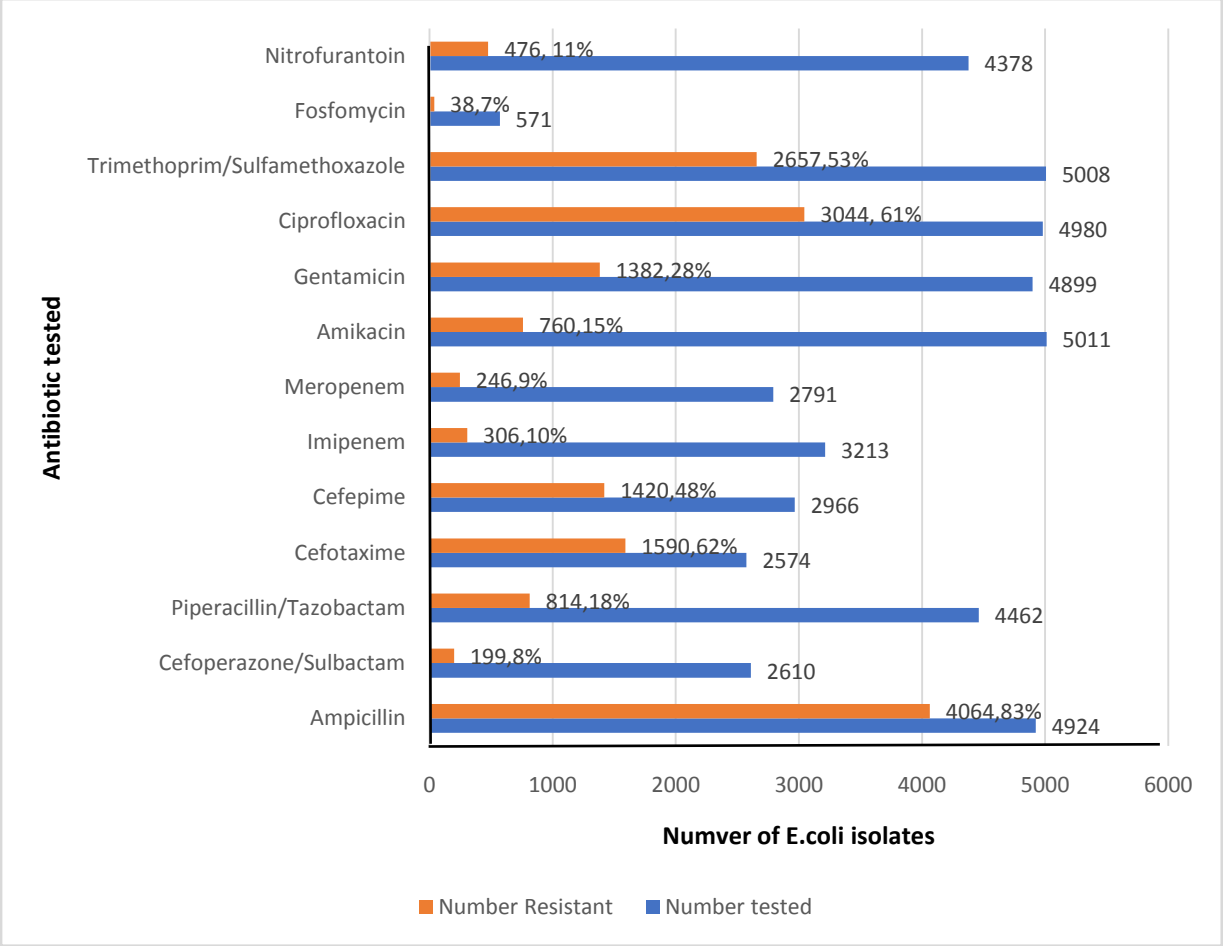

Figure 13 Resistance profile of E. coli (N=5,718)

Antibiotic tested	PA+OSBF(N=913)			Blood{N=287)			Urine(N=4518)		
	Number tested	Number Resistant	%R	Number tested	Number Resistant	%R	Number tested	Number Resistant	%R
Ampicillin	881	744	84	267	223	84	3776	3097	82
Cefoperazone/Sulbactam	617	33	5	183	17	9	1810	149	8
Piperacillin/Tazobactam	858	170	20	235	56	24	3369	588	17
Cefotaxime	420	242	58	125	82	66	2029	1266	62
Cefepime	582	270	46	195	94	48	2189	1056	48
Imipenem	599	55	9	196	19	10	2418	232	10
Meropenem	708	70	10	210	20	10	1873	156	8
Amikacin	852	140	16	265	51	19	3894	569	15
Gentamicin	863	265	31	239	78	33	3797	1039	27
Ciprofloxacin	884	546	62	247	158	64	3849	2340	61
Trimethoprim/Sulfamethoxazole	702	367	52	239	134	56	4067	2156	53
Fosfomycin							571	38	7
Nitrofurantoin							4378	476	11

Table 8. Specimen wise resistance profile of E. coli (N=5,718)

