Kerala Antimicrobial Resistance Surveillance Network

(KARS-NET)

Annual Report 2023

(Data from January to December 2022)

HANDLE ANTIMICROBIALS WITH CARE

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Contents

Abbreviations

AMR	Antimicrobial resistance
AST	Antimicrobial susceptibility testing
BMD	Broth microdilution
CLSI	Clinical and Laboratory Standards Institute
CRE	Carbapenem resistant Enterobacterales
EQAS	External quality assessment scheme
ESBL	Extended spectrum beta-lactamase
GLASS	Global Antimicrobial Resistance Surveillance System
ICU	Intensive care unit
ID	Identification
IPD	In-patient
IQC	Internal quality control
KARSAP	Kerala Antimicrobial Resistance Strategic Action Plan
KARS-NET	Kerala Antimicrobial Resistance Surveillance Network
LIMS	Laboratory information management system
MRSA	Methicillin resistant Staphylococcus aureus
NCDC	National Centre for Disease Control
NFGNB	Non-fermenting Gram-negative bacilli
OPD	Outpatient
OSBF	Other sterile body fluids
PA	Pus aspirate
R I S	Resistant Intermediate Sensitive
SDGs	Sustainable Development Goals
SOP	Standard operating procedure
TMP-SMX	Trimethoprim sulfamethoxazole
VRE	Vancomycin resistant Enterococcus species
WHO	World Health Organization

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Executive summary

The Government of Kerala in collaboration with Ministry of Health and Family Welfare and WHO Country Office for India officially launched the Kerala Antimicrobial Resistance Strategic Action Plan (KARSAP) on 25 October 2018. Antimicrobial resistance (AMR) has emerged as a significant public health threat that requires urgent attention. In order to strengthen and expand the AMR surveillance network in Kerala, Kerala Antimicrobial Resistance Surveillance Network (KARS-NET) was established in 2019. The objectives of the network were to foster standardization, to strengthen and expand AMR surveillance in Kerala, to analyze and report KARS-NET data to State Government and NCDC on regular basis, to contribute towards the estimation of extent, burden and monitoring of AMR in Kerala and to detect emerging resistance and it's spread in Kerala. The network of laboratories over the years has expanded from 21 labs in 9 districts to 31 labs across 11 districts in a phased manner (Figure 1). Priority pathogens under surveillance currently include eight commonly isolated pathogens from identified specimens. The WHONET software is used for the collection and analysis of antimicrobial susceptibility data.

This annual report covers the AMR data from 1 January to 31 December 2022. A total of 23 surveillance laboratories from 11 districts submitted their data during this period. Antimicrobial susceptibility (AST) data of 30,753 priority pathogens, along with the demographic information of the patients from whom these pathogens were isolated, were reported under KARS-NET during 2022. After data deduplication, data from 27,604 unique patient isolates were analysed; 49% (13,443) of reported isolates were from male patients; 51% (13,962) were from female patients.

Urine was the most reported specimen 50.2% (13,859), followed by pus aspirate 34.7% (9,582), blood 12% (3,320), other sterile body fluids 3% (837) and stool 0.02% (6). The most frequently reported priority pathogen from all specimens was *E. Coli* (38.9%), followed by *Klebsiella species* (24.8%), *S. aureus* (12.0%), *Pseudomonas species* (12%), *Enterococcus species* (6.3%), *Acinetobacter species* (5.8%) and *Salmonella enterica* serotype Typhi and Paratyphi (0.1%).

Among the reported *Staphylococcus* isolates, 27.47% were methicillin resistant *Staphylococcus aureus* (MRSA) and only 1 isolate from blood culture was linezolid resistant. Vancomycin resistant *Enterococci* (VRE) from blood culture was 2% whereas linezolid resistance was found to be 1%. Extended spectrum beta-lactamase (ESBL) was observed in 67% of *E. coli* and 73% of *Klebsiella spp*. isolated from blood specimens. With respect to carbapenem resistant Enterobacterales (CRE) in blood, 10% resistance was observed in *E. coli* and 43 % in *Klebsiella spp*. *Salmonella typhi* isolated from blood cultures showed 42% resistance to ciprofloxacin.

Resistance to imipenem was observed in 53% blood isolates of *Acinetobacter spp*. carbapenem resistance was observed in 14% of *Pseudomonas spp*. from blood. Resistance to colistin was observed to be < 1 % among gram negative bacterial isolates.

Kerala Antimicrobial Resistance Surveillance Network (KARS-NET)

Antimicrobial resistance (AMR) is a growing threat to public health which needs urgent attention. Government of India has already taken a series of initiatives to combat this burgeoning problem. One such initiative is the National Programme on Antimicrobial Resistance Containment, launched in 2013, during the Twelfth Five-Year Plan (2012-2017). This programme is coordinated by National Centre for Disease Control (NCDC), New Delhi. One of the objectives of the programme is to generate quality AMR surveillance data in order to generate evidence of AMR in the country to guide the plan of action to contain AMR.

Kerala Antimicrobial Resistance Strategic Action Plan (KARSAP) was the first subnational 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 Network (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. From 2019, with the technical support from World Health Organization (WHO), the network was expanded to 31 laboratories from both public and private sectors. The data generated by KARS-NET is submitted to the Global Antimicrobial Resistance Surveillance System (GLASS) from 2021 onwards.

The 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 KARS-NET, 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 eight key priority pathogens responsible for the highest antibiotic resistance rates among bacteria that commonly cause human infections.

The eight priority pathogens monitored by KARS -Net are:

1. *Staphylococcus aureus*
2. *Enterococcus* species
3. *Escherichia coli*
4. *Klebsiella* species
5. *Pseudomonas* species
6. *Acinetobacter* species
7. *Salmonella enterica* serotype Typhi
8. *Salmonella enterica* serotype Paratyphi A & B

KARS-NET includes 16 government medical college hospitals and laboratories, 3 semi-autonomous institutions, 12 private medical colleges, hospitals and laboratories (Figure 1). Of these 31 sites, AMR surveillance data was received for the period of one year from 1 January to 31 December 2022 from 23 network centres from 11 districts in Kerala.

The clinical specimens currently included under KARS-NET are:

- Blood
- Urine
- Pus aspirate (PA)
- Other sterile body fluids (OSBF)
- Stool (only for *Salmonella* Typhi and Paratyphi)

Table 1: Pathogens and specimens included under surveillance

	S.aureus	*Enterococcus spp.*	*Klebsiella spp.*	*E. coli*	*Acinetobacter spp.*	*Pseudomonas spp.*	*Salmonella Typhi/ Paratyphi*
Blood	●	●	●	●	●	●	●
Urine	X	●	●	●	●	●	X
PA	●	●	●	●	●	●	X
OSBF	●	●	●	●	●	●	X
Stool	X	X	X	X	X	X	●

X- specimen not collected for this pathogen

All the participating network sites report the monthly AMR data of the eight priority pathogens from the above-mentioned specimen types to the Department of Microbiology, Government Medical College, Thiruvananthapuram. The feedback regarding the AMR data is being provided to the network sites. The network sites are mandated to implement internal quality control as an essential component of quality assurance in antimicrobial susceptibility testing and also participate in the External Quality Assessment Scheme (EQAS). Continuous support is provided to the programme sites to improve specimen collection, bacterial culture, identification of pathogens and their antimicrobial susceptibility testing (AST) which includes provision of continuous virtual and/or hands-on trainings. Onsite support visits and onsite trainings are also conducted for handholding the sites to strengthen bacteriology laboratory capacity by improving the quality of culture and AST practices. In addition, trainings and workshops on WHONET software to streamline AMR surveillance data flow from network sites are regularly organised.

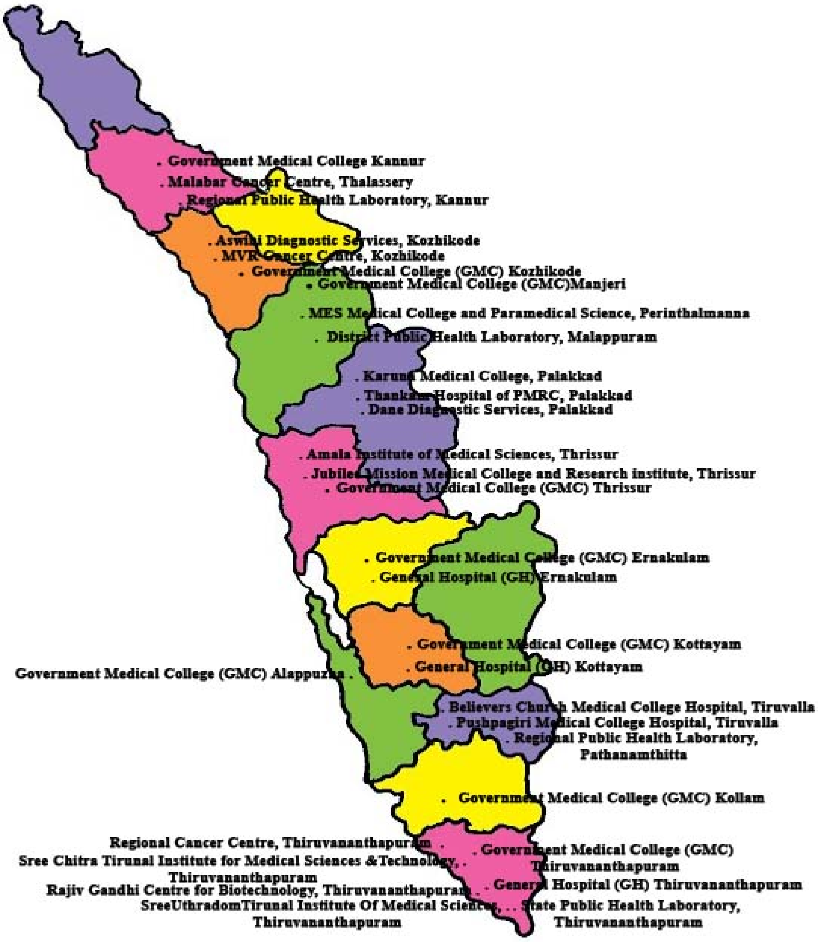

Figure 1: Institutions under Kerala AMR Surveillance Network (KARS-NET)

The laboratories under KARS-NET follow a standardised approach for AMR data collection, analysis, and reporting using WHONET. 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 AST, including frequent trouble shooting sessions for WHONET data management. Onsite support visits were also conducted in 2021 and 2022 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.

Data collection

The WHONET software is used for the collection and analysis of the AST data generated by the manual testing methods and the automated systems at the programme sites. WHONET is a free open source Windows application for management of microbiology laboratory data on antimicrobial susceptibility testing, developed by WHO Collaborating Centre for Surveillance of AMR at the Brigham and Women's Hospital at Harvard University. WHONET is used for global surveillance efforts in many countries worldwide.

The classification of the isolates as susceptible, intermediate or resistant is based on the Clinical & Laboratory Standards Institute (CLSI) guidelines. During 2022, AST data of 30,753 priority pathogens, along with the demographic information of the patients from whom these pathogens were isolated, was reported from 23 sites in 11 districts.

All sentinel sites submitted the data monthly after validation by the AMR nodal officer at the sites. The monthly data submitted by the sites was screened and analysed and the detailed feedback was provided to them for each month and based on feedback the corrected WHONET files were received.

Data analysis

The analysis of cumulative data for the year 2022 has been performed by the Department of Microbiology, Government Medical College Thiruvananthapuram, based on which this annual report has prepared. The AST data includes data of conventional disk diffusion method, Broth-micro dilution (BMD) method and data generated through the automated antimicrobial susceptibility testing systems.

a. Data deduplication

As a first step for data analysis, a single file was created from all the cumulative AMR data files. During this step, duplicate isolates for the same patients have been excluded from the database files. Before starting the de-duplication process, variables containing information about the patient was checked and variables were generated if required, e.g., patient ID number, age, sex, location, department, AST in values (mm or µg/ml) etc. For analysis, only one result was considered for each patient per specimen type and per pathogen. For example, if two blood cultures from the same patient yielded growth of *E. coli*, only the first has been included in the data; if the growth of E. coli was detected in one culture and of *K. pneumoniae* in the other, both results have been considered. If there is the growth of *E. coli* in one blood culture and in one urinary culture from the same patient, both specimen types have been included. From each patient, only the first isolate of a given species recovered during the investigated time interval was included, regardless of its susceptibility profile. The total number of isolates from unique patients (after de-duplication) is 27,604 (Figure 2).

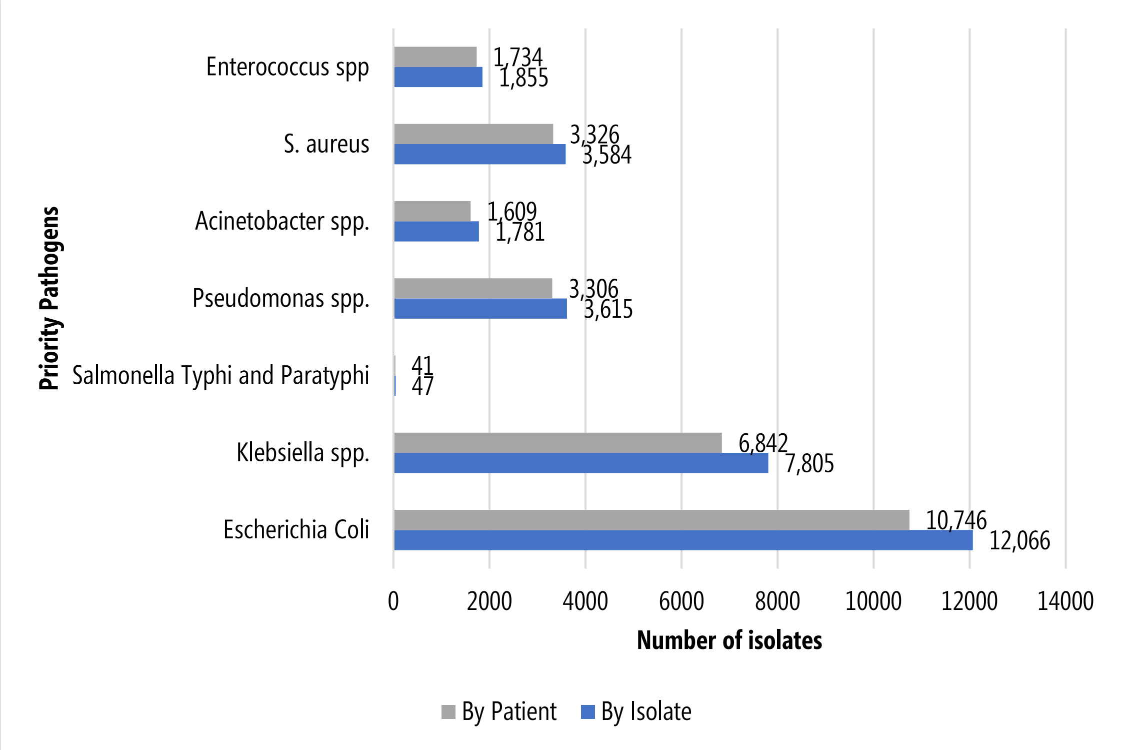

Figure 2: Priority pathogens before and after de-duplication

b. Demography and distribution of priority pathogens

Among the total of 27,604 unique patients, 49% pathogens were isolated from male patients as compared to female patients (51%). Age data was available for 99% of unique patient isolates. The highest proportion of unique patients contributing to the AST data belong to mature working age group that is 55-64 years whereas the lowest number of pathogens (2%) are reported from age group of 85-100 years (Figure 3).

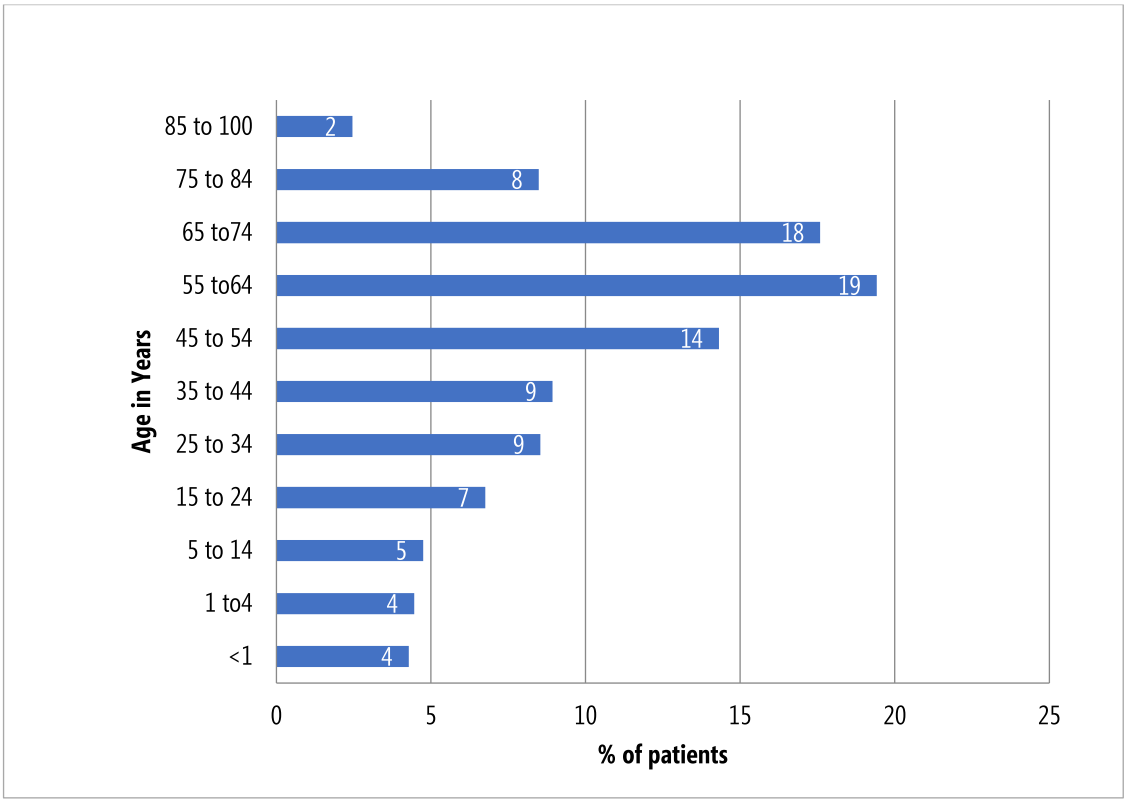

Figure 3: Distribution of isolates based on age

Of the total unique isolates (after de-duplication; 27,604) the following was the specimen distribution:

- Urine – 13,859 (50.20%)
- Blood – 3,320 (12.02%)
- Pus aspirate (PA) – 9,582 (34.71%)
- Other sterile body fluids (OSBF) – 837(3.03%)
- Stool – 6

The number of isolates reported in the year 2022 has increased over that reported last year. In 2022 AMR surveillance data, the most commonly isolated priority pathogen is *E. coli* (39%), followed by *Klebsiella species* (25%), *S. aureus* (12%), *Pseudomonas species* (12%), *Acinetobacter species* (6%) *Enterococcus species* (6%) and *Salmonella enterica* serovar Typhi and Paratyphi 0.1% (Figure 4).