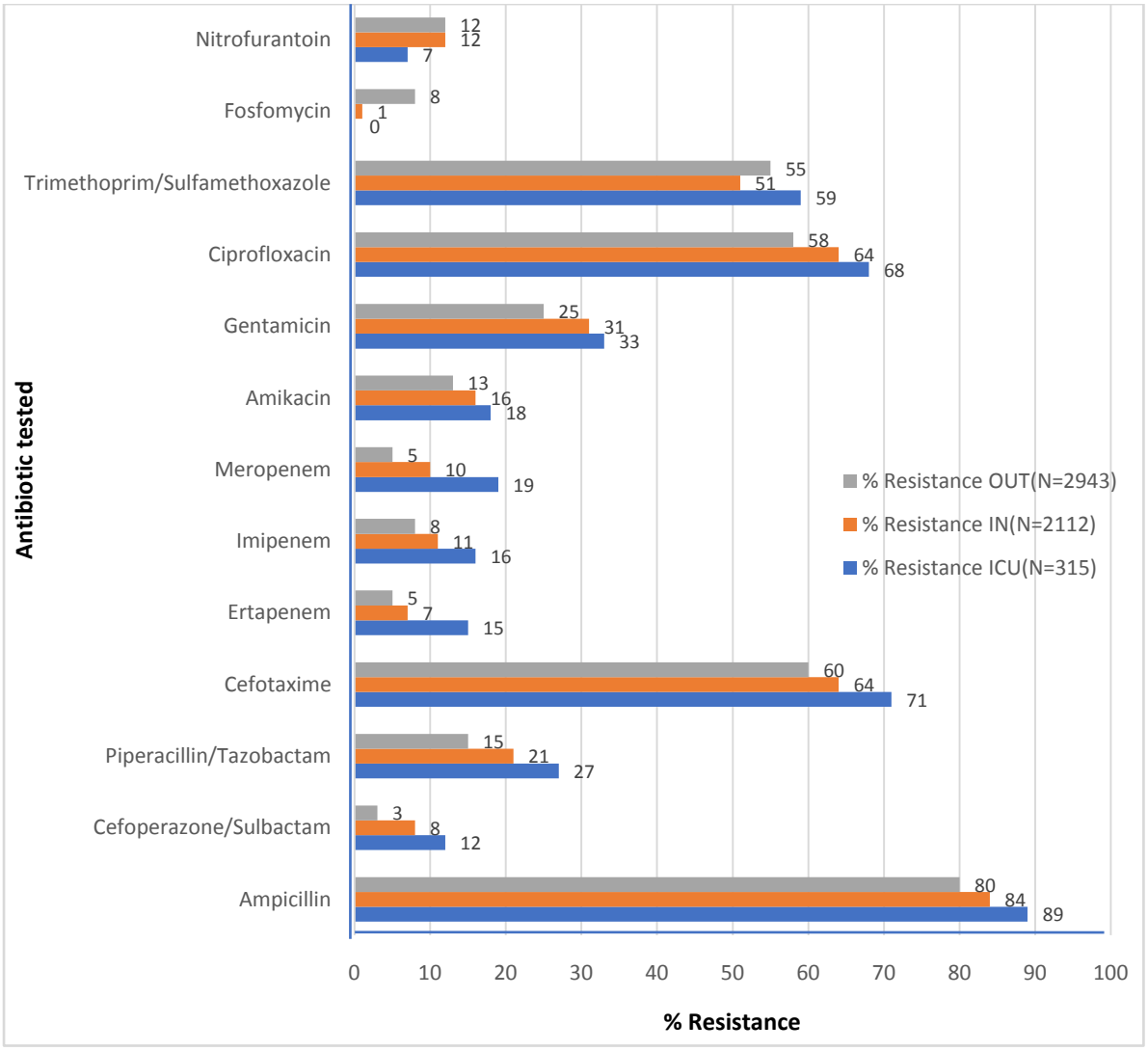

Figure 14 Resistance profile of *E. coli* isolates from blood, urine, PA & OSBF from different location types in healthcare facilities

Klebsiella species

A total of 4692 *Klebsiella* spp. isolates were reported from 3441 unique patients in the year 2021. Similar to the *E. coli* highest number of *Klebsiella* spp. are reported from urine samples followed by PA & OSBF and blood (Fig. 5). Beta-lactam antibiotic resistance observed among blood culture isolates is 67% to Cefotaxime, 65% to Cefepime, 43% to Imipenem and 47% to Meropenem. For beta lactam + beta lactam inhibitor Piperacillin/tazobactam 59% resistance is reported. (Table 9) For urinary isolates, beta lactam antibiotic resistance in urine is 61% to Cefotaxime, 48% to Cefepime, 21% to Imipenem and 26% to Meropenem. Resistance of PiperacillinTazobactam is 33% (Table 9).

Beta lactam antibiotic resistance in PA & OSBF isolates is 65% to Cefotaxime, 59% to Cefepime, 24 % to Imipenem and 32%to Meropenem. 47% isolates are resistant to beta lactam + beta lactam inhibitor ,Piperacillin/tazobactam (Table 9).

Amikacin resistance is observed in 32% isolates from PA & OSBF,43% in blood and in 24% isolates from urine. The Colistin susceptibility testing has been done using the broth microdilution method as per CLSI document M02 and M100, though for a limited number of isolates. Klebsiella spp. isolates showed more than 30% resistance to all the beta lactam antibiotics tested. (Fig. 15). Klebsiella species showed alarmingly high resistance to 3rd and 4th generation cephalosporins (75% to Cefotaxime, 70% to Cefepime) and carbapenem (39% to Imipenem, 47% to Meropenem) in ICU patients (Fig. 16)