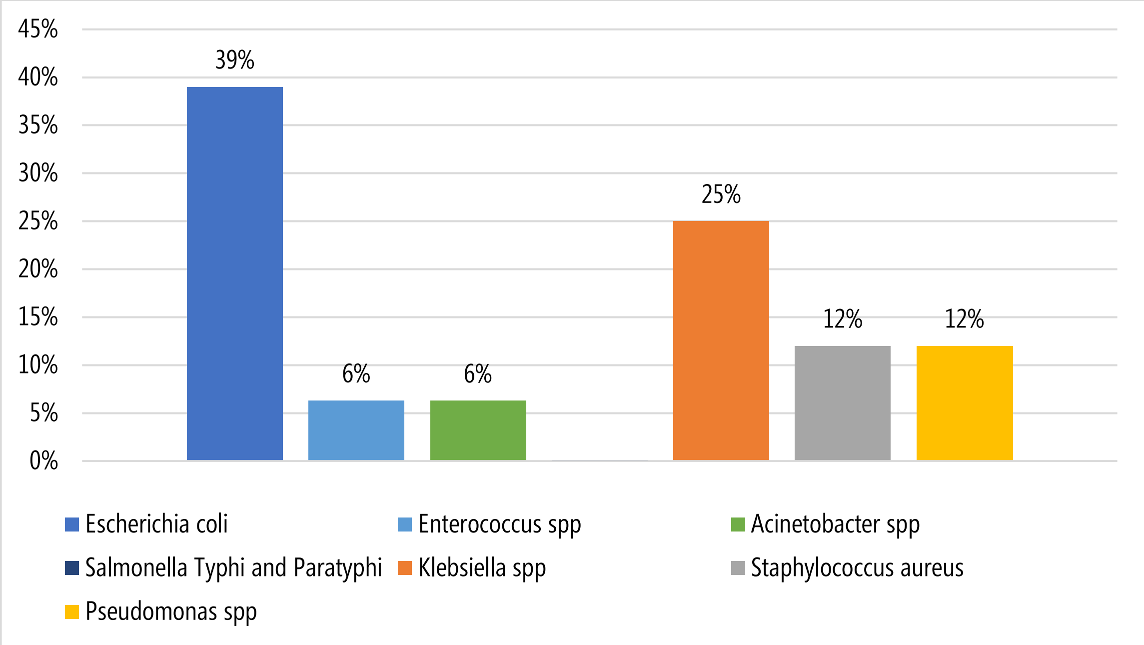

Figure 4: Distribution of AMR surveillance priority pathogens

Among all specimen types, highest number of *E. coli* (59%) were isolated from urine samples. From blood specimen the highest number of priority pathogen isolated was *Klebsiella* spp. (25%) and in pus aspirate it was *Staphylococcus aureus* (26%). While the lowest number of pathogens isolated from blood was *Salmonella enterica* serovar Typhi and Paratyphi (1%). The most commonly isolated pathogen from OSBF was *Klebsiella* spp. (31%). Lowest percentage of pathogen isolated from PA was *Enterococcus* species (6%) and *Acinetobacter* spp. (6%) whereas from OSBF it was *Staphylococcus aureus* (9%) and *Enterococcus* species (9%). (Table 2, Figure 5)

Table 2: Specimen-wise isolation of priority pathogens

Priority pathogens	**Blood (%)**	**PA (%)**	**OSBF (%)**	**Urine (%)**
Escherichia coli	617 (19%)	1801 (19%)	173 (21%)	8155 (59%)
Klebsiella spp.	819 (25%)	2167 (23%)	260 (31%)	3596 (26%)
Salmonella Typhi and Paratyphi	35 (1%)			
Pseudomonas spp.	291 (9%)	1889 (20%)	151 (18%)	975 (7%)
Acinetobacter spp.	614 (18%)	606 (6%)	105 (13%)	284 (2%)
S. aureus	714 (21%)	2,540 (26%)	72 (9%)	
Enterococcus spp.	230 (7%)	579 (6%)	76 (9%)	849 (6%)
Total	**3,320**	**9,582**	**837**	**13,859**

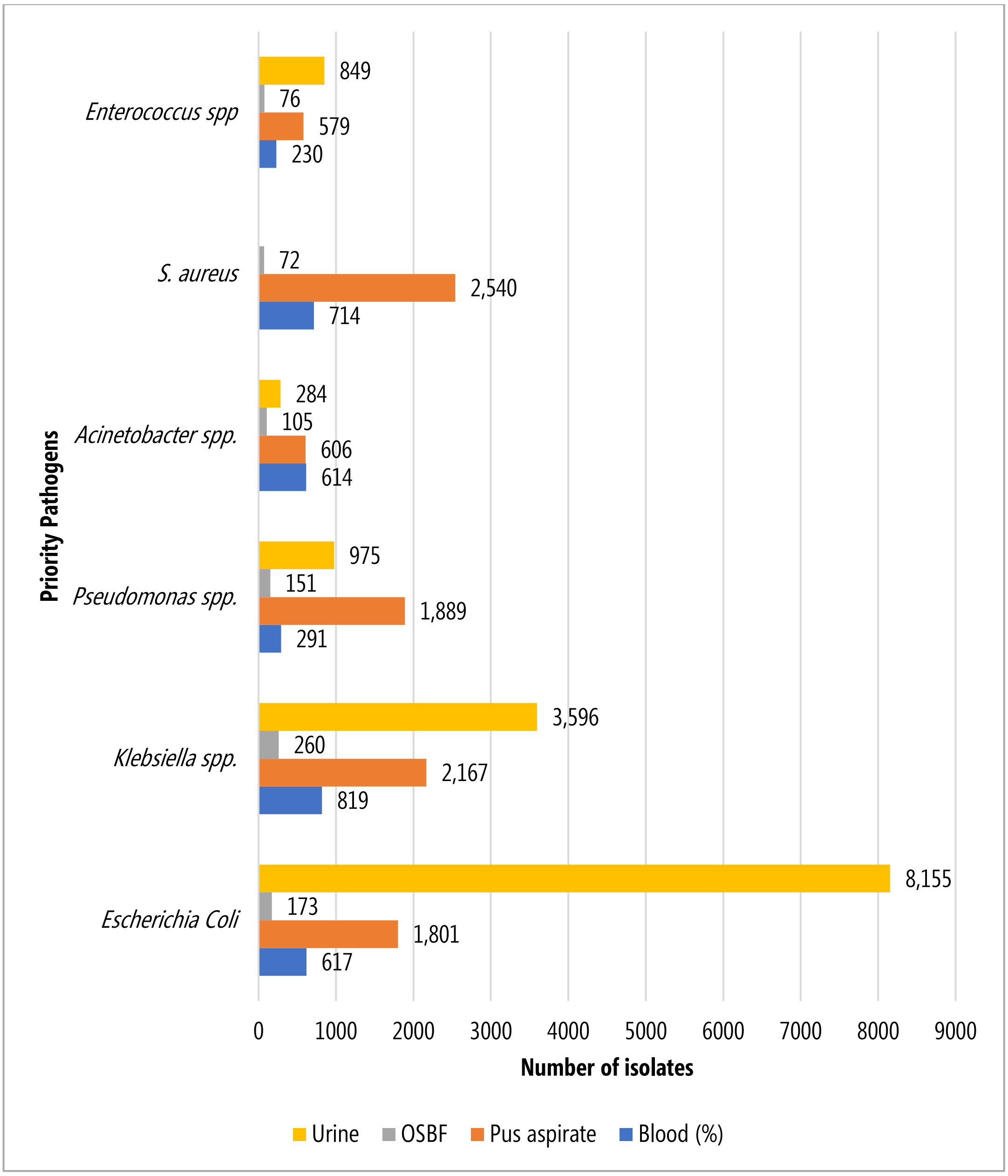

Figure 5: Specimen wise distribution of AMR surveillance of priority pathogens

Out of the 27,604 isolates, 49% are from in-patients (IPD), 35% from out-patients (OPD), 13% from intensive care unit (ICU) patients and for 6% of isolates, location type data was not available (Figure 6). The most commonly isolated pathogen from IPD and OPD was *E. coli*. In IPD patients, maximum isolates are of *E. coli* (37%) followed by *Klebsiella* spp. (26%), *Pseudomonas* spp. (12%), *S. aureus* (12%), *Enterococcus* spp. (7%) and *Acinetobacter* spp. (6%). Among isolates from OPD patients, after *E. coli* (45%) second highest pathogen isolated is *Klebsiella* spp. (22%). In ICU facilities, *Klebsiella* spp. (31%) was the most commonly isolated pathogen, followed by *E. coli* (29%) and *Acinetobacter* spp. (13%). (Table 3, Figure 6)

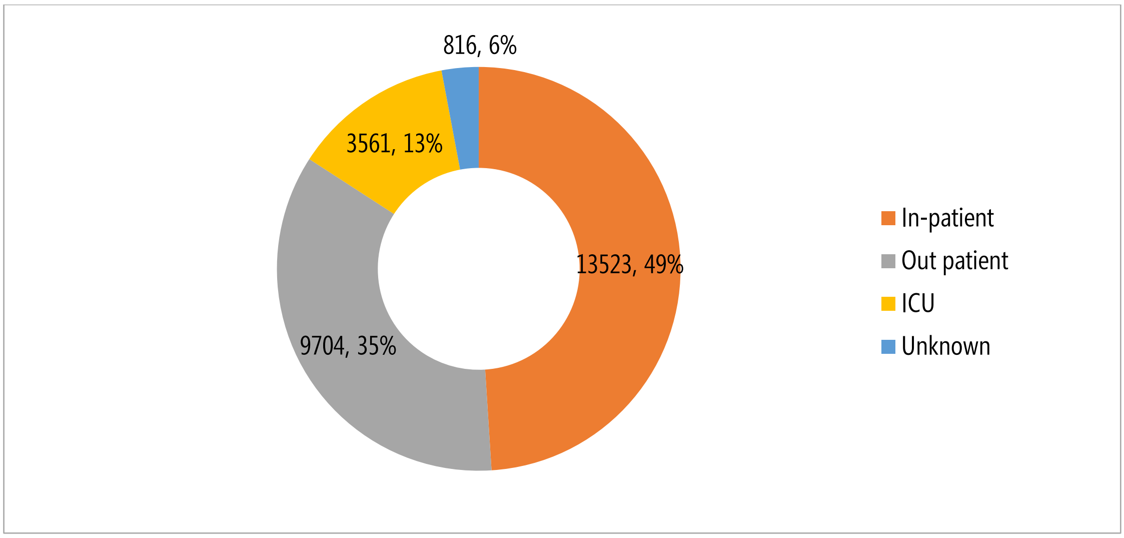

Figure 6: Location-wise distribution of isolates

Table 3: Location-wise distribution of priority pathogens

Priority pathogens	ICU (%)	IPD (%)	OPD (%)
Escherichia coli	1,019 (29%)	5,004 (37%)	4,360 (45%)
Klebsiella spp.	1,102 (31%)	3,477 (26%)	2,112 (22%)
Salmonella Typhi and Paratyphi**	2	33	3
Pseudomonas spp.	413 (12%)	1,640 (12%)	1,167 (12%)
Acinetobacter spp.	457 (13%)	808 (6%)	296 (3%)
S. aureus	287 (8%)	1,635 (12%)	1,284 (13%)
Enterococcus spp.	281 (8%)	926 (7%)	482 (5%)
Total (N)*	**3,561**	**13,523**	**9,704**

* N is the number of isolates for which location type was available in the submitted data
**Due to low numbers, percentages were not computed

AMR profile of priority pathogens

The data collected under KARS-NET is for selected antibiotics only as per the NCDC AMR surveillance data management SOP. This AMR surveillance data is from patients visiting the OPD, IPD and ICU of the hospitals.

a. Gram positive cocci

AMR surveillance under KARS-NET covers 2 important globally prevalent gram-positive bacterial pathogens i.e., *Staphylococcus aureus* and *Enterococcus species*. The AST data of 5,439 Gram positive cocci have been submitted by KARS-NET sites, of which 5060 isolates are from unique patients.