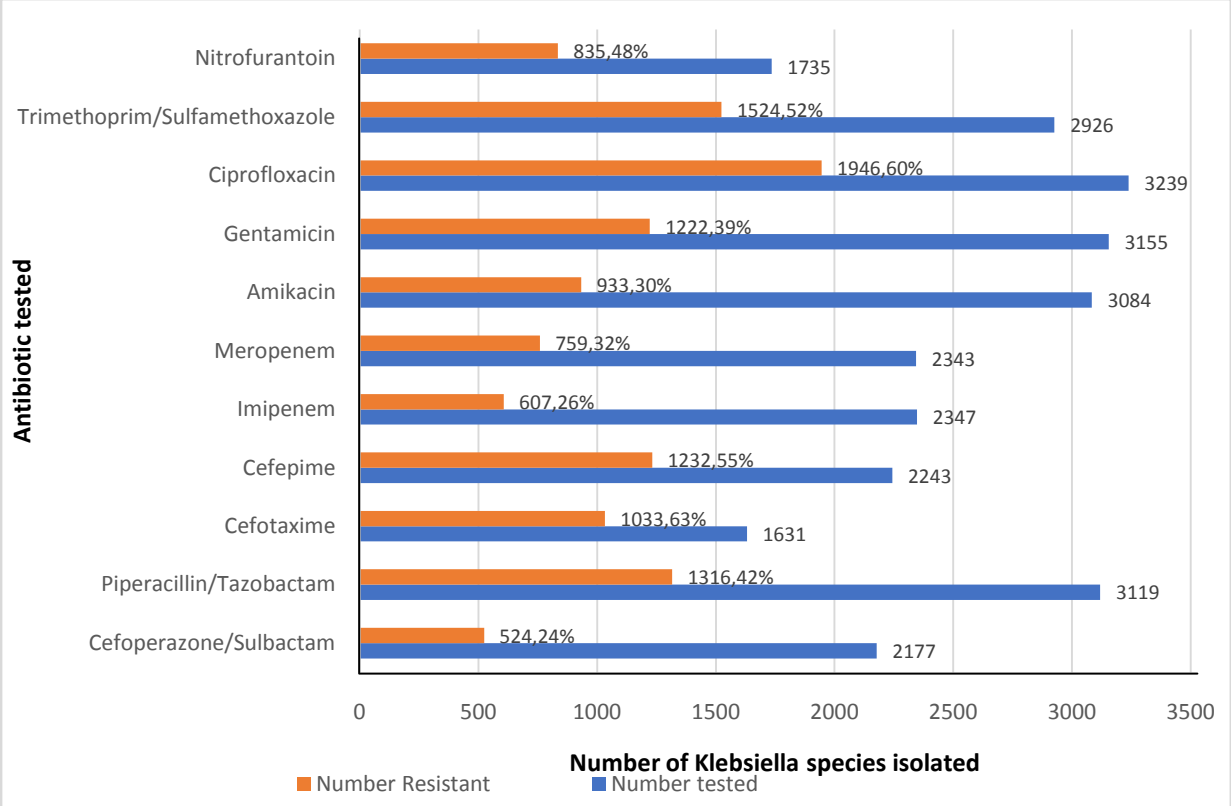

Figure 15 Resistance profile of Klebsiella species (N= 3,441)

Antibiotic tested	PA+OSBF(N=1167)			Blood{N=533)			Urine(N=1741)		
	Number tested	Number Resistant	%R	Number tested	Number Resistant	%R	Number tested	Number Resistant	% R
Cefoperazone/ Sulbactam	882	174	20	406	121	30	889	229	26
Piperacillin/ Tazobactam	1119	527	47	518	307	59	1482	482	33
Cefotaxime	511	334	65	224	151	67	896	548	61
Cefepime	773	456	59	405	264	65	1065	512	48
Imipenem	800	194	24	383	163	43	1164	250	21
Meropenem	955	302	32	462	217	47	926	240	26
Amikacin	1078	348	32	509	219	43	1497	366	24
Gentamicin	1103	479	43	485	243	50	1567	500	32
Ciprofloxacin	1133	722	64	511	347	68	1595	877	55
Trimethoprim/ Sulfamethoxazole	908	518	57	451	263	58	1567	743	47
Nitrofurantoin	63	51	81	19	8	42	1653	776	47

Table 9. Specimen wise resistance profile of Klebsiella species (N= 3,441)

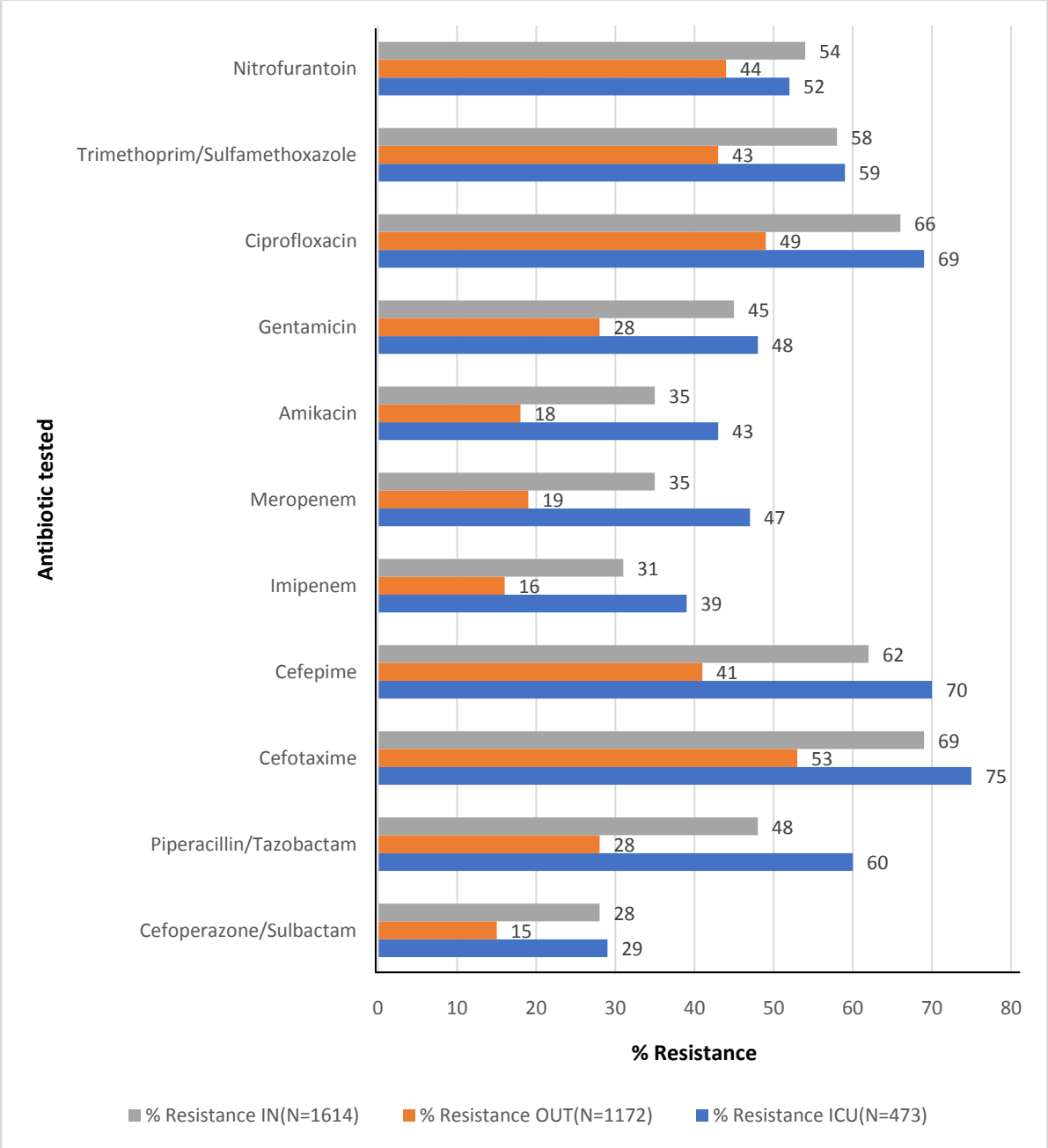

Figure 16 Resistance profile of Klebsiella species (N= 3,441) from blood, urine, PA & OSBF from different location types in healthcare facilities

Salmonella enterica serotypes Typhi and Paratyphi

During 2021, only 8 isolates of *Salmonella Typhi* and 2 isolates each of *Salmonella Paratyphi A and B* were obtained. (Table 10). Resistance to Ciprofloxacin and TMP/SMX were seen in *Salmonella Typhi*, resistance of Ciprofloxacin seen in *Salmonella Paratyphi A* and resistance to Ciprofloxacin and Ampicillin seen in *Salmonella Paratyphi B.*

Antibiotic tested	S.Typhi (N=8)		S. Paratyphi A (N=2)		S. Paratyphi B (N=2)	
	Number tested	Number Resistant	Number tested	Number Resistant	Number tested	Number Resistant
Ampicillin	8	2	2	0	2	2
Ceftriaxone	7	0	2	0	2	0
Imipenem	3	0	0	0	0	0
Ciprofloxacin	8	5	2	2	2	1
Trimethoprim/ Sulfamethoxazole	6	4	1	0	2	0
Azithromycin	2	0	1	0	1	0
Chloramphenicol	3	1	2	0	2	0

Table 10 Resistance profile of Salmonella enterica serotype Typhi and Paratyphi isolated (N= 12)

ii. Non-Fermenting Gram-Negative Bacilli

Two important non-fermenting gram-negative bacilli (NFGNB) included in the priority pathogen list for AMR surveillance under KARS-Net are *Pseudomonas* spp. and *Acinetobacter* spp. Total of 3,157 NFGNB are reported from 2,466 unique patients. Among the NFGNB, *Pseudomonas* spp. is the commonest isolate 1,556 (11%), followed by *Acinetobacter* spp. 910 (6%) (Fig. 3).

Pseudomonas species

A total of 2,040 *Pseudomonas* spp. isolates are reported from 1,556 unique patients. In PA & OSBF highest resistance (30%) is observed to Ceftazidime and Ciprofloxacin (Fig. 17, Table 11).*Pseudomonas* spp. has been isolated from 11% of ICU patients (Fig. 8). Among the isolates from ICU, highest resistance (40%) is observed to beta-lactam antibiotic Ceftazidime(Fig. 18). Resistance to Imipenem is 21% in ICU isolates, followed by 15% in inpatient isolates and 12% in outpatient isolates.

Antibiotic tested	Blood(N=212)			PA+OSBF{N=887)			Urine(N=457)		
	Number tested	Number Resistant	%R	Number tested	Number Resistant	%R	Number tested	Number Resistant	%R
Piperacillin/ Tazobactam	202	21	10	810	110	14	378	49	13
Ceftazidime	191	41	21	796	235	30	372	110	30
Imipenem	148	25	17	672	78	12	318	61	19
Meropenem	175	30	17	556	90	16	323	50	15
Amikacin	208	29	14	793	147	19	381	74	19
Gentamicin	187	29	16	763	175	23	393	82	21
Ciprofloxacin	207	38	18	796	242	30	392	119	30

Table 11 Specimen wise resistance profile of *Pseudomonas* species (N = 1,556)

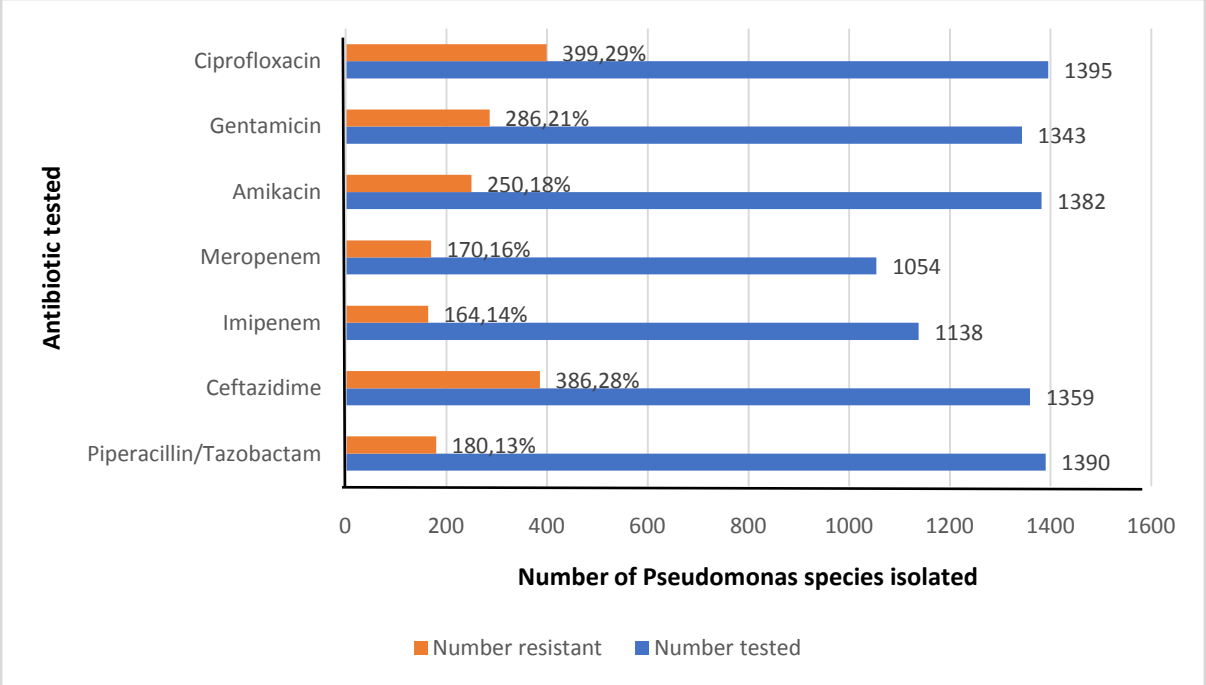

Figure 17 Resistance profile of *Pseudomonas* species (N= 1,556)