Staphylococcus aureus

Staphylococcus aureus constituted 12% of all the isolates (Figure 4). Data of a total of 3,584 *S. aureus* isolates was submitted by the KARS-NET sites of which 3,326 isolates are from unique patients. AST analysis of 3,326 isolates indicated that *S. aureus* isolation rate from blood was 21%, 26% from PA and 9% from OSBF. Resistance to methicillin was observed in 38% isolates from blood, and resistance to methicillin in isolates from PA and OSBF was found to be 24% and 31%, respectively (Table 4). Erythromycin resistance was observed in 69% of *S. aureus* isolated from blood, 54% from PA and 62% from OSBF (Table 4). The MRSA resistance from all the three specimens was 27%. *S. aureus* was the most commonly isolated Gram-positive bacteria from each location type. Distribution of *S. aureus* isolates reported under the programme in 2022 is from 8% of ICU patients, 12% of IPD patients and 13% of OPD patients (Table 3). MRSA isolated from IPD patients was 40% followed by ICU and OPD patients 17% and 33% respectively (Figure7).

Table 4: Resistance profile of *Staphylococcus aureus*

Antibiotic tested	Blood (N= 714)			PA (N= 2,540)			OSBF (N=72)		
	Number tested	Number Resistant	Resistance (%)	Number tested	Number Resistant	Resistance (%)	Number tested	Number Resistant	Resistance (%)
Cefoxitin	552	210	38	1,862	451	24	65	20	31
Amikacin	106	2	2	929	31	3	15	0	*
Gentamicin	645	146	23	2,020	292	14	53	10	19
Ciprofloxacin	246	98	40	1,927	879	46	44	25	57
Trimethoprim/ Sulfamethoxazole	607	122	20	2,404	234	10	69	5	7
Clindamycin	523	142	27	2,205	363	16	67	13	19
Erythromycin	685	473	69	2,488	1341	54	71	44	62
Linezolid	630	1	0	2,284	9	0	63	0	0
Teicoplanin	72	0	0	676	6	1	10	1	*
Doxycycline	158	5	3	1,263	34	3	39	1	3
Vancomycin	438	0	0	1,029	0	0	22	0	*

*Due to number tested being <30, percentages were not computed

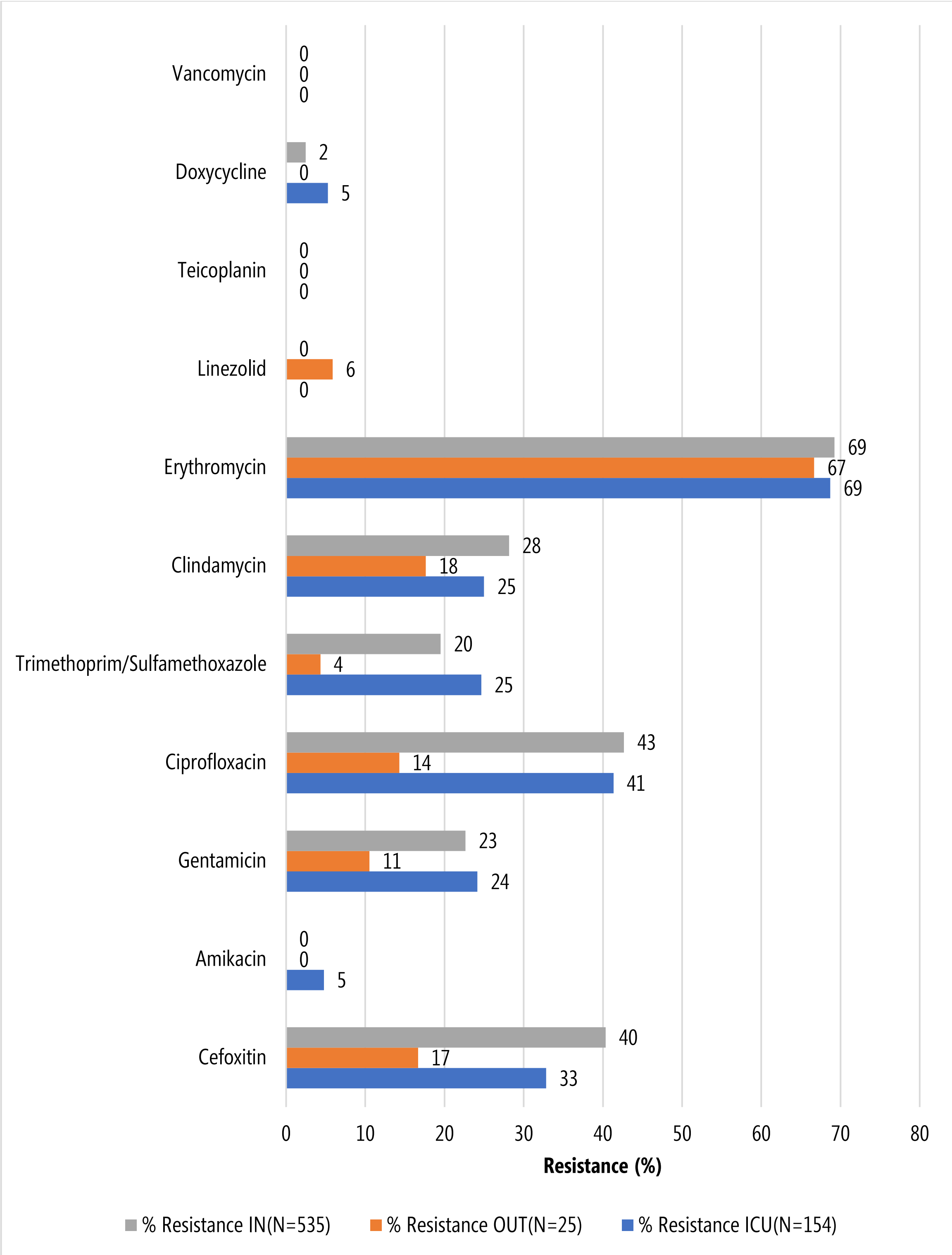

Figure 7: Resistance profile of S. aureus isolated from blood from different location types

Enterococcus species

Enterococcus species constituted 6% of all isolates (Figure 4). A total of 1,855 *Enterococcus species* isolate data was submitted by the KARS-NET sites during 2022 of which 1,734 isolates were from unique patients. Reported *Enterococcus species* represent 7% of blood culture isolates, 9% of OSBF isolates, 6% of urine isolates and PA each (Table 2).

Among the *Enterococcus species* isolated from blood, pus aspirate and OSBF specimens, the highest resistance is observed to erythromycin i.e., 74%, 68% and 63%, respectively. Next highest resistance is observed to doxycycline in three specimen types i.e., blood, pus aspirate and OSBF specimens which is 55%, 33% and 63% respectively whereas in urine specimens the highest resistance was observed to tetracycline (72%), and the second highest resistance was observed in ciprofloxacin (68%). Among urinary isolates, 5% resistance to vancomycin and 1% resistance to linezolid was seen. The blood isolates showed 2% resistance to vancomycin and 1% resistance to linezolid. The PA isolates showed 1% resistance to both vancomycin and linezolid whereas OSBF isolates showed 1% linezolid resistance and 2% vancomycin resistance. The vancomycin resistance from all the four specimen is 3%. The reported *Enterococcus species* were from 8% of ICU patients, 7% of IPD patients and 5% of OPD patients. (Table 3)

Table 5: Resistance profile of *Enterococcus* species

Antibiotic tested	Blood (N=230)			Pus aspirate (N=579)			OSBF (N=76)			Urine (N=849)		
	Number tested	No. Resistant	Resistance %	Number tested	No. Resistant	Resistance %	Number tested	No. Resistant	Resistance %	Number tested	No. Resistant	Resistance %
Ampicillin	178	90	51	498	92	18	52	22	42	625	205	33
Gentamicin-HLAR	202	84	42	479	93	19	62	13	21	553	190	34
Ciprofloxacin										695	471	68
Erythromycin	199	147	74	514	348	68	65	41	63			
Linezolid	202	3	1	522	5	1	72	1	1	736	11	1
Vancomycin	204	5	2	508	7	1	64	1	2	699	35	5
Teicoplanin	41	2	5	184	5	3	30	0	0	356	13	4
Doxycycline	64	35	55	165	55	33	32	20	63	20	13	*
Fosfomycin										103	6	6
Tetracycline										628	450	72
Nitrofurantoin										572	133	23

*Due to number tested being < 30, percentages were not computed

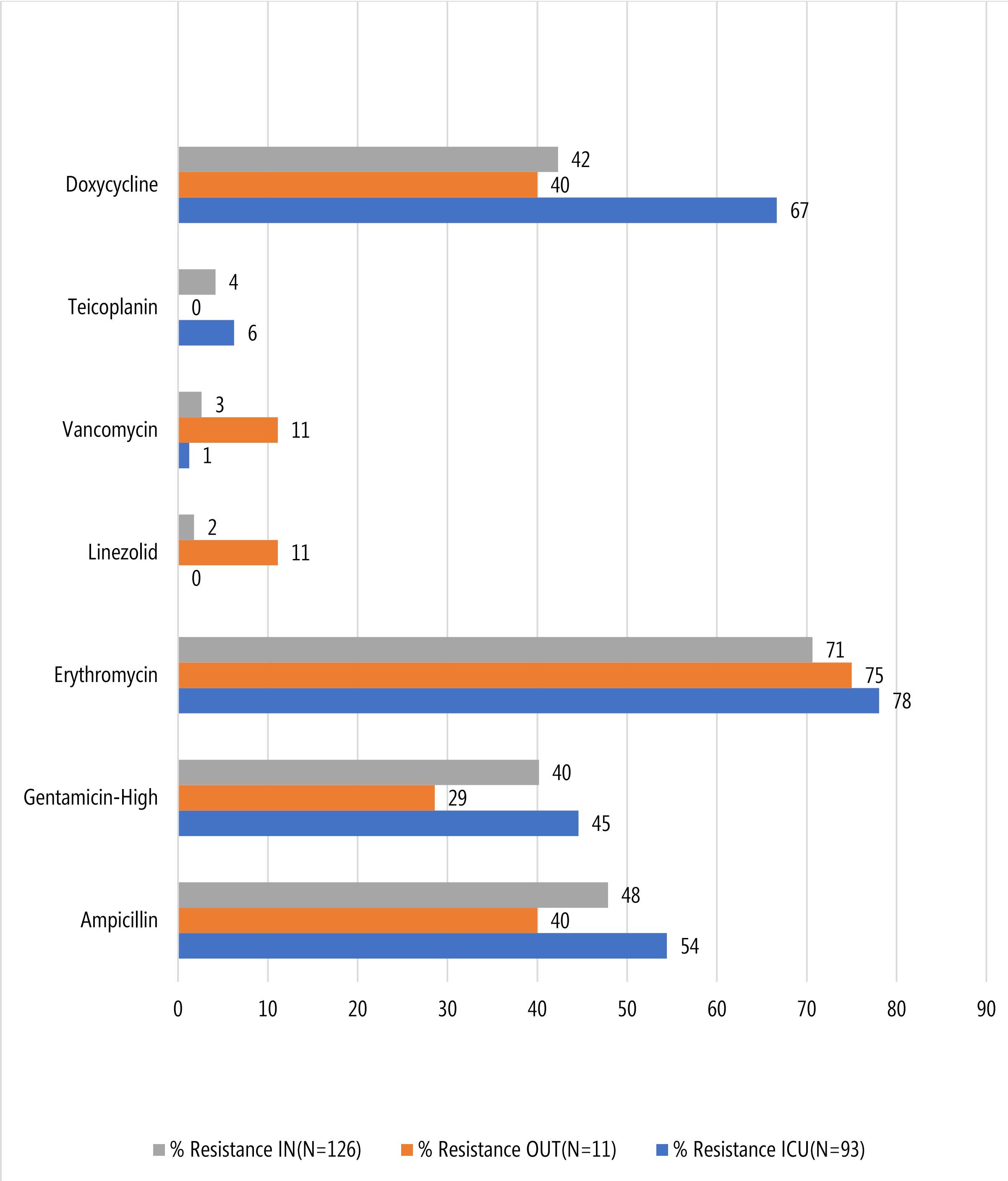

Figure 8: Resistance profile of Enterococcus species isolated from blood from different location types

b. Gram negative bacilli

Under KARS-NET, six commonly isolated gram-negative bacilli of public health importance are included for AMR surveillance. These are *E coli*, *Klebsiella species, Pseudomonas species*, *Acinetobacter species* and *Salmonella enterica* serovar Typhi and Paratyphi. AST data of 25,314 isolates of gram-negative bacilli have been reported from 22,544 unique patients during the reporting period.

i. Enterobacteriaceae

E. coli, *Klebsiella species* and *Salmonella enterica* serovar Typhi and Paratyphi AST data submitted by network sites accounted for 19,918 (65%) isolates from 17,629 (64%) unique patients. Thus, in concordance to previous annual report, this year also maximum isolates belonged to the Enterobacteriaceae family.

Escherichia coli

A total of 12,066 *E. coli* AST data has been reported from 10,746 unique patients. *E. coli* constituted 39% of data reported from unique patients for the year 2022. The highest number of *E. Coli* was reported from urine samples, followed by PA, blood & OSBF (Table 2). Ampicillin resistance in *E. Coli* was observed to be more than 80% in all specimen types. For third generations cephalosporin, cefotaxime resistance was observed in >60 % from *E. coli* isolated from all specimen types. Among blood isolates of *E. coli*, 67% were ESBL positive. Carbapenem resistance observed in *E. coli* isolates from blood was up to 10%. For non-beta-lactam antibiotics, 63% resistance was observed to ciprofloxacin and 49% to trimethoprim-sulfamethoxazole (TMP/SMX). Around 9% resistance to nitrofurantoin was seen in urinary isolates (Table 6). Twenty four percent blood isolates showed resistance to piperacillin tazobactam. 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. The carbapenem resistance in isolates from all the four specimens was 10% (Table 6, Figure 8).

Table 6: Resistance profile of *Escherichia coli*

Antibiotic tested	Blood (N=617)			PA (N=1,801)			OSBF(N=173)			Urine(N=8,155)		
	Number tested	Number resistant	Resistance %	Number tested	Number resistant	Resistance %	Number tested	Number resistant	Resistance %	Number tested	Number resistant	Resistance %
Ampicillin	457	400	88	1619	1436	89	148	118	80	6109	5119	84
Amoxicillin/ Clavulanic acid	295	98	33	585	173	30	75	26	35	3569	800	22
Cefoperazone/ Sulbactam	497	24	5	1366	41	3	129	7	5	4904	184	4
Piperacillin/ Tazobactam	591	139	24	1717	415	24	171	36	21	6760	1073	16
Cefuroxime	299	202	68	566	393	69	46	29	63	4040	2511	62
Ceftriaxone	337	226	67	1160	766	66	119	67	56	4733	2986	63
Cefotaxime	317	195	62	1112	708	64	106	68	64	4530	2825	62
Cefepime	518	244	47	1448	729	50	138	61	44	6785	3095	46
Ertapenem	171	14	8	349	32	9	17	3	18	2126	109	5
Imipenem	466	41	9	1277	165	13	116	19	16	5862	654	11
Meropenem	560	55	10	1582	156	10	161	11	7	5776	552	10
Amikacin	591	64	11	1681	229	14	170	17	10	6625	533	8
Gentamicin	588	160	27	1741	522	30	171	41	24	7328	1545	21
Ciprofloxacin	607	380	63	1775	1128	64	171	113	66	7610	4390	58
Trimethoprim/ Sulfamethoxazole	523	258	49	1484	659	44	141	58	41	7652	3428	45
Colistin	248	0	0	919	0	0	54	0	0	1775	0	0
Fosfomycin										790	18	0
Nitrofurantoin										7648	707	9

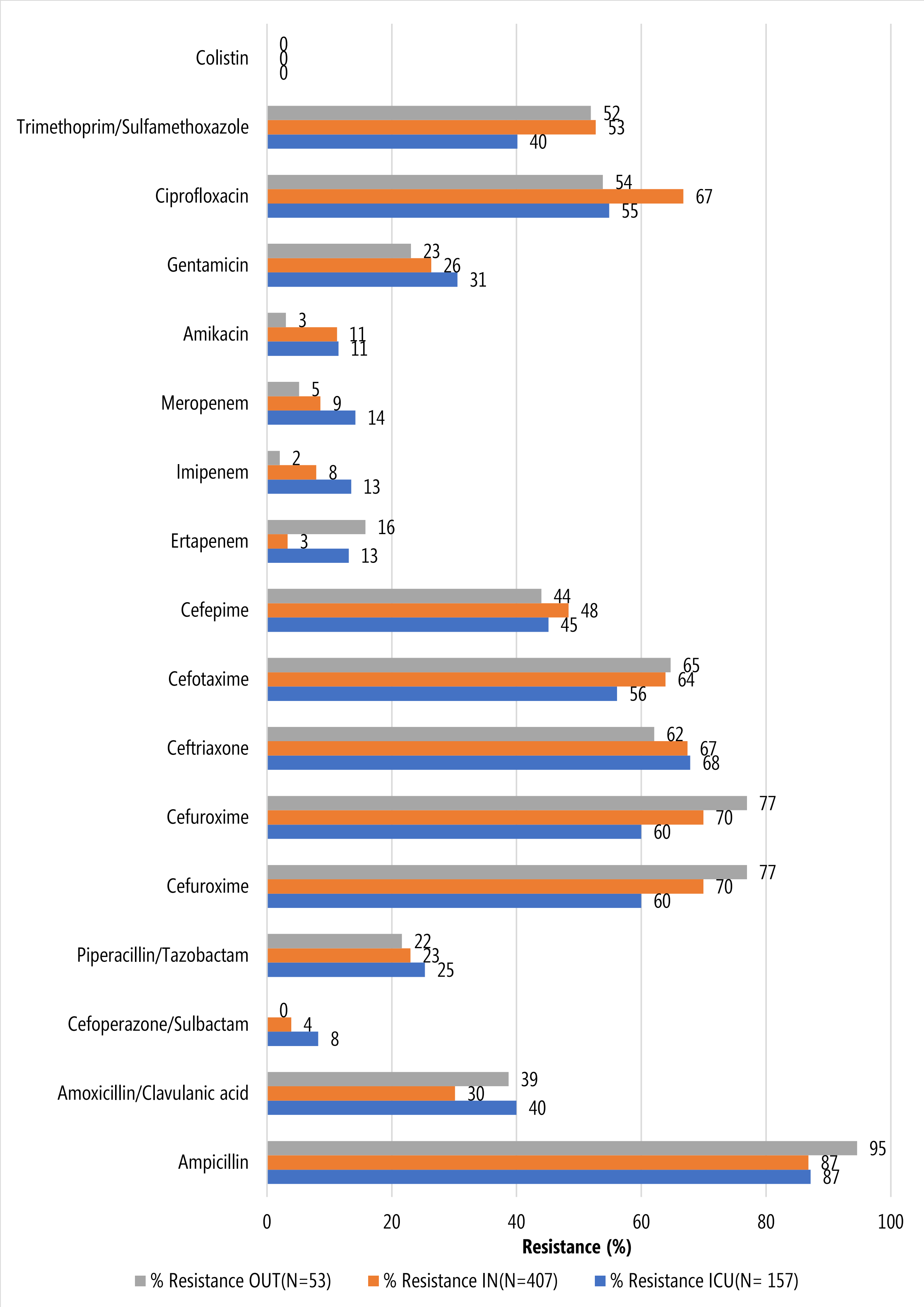

Figure 9: Resistance profile of Escherichia coli isolated from blood from different location types