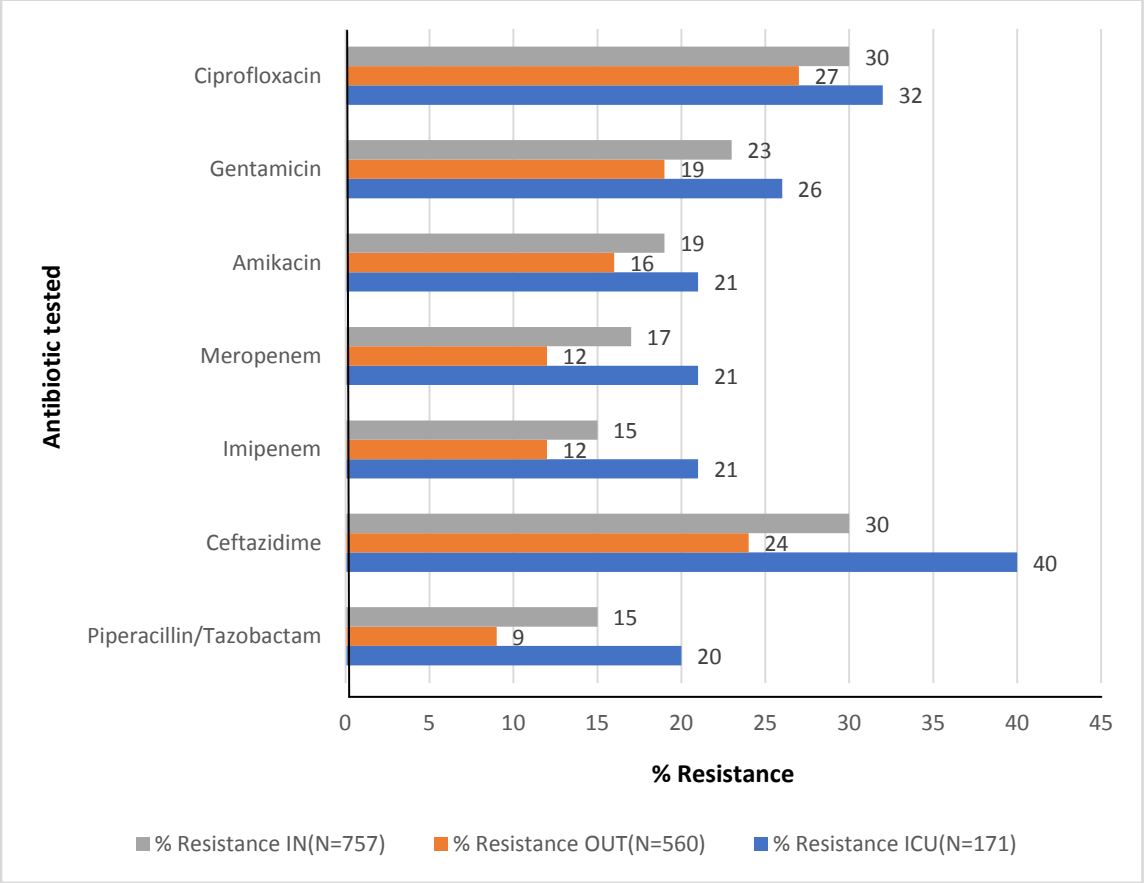

Figure 18 Resistance profile of *Pseudomonas* species isolated from blood, urine, PA+OSBF from different location types in healthcare facilities

Acinetobacter species

A total of 1,117*Acinetobacter* spp. isolates are reported from 910 unique patients. *Acinetobacter* species constitutes 6% of the total isolates reported during 2021 (Fig. 3). The majority of *Acinetobacter* spp. are isolated from IPD patients (416), followed by ICU (272) & OPD (157) (Fig. 8). The Acinetobacter spp. isolates are more from blood (358) than from PA & OSBF (357) and urine (195) (Table 12). Resistance profile is given in Figure 19.

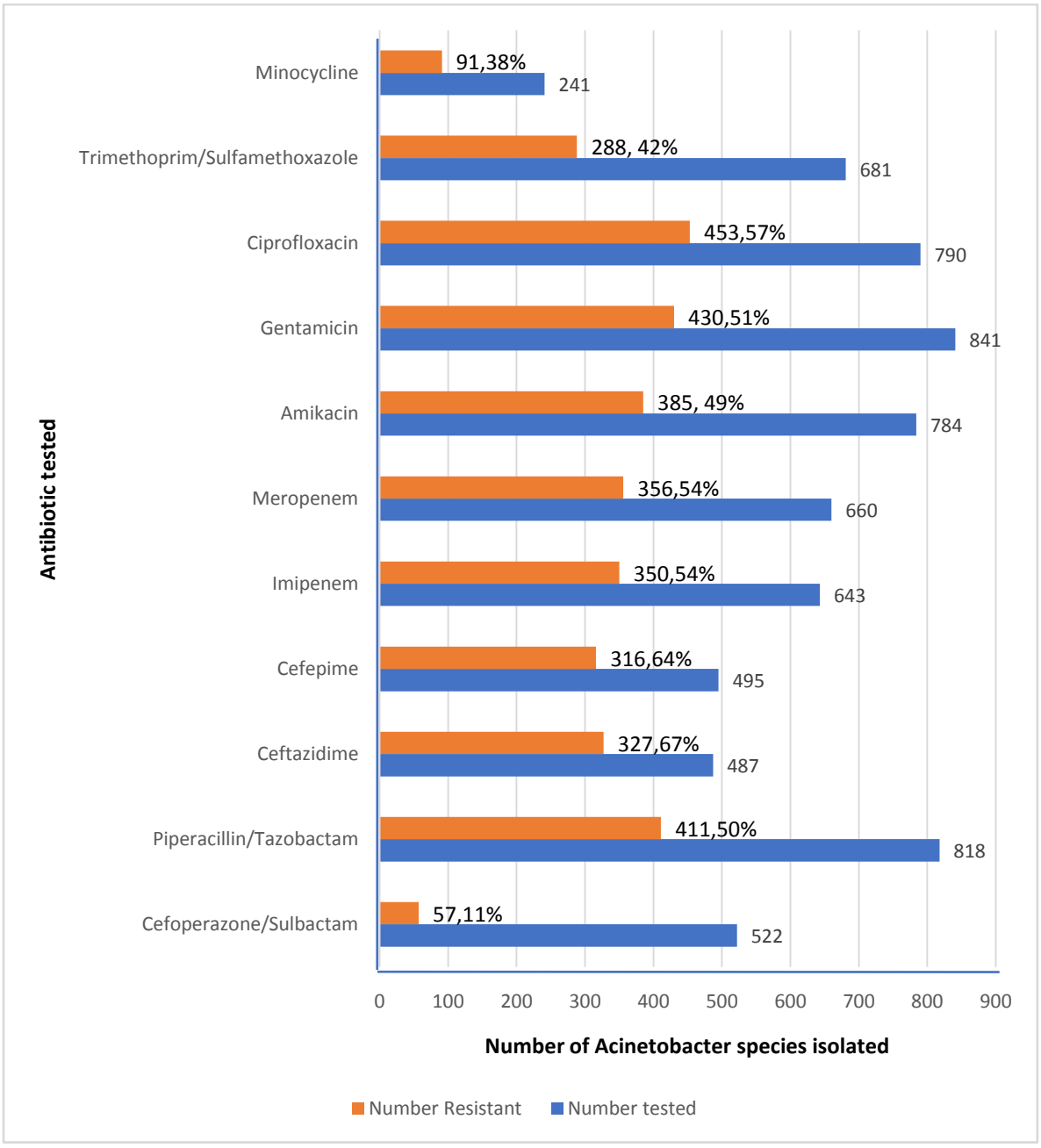

Figure 19 Resistance profile of *Acinetobacter* species (N=910)

Significantly higher resistance is observed in isolates from ICU: 81% to Ceftazidime, 71% to Ciprofloxacin, 69% to piperacillin/tazobactam and 76% to Imipenem (Fig. 20). In blood culture isolates, highest resistance is reported to Cefepime (66%). (Table 12)

Antibiotic tested	Blood(N=358)			PA+OSBF{N=357)			Urine(N=195)		
	Number tested	Number Resistant	%R	Number tested	Number Resistant	%R	Number tested	Number Resistant	%R
Cefoperazone/ Sulbactam	244	20	8	199	28	14	79	9	11
Piperacillin/ Tazobactam	344	168	49	323	212	66	151	31	21
Ceftazidime	225	142	63	190	148	78	72	37	51
Cefepime	225	149	66	199	143	72	71	24	34
Imipenem	263	146	56	259	174	67	121	30	25
Meropenem	269	139	52	286	188	66	105	29	28
Amikacin	336	174	52	301	177	59	147	34	23
Gentamicin	322	177	55	341	209	61	178	44	25
Ciprofloxacin	322	178	55	315	229	73	153	46	30
Trimethoprim/ Sulfamethoxazole	281	120	43	252	131	52	148	37	25
Minocycline	138	47	34	88	35	40	15	9	60

Table 12. Specimen wise resistance profile of *Acinetobacter* species (N= 910)

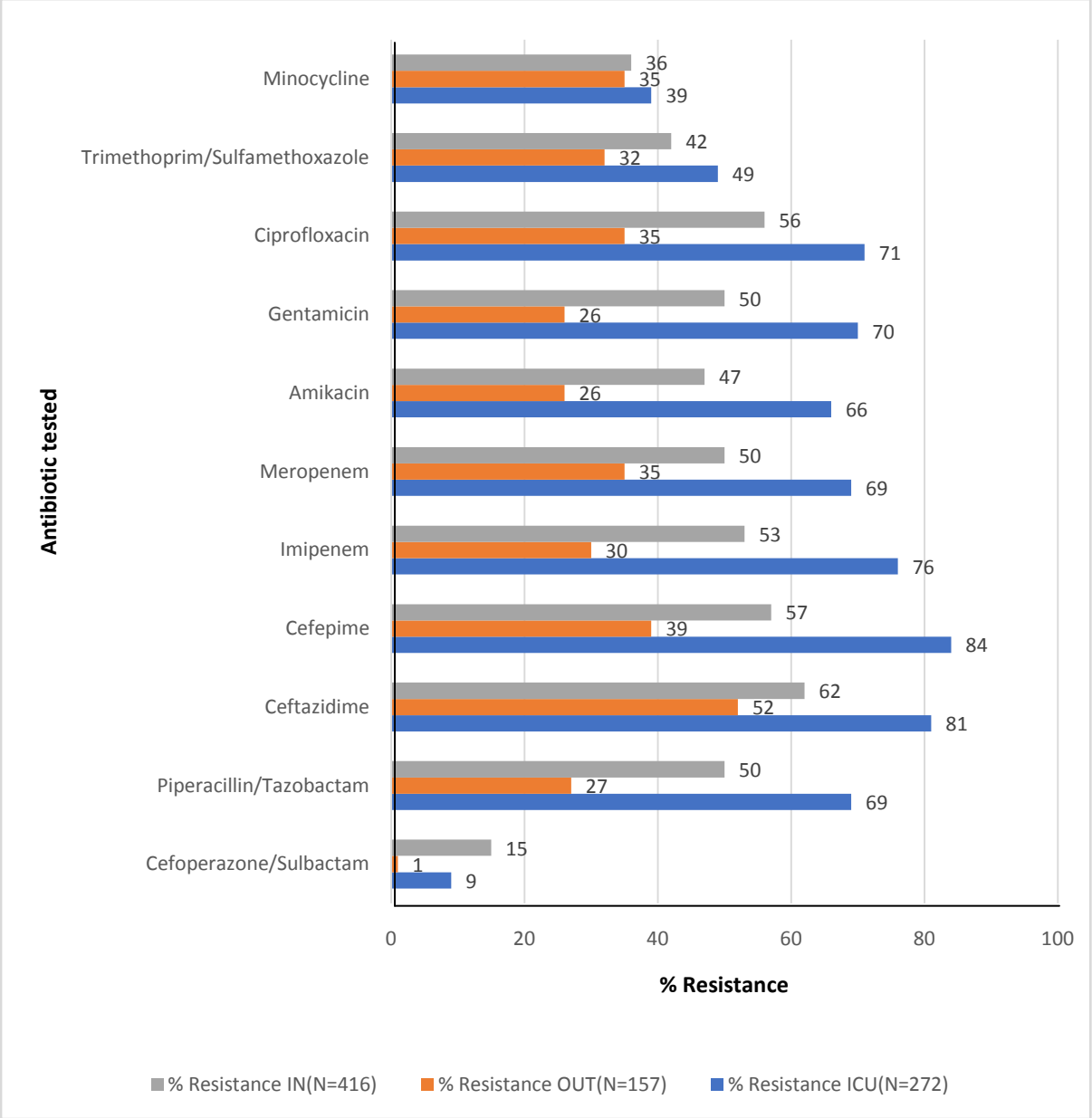

Figure 20 Resistance profile of *Acinetobacter* species isolated from blood, urine, PA+OSBF from different location types in healthcare facilities

Imipenem-resistance reported in Acinetobacter spp. during 2021 is high: 76% in ICU, 53% in IPD patients and 30% in OPD patients (Fig. 20). Minocycline is an alternate antimicrobial option to treat *Acinetobacter* infections. Monitoring its resistance profile is also essential for the treatment of such infections.