Klebsiella species

High level of resistance was observed in *Klebsiella spp*. isolates from all specimen types and for all antibiotics except for colistin. Total of 3,596 *Klebsiella species* were isolated from urine specimens. ESBL positivity was observed in 73% of blood isolates. Cefotaxime resistance in the blood isolates is 73% followed by 62% in PA isolates, 57% in OSBF isolates and 55% in urine isolates. Ciprofloxacin resistance in all isolates ranged from 70% to 54% and amikacin resistance ranged from 34% to 19%. Highest resistance to carbapenem was observed in *Klebsiella spp*. from blood i.e., 43% compared to the other specimen types (Figure 9). Highest resistance to ertapenem was observed in Klebsiella species from blood i.e., 37% compared to other specimen types, and colistin resistance was 3% in blood and 1% in urine specimens.

Table 7: Resistance profile of *Klebsiella* species

Antibiotic tested	Blood (N=819)			Pus aspirate (N=2,167)			OSBF (N=260)			Urine (N=3,596)		
	Number tested	Number resistant	Resistance %	Number tested	Number resistant	Resistance %	Number tested	Number resistant	Resistance %	Number tested	Number resistant	Resistance%
Amoxicillin/ Clavulanic acid	266	139	52	579	249	43	90	38	42	1,591	610	38
Cefoperazone/ Sulbactam	644	98	15	1,812	147	8	189	24	13	2,405	276	11
Piperacillin/ Tazobactam	801	445	56	2,080	943	45	254	100	39	3,099	1045	34
Cefuroxime	250	179	72	656	426	65	69	40	58	1,925	1082	56
Ceftriaxone	412	291	71	1552	917	59	164	87	53	2,059	1104	54
Cefotaxime	467	341	73	1471	914	62	159	91	57	2,196	1198	55
Cefepime	675	427	63	1,865	1,069	57	203	100	49	3,032	1360	45
Ertapenem	106	39	37	360	99	28	23	5	22	977	180	18
Imipenem	554	246	44	1,742	617	35	168	57	34	2,684	618	23
Meropenem	757	326	43	1,989	655	33	243	65	27	2,742	634	23
Amikacin	802	275	34	2,062	610	30	250	57	23	3,104	576	19
Gentamicin	793	395	50	2,102	824	39	256	81	32	3,332	874	26
Ciprofloxacin	806	561	70	2,150	1,296	60	253	138	55	3,438	1858	54
Trimethoprim/ Sulfamethoxazole	629	321	51	1,897	873	46	207	74	36	3,426	1409	41

Antibiotic tested	Blood (N=819)			Pus aspirate (N=2,167)			OSBF (N=260)			Urine (N=3,596)		
	Number tested	Number resistant	Resistance %	Number tested	Number resistant	Resistance %	Number tested	Number resistant	Resistance %	Number tested	Number resistant	Resistance%
Colistin	333	9	3	1,335	4	0	93	0	0	872	8	1
Doxycycline	122	84	69	56	22	39	22	6	27			
Tigecycline	392	52	13	1,237	26	2	119	6	5			
Nitrofurantoin										3,284	1,427	43

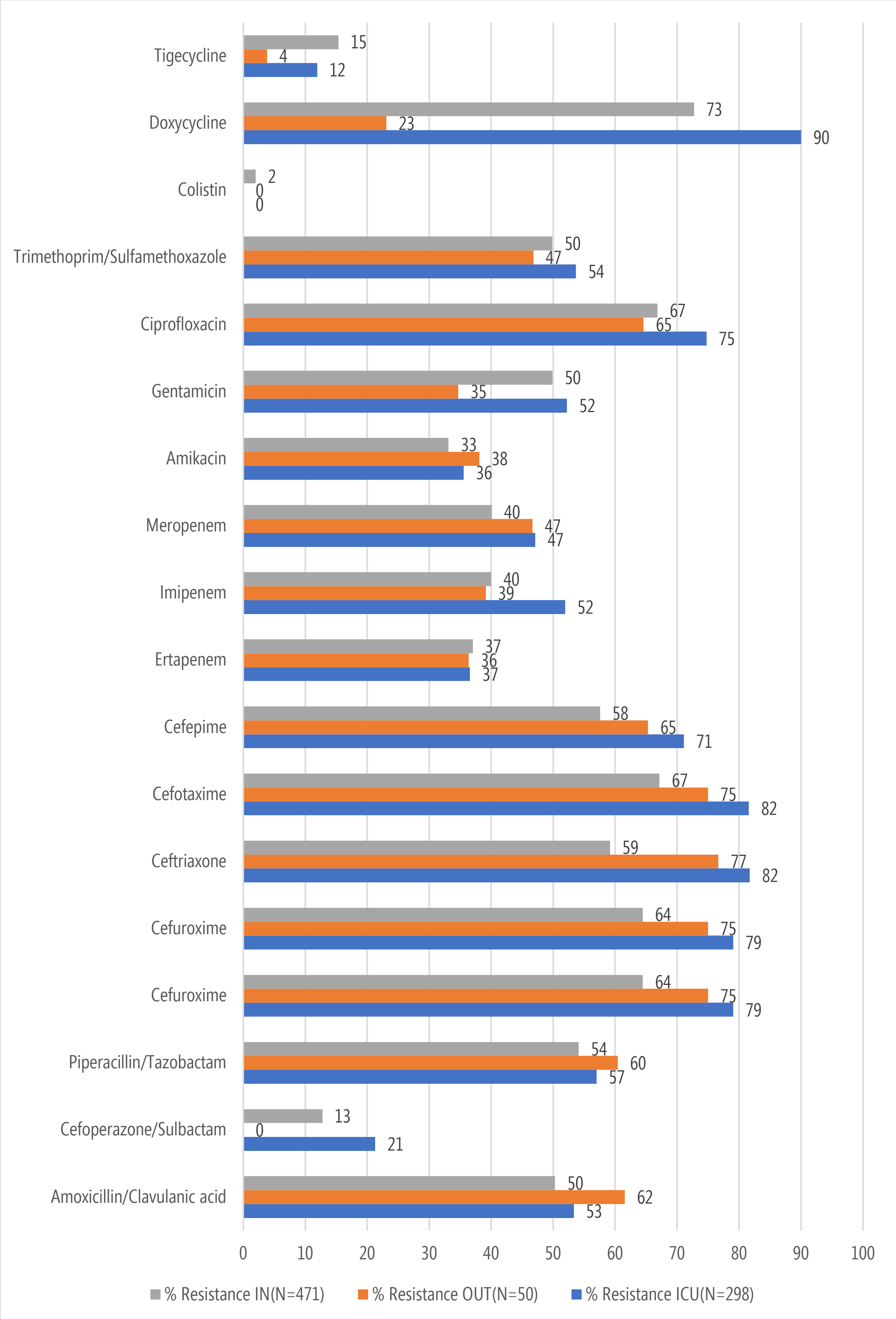

Figure 10: Resistance profile of Klebsiella species isolated from blood from different location types

Salmonella enterica Typhi and Paratyphi

This year network sites submitted AMR surveillance data of 47 Salmonella enterica serovar Typhi and Paratyphi isolates of which 41 isolates were from unique patients. Low resistance to first-line antibiotics (26% ampicillin and 5% chloramphenicol) was observed compared to ciprofloxacin (42%).

Table 8: Resistance profile of *Salmonella enterica* Typhi and Paratyphi

Antibiotic tested	S. Typhi (N=34)			S. Paratyphi A (N=3)		S. Paratyphi B (N=4)	
	Number tested	Number Resistant	% Resistant	Number tested	Number Resistant	Number tested	Number Resistant
Ampicillin	31	8	26	3	0	4	4
Ceftriaxone	28	1	4	3	0	4	4
Imipenem	11	0	0	3	0	0	0
Ciprofloxacin	33	14	42	3	3	4	4
Azithromycin	14	1	7	1	0	3	3
Chloramphenicol	20	1	5	2	0	2	2

ii. Non-fermenting Gram-negative bacilli

Among the non-fermenting Gram-negative bacilli (NFGNB) collected during Jan-Dec 2022 across all KARS -Net sites, *Pseudomonas species* (3,306) was the most commonly isolated pathogen followed by *Acinetobacter species* (1,609). Similar isolation rates of NFGNB were observed last year.

Pseudomonas species

Pseudomonas species isolated from blood showed 14% resistance to meropenem and 17% to piperacillin tazobactam. Isolates from blood in ICU, IPD and OPD patient facilities showed high resistance to ceftazidime i.e., 52%, 33% and 23%, respectively. Carbapenem-resistance was observed in 14% of *Pseudomonas spp*. isolated from blood and 22% from urine specimen.

Table 9: Resistance profile of *Pseudomonas* species

Antibiotic tested	**Blood** (N=291)			**Pus aspirate** (N=1,889)			**OSBF** (N=151)			**Urine** (N=975)		
	Number tested	Number resistant	Resistance%	Number tested	Number resistant	Resistance%	Number tested	Number resistant	Resistance%	Number tested	Number resistant	Resistance%
Piperacillin/ Tazobactam	285	49	17	1,851	301	16	145	27	19	935	136	15
Ceftazidime	262	95	36	1,803	605	34	132	51	39	849	274	32
Aztreonam	62	13	21	200	40	20	6	2	33	247	66	27
Imipenem	177	26	15	1,636	280	17	68	18	26	757	179	24
Meropenem	237	33	14	1,585	207	13	122	29	24	777	168	22
Amikacin	285	65	23	1,606	321	20	140	40	29	779	173	22
Gentamicin	286	80	28	1,854	517	28	146	51	35	937	221	24
Ciprofloxacin	245	63	26	1,804	634	35	110	46	42	947	321	34
Colistin	95	0	0	1,202	0	0	35	0	0	261	1	0

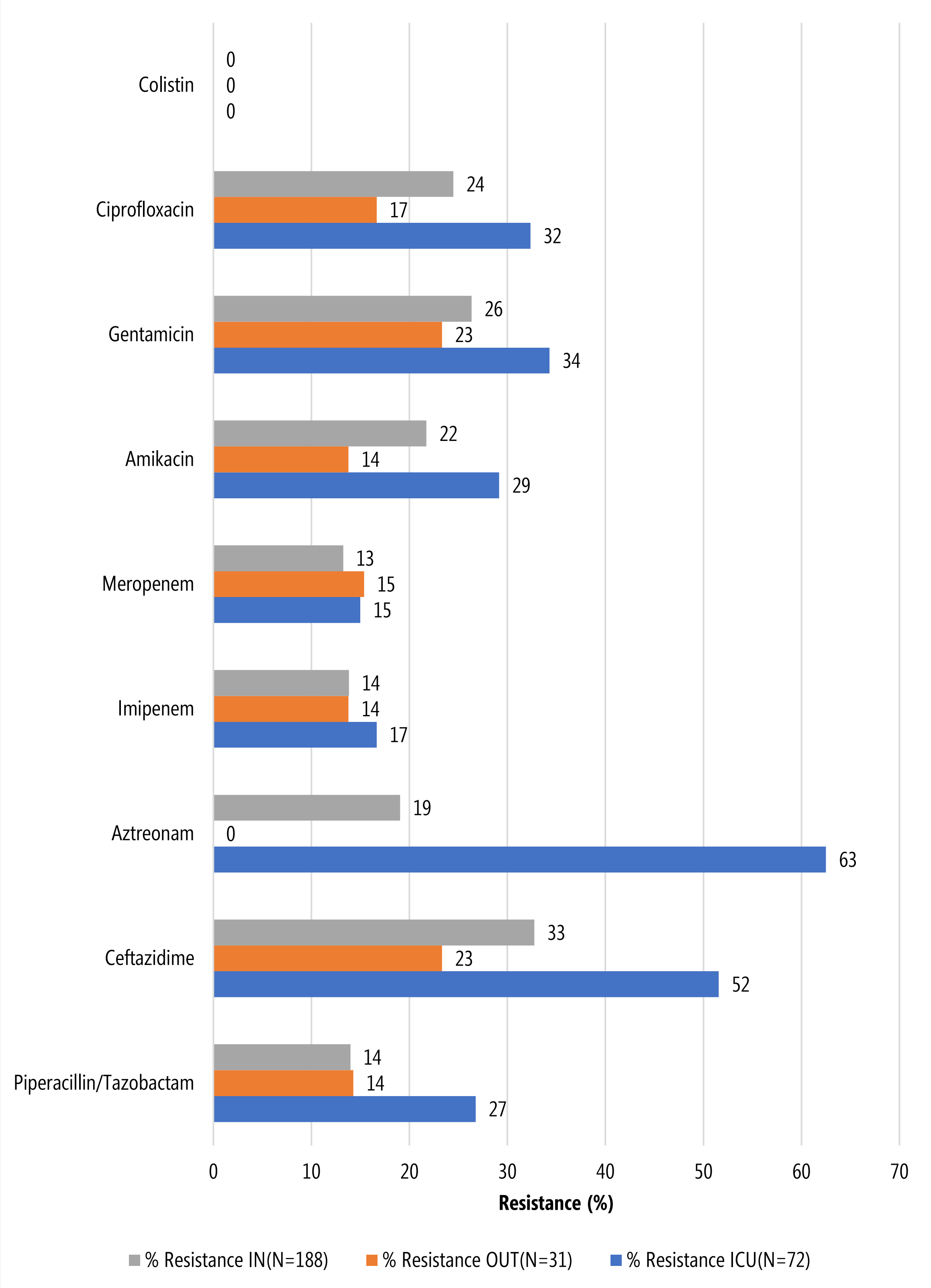

Figure 11: Resistance profile of Pseudomonas species isolated from blood from different location types

Acinetobacter species

Data from a total of 1,781 *Acinetobacter species* isolates was submitted by network sites, of which 1,609 were from unique patients. Majority of *Acinetobacter spp*. reported under KARS -Net were from blood cultures (614). 53% resistance to imipenem was observed in blood isolates. *Acinetobacter spp*. isolated from all specimen types showed highest resistance to ceftazidime.

Table 10: Resistance profile of *Acinetobacter* species

Antibiotic tested	Blood (N=614)			Pus aspirate (N=606)			OSBF (N=105)			Urine (N=284)		
	Number tested	Number resistant	Resistance %	Number tested	Number resistant	Resistance %	Number tested	Number resistant	Resistance %	Number tested	Number resistant	Resistance %
Cefoperazone/ Sulbactam	323	28	9	408	7	2	58	7	12	111	8	7
Ampicillin/ Sulbactam	38	11	29	92	44	48	4	0	0	55	18	33
Piperacillin/ Tazobactam	593	282	48	589	371	63	103	58	56	245	70	29
Ceftazidime	337	202	60	499	341	68	56	43	77	148	57	39
Imipenem	352	185	53	532	349	66	61	44	72	188	67	36
Meropenem	466	219	47	533	324	61	77	49	64	154	47	31
Amikacin	592	244	41	572	333	58	100	58	58	233	67	29
Gentamicin	603	279	46	595	361	61	102	66	65	266	86	32
Ciprofloxacin	571	282	49	576	382	66	81	55	68	257	94	37
Trimethoprim/ Sulfamethoxazole	427	189	44	558	318	57	75	35	47	242	50	21
Colistin	222	0	0	398	0	0	41	0	0	41	0	0
Minocycline	256	70	27	324	101	31	37	14	38	42	6	14
Tigecycline	247	2	1	386	3	1	52	0	0	34	2	6
Tetracycline										78	20	26

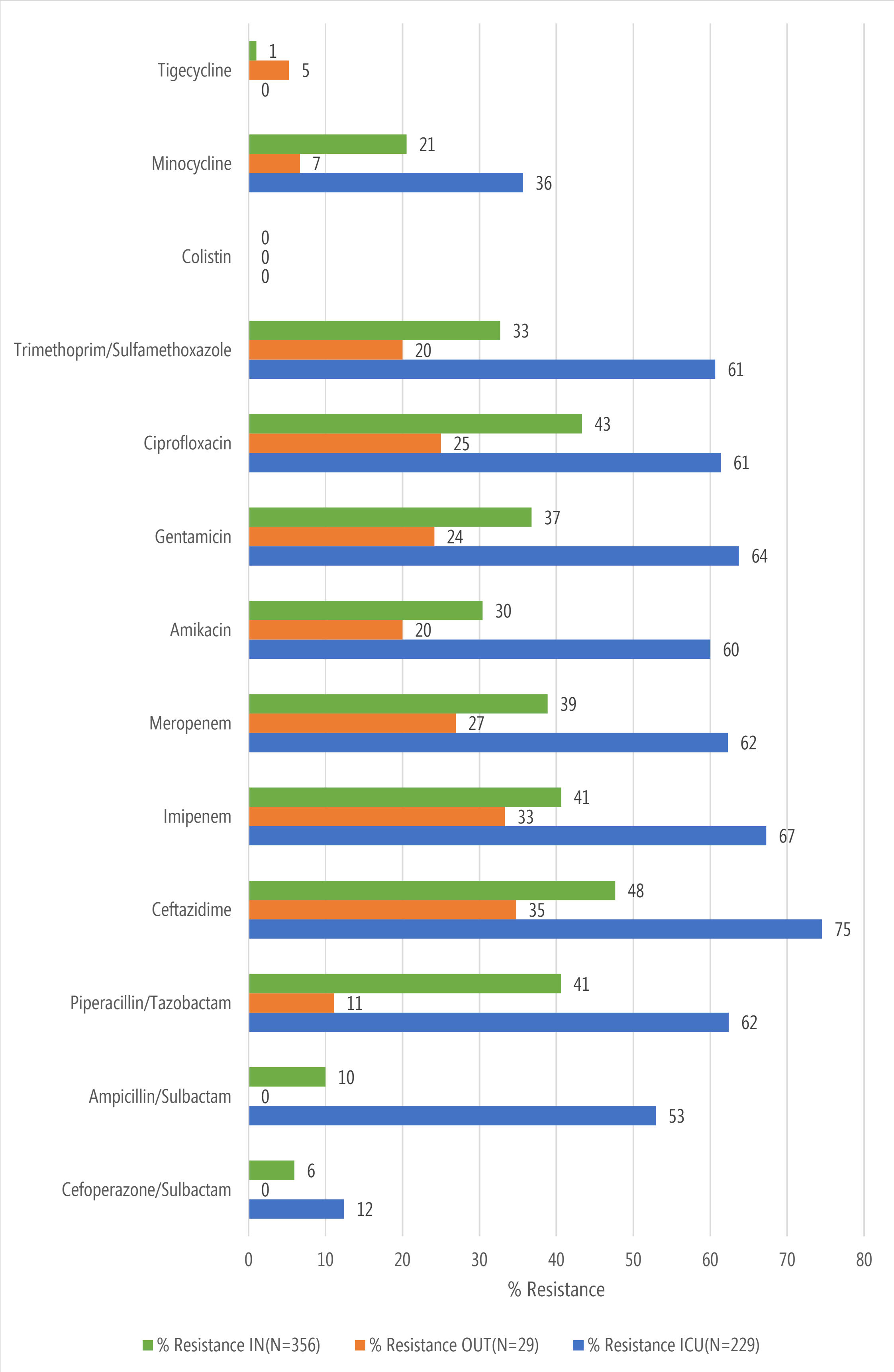

Figure 12: Resistance profile of Acinetobacter species isolated from blood from different location types

Trends of AMR in Kerala over 4 years

The trends of AMR in Kerala over four years (2018-2022) were analysed from the KARS-NET data. The data for 2020 was not included as most of the centres were unable to test and report AMR due to the pandemic. It was observed that ESBL production as well as carbapenem resistance has been increasing over the years (Figures 12 and 13). The limitation of the data is that most of the centres are tertiary care centres, and the data may not be representative of the community. The apparent decrease in MRSA in 2021 may 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 centres being COVID care centres**.** VRE rates have also increased over the last three years (Figure14).