6. Trends of AMR in Kerala over 3 years

We have tried to analyse the trends of Antimicrobial resistance in Kerala over 3 years (2018, 2019 and 2021) from the KARS-Net data. 2020 data is not included as most of the centres have not reported owing to the pandemic. We can see that ESBL production as well as Carbapenem resistance has been rising over the years (Fig 21, Fig 22). The limitation of the data is that most of our centres are tertiary care centres and the data may not be a true representative of the community data. The apparent decrease in MRSA can be attributed to the non uniformity in data from some centres in the initial months of 2021 owing to the subsequent waves of pandemic in the state and majority of our centres being COVID care centres**.**VRE rates have increased in these years (Fig23).

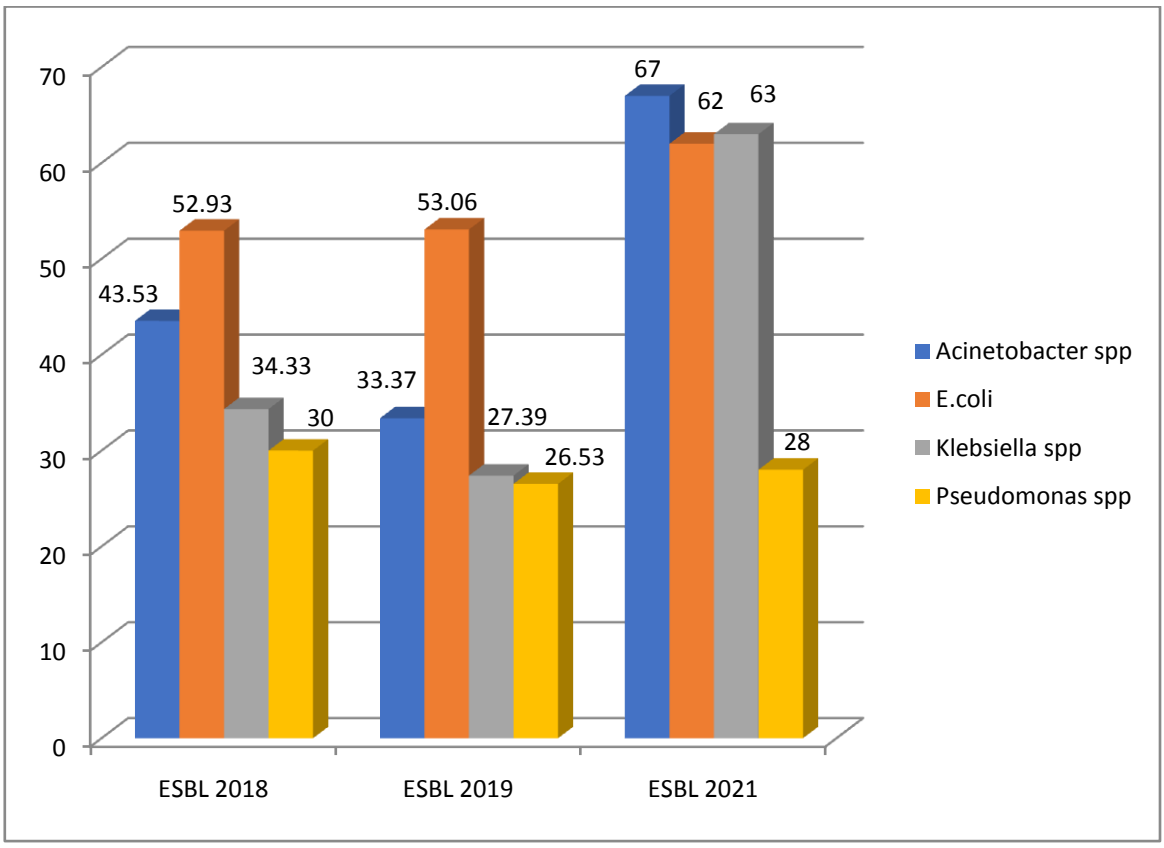

Figure 21 Trends of ESBL – evidence from KARS-Net over 3 years

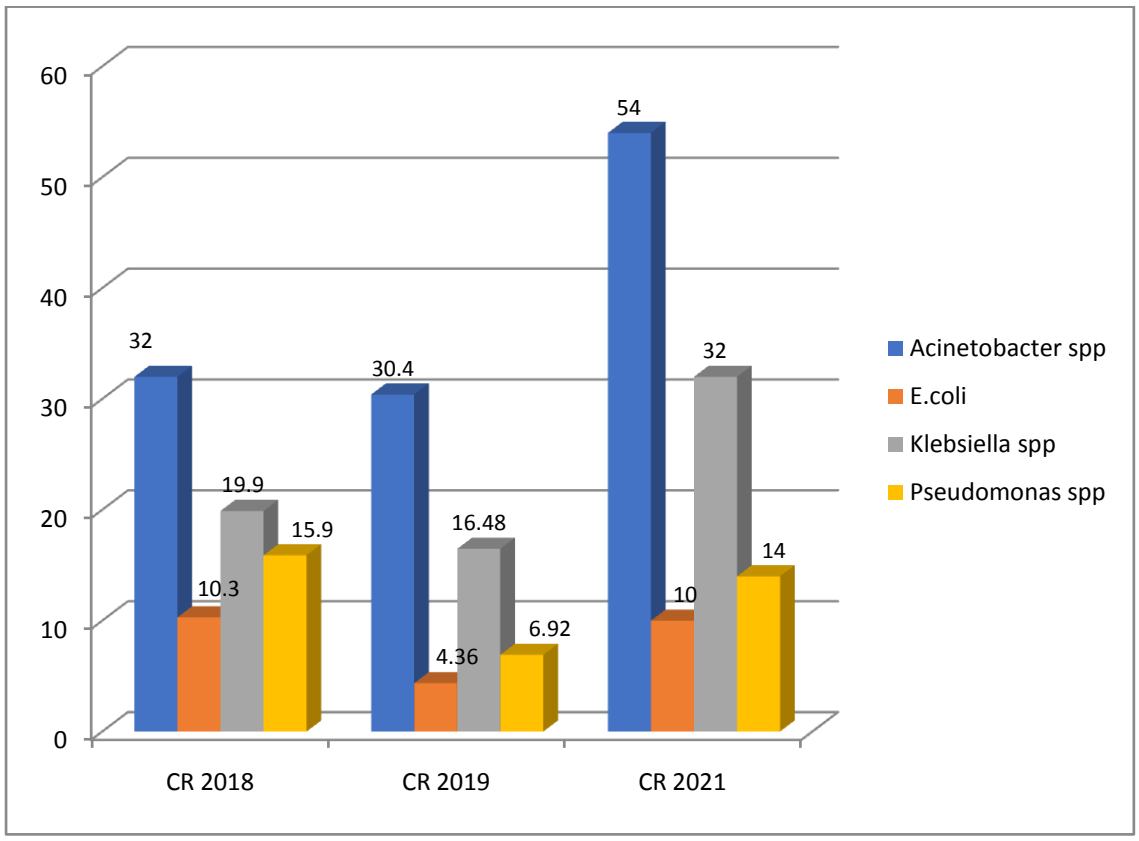

Figure 22 Trends of Carbapenem resistance – evidence from KARS-Net over 3 years

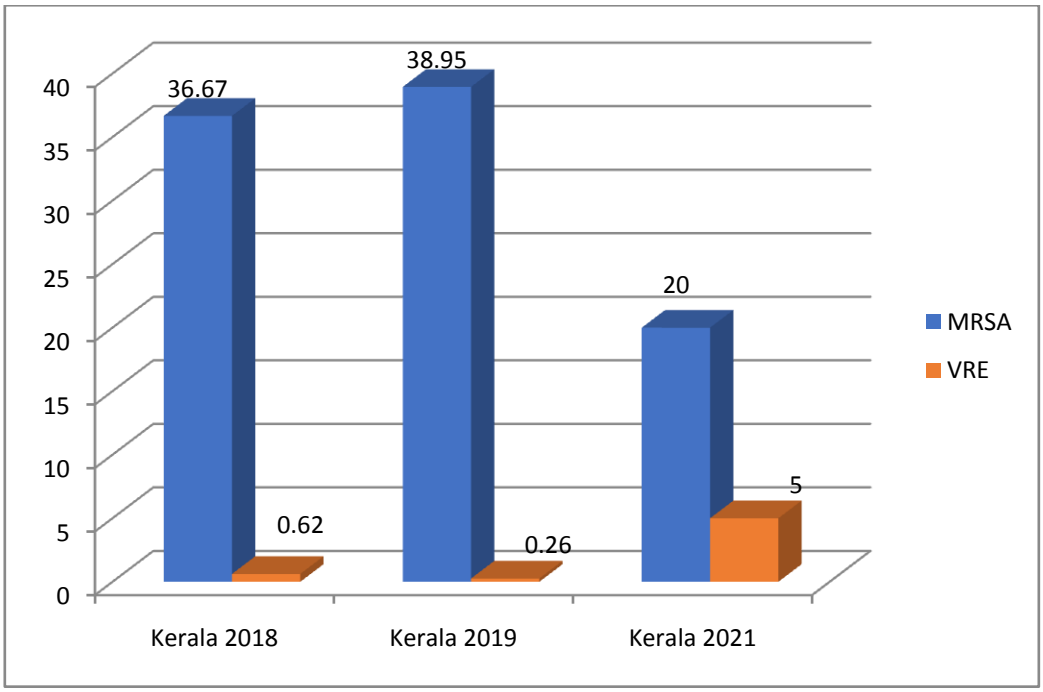

Figure 23 Trends of MRSA and VRE – evidence from KARS-Net over 3 years

7. Discussion

Antimicrobial resistance (AMR) is a global health challenge that threatens the achievement of Sustainable Development Goals (SDGs) related to health for all. WHO has declared AMR as one of the top 10 global public health threats. Under KARSAP, KARS-Net is going to annually generate the State AMR Surveillance report. KARS-Net activities include capacity building of a network of medical college laboratories to detect AMR surveillance. AMR surveillance under KARS-Net includes standardised collection, analysis and compilation of AMR data from the network sites. The compiled data is used to generate the annual State AMR surveillance report which will be shared with stakeholders at state level and will be made available in the public domain. This network data is also submitted to NCDC through which the data is finally submitted to WHO's Global AMR Surveillance System (GLASS). This report for the year 2021 presents analysed data from 18 sentinel sites located in 8districts of Kerala. Quality of AMR surveillance data submitted by the sites has been ensured by continuous support in the form of trainings based on standard operating procedures for data management, antimicrobial susceptibility testing, and other technical guidelines developed by NCDC and the state. In addition, monthly feedback on AMR data are provided to the network sites. Network laboratories have played an essential role in improving the patient demographic & AST data compliance. Most sites have also become stringent in conducting internal quality control of antibiotic discs as per recommendations under the programme. Certain limitations that could affect this data are lack of strict compliance to the internal quality control SoPs by some sites . Including data from greater number of centres would make the data more representative for the state. E. coli is the most commonly reported pathogen (40%) in the AMR Surveillance data of 2021.*Escherichia coli* is the predominant isolate from urine samples (61%) , *Klebsiella* spp is the most common pathogen isolated from blood samples (27%) and *S. aureus* is the most common pathogen isolated from PA & OSBF (27%). E. coli is the commonest pathogen isolated(50%) from out patients as well as in patients (35%) whereas *Klebsiella* spp. is the predominant pathogen isolated (32%) in ICU settings.

Methicillin-resistant S. aureus (MRSA) isolates was found to be 20% in this year. Due to lack of uniformity in testing method especially MIC determination by MBD method, data of Vancomycin resistance in *S. aureus* and Colistin Resistance in Gram negative bacilli are

not included in the report. Among 5% of Enterococci isolated from blood and urine Vancomycin resistance is observed. Probable ESBL production as evidenced by resistance to 3rd generation cephalosporins was found to be 62%,63%, 28% and 67% in *E.coli, Klebsiella spp, Pseudomonas spp and Acinetobacter spp* respectively. The resistance to Carbapenem was found to be 10% in *E.coli*, 32% in *Klebsiella* spp, 14% in *Pseudomonas* spp and 54% in *Acinetobacter* spp. Strengthening local infection prevention and antimicrobial stewardship practices at healthcare facilities in the country and initiating multisectoral action as stated in the KARSAP is the need of the hour.