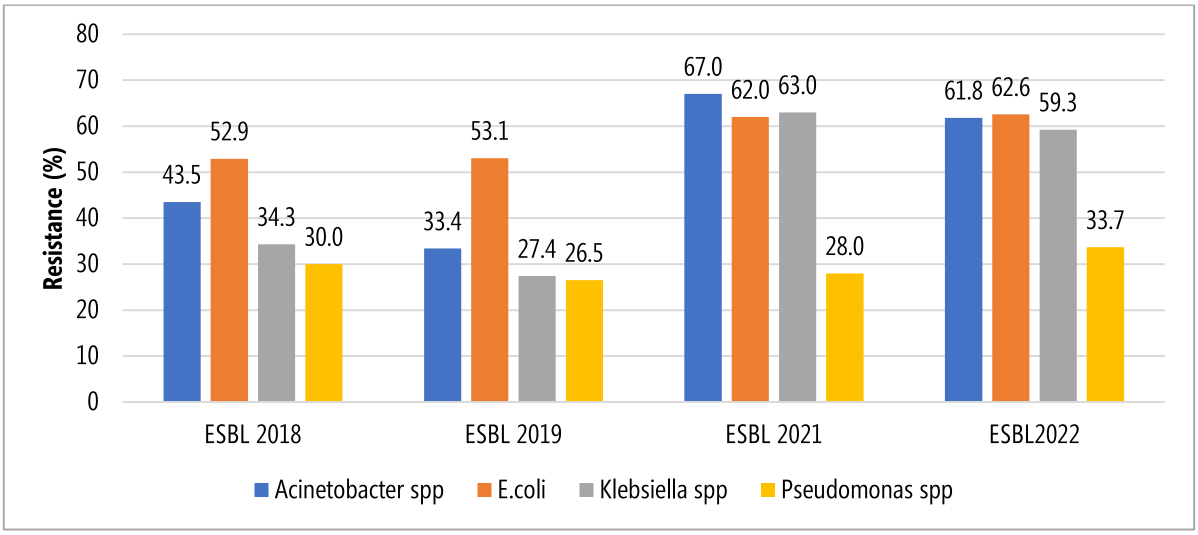

Figure 13: Trends of ESBL – evidence from KARS-NET over 4 years

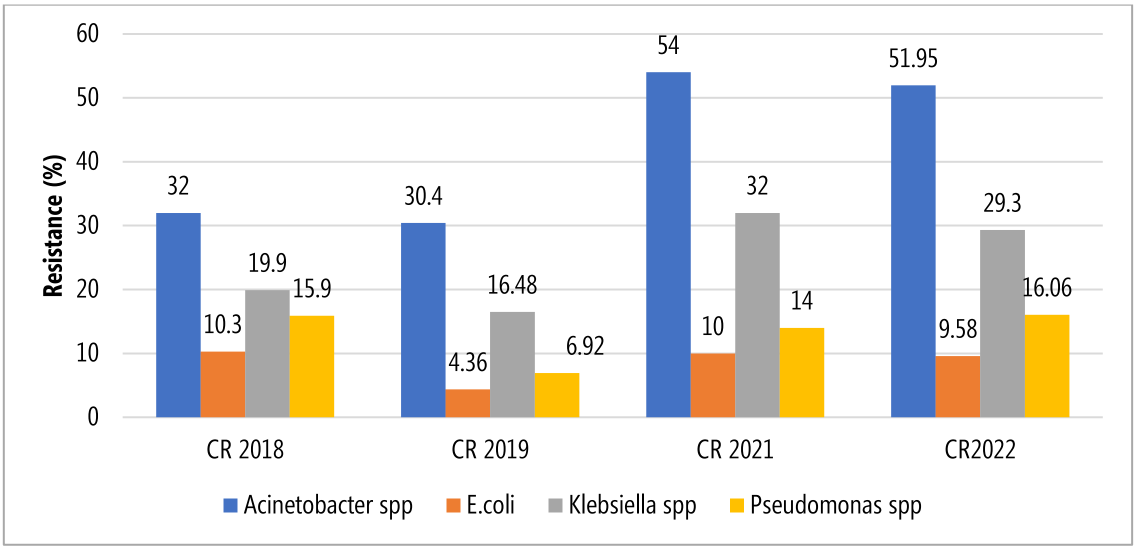

Figure 14: Trends of Carbapenem resistance – evidence from KARS-NET over 4 years

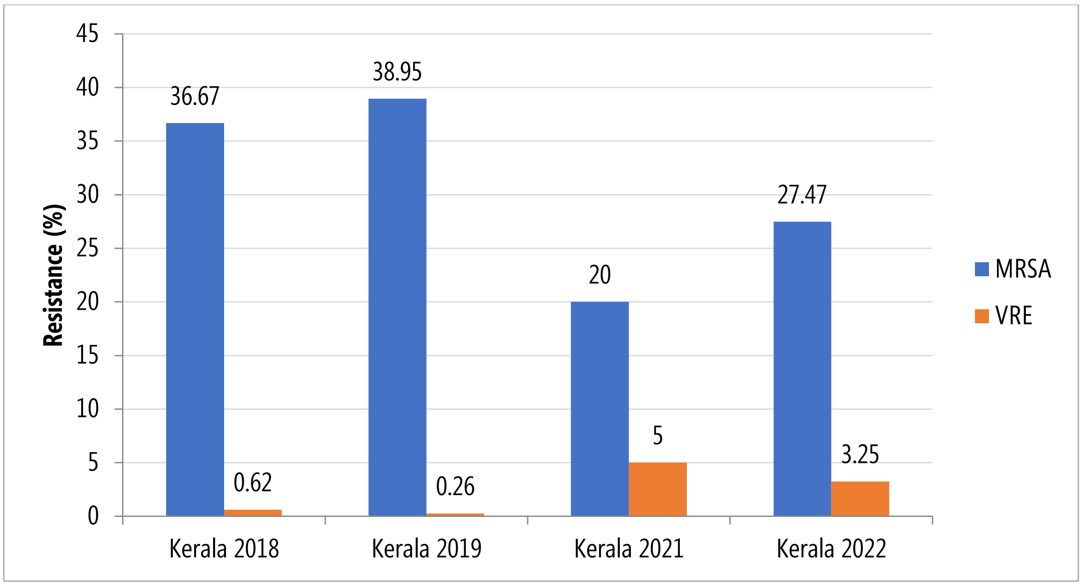

Figure 15: Trends of MRSA and VRE – evidence from KARS-NET over 4 years

Discussion

Strengthening global, national and local AMR surveillance is critical for AMR containment as it is the basis for designing and implementing evidence-based strategies, monitoring the effectiveness of public health interventions and detecting new trends and threats. AMR poses a significant global health challenge threatening the attainment of Sustainable Development Goals (SDGs) related to health. WHO declared AMR as one of the ten global public health threats in 2019 and an emergent health challenge for the decade in 2020.

KARS-NET compiles the State AMR surveillance report annually. The activities under KARS-NET include capacity building of a network of government and private medical colleges and laboratories for AMR surveillance. KARS-NET has been expanded in a phased manner to 11 districts across the state. AMR surveillance under KARS-NET includes standardised collection, analysis and compilation of AMR data from all the network sites. The compiled data is used to generate the annual State AMR surveillance report which is shared with all the network sites under KARS-NET and to the stakeholders at the State level. This network data is also submitted annually to NCDC for submission in WHO's GLASS.

This report for the year 2022 presents analysed data from 23 sentinel sites located in 11 districts of Kerala. Compared to the previous year's Kerala AMR surveillance report which included 2021 data from 18 network sites, the number of sites submitting the AMR data during 2022 has increased to 23 network sites. 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, internal quality control (IQC) and other technical guidelines developed by NCDC. The number of centres performing colistin BMD has increased compared to the previous years. The monthly feedbacks on AMR data are provided to the network laboratories have played an essential role in improving the patient demographic & AST data compliance. Most sites have adopted stringent internal quality control of antibiotic discs as per recommendations under the programme.

E. coli was the most commonly isolated pathogen (39%) in the AMR surveillance data of 2022 which is similar to the previous year report. Amongst urinary isolates, *E. Coli* was the most commonly isolated pathogen (59%) while *Klebsiella spp.* (25%) was the most commonly isolated pathogen from blood specimen and this finding corroborated with the previous year reports. *Klebsiella spp*. was the most predominant pathogen isolated from OSBF (31%). *Staphylococcus aureus* was the most predominant pathogen isolated from PA (26%). In terms of location type, *E coli* was predominantly isolated from

OPD (45%) and IPD (37%) settings whereas *Klebsiella spp*. were more commonly isolated in the ICU setting (31%). Similar pathogen burden in respective location types was also seen in the previous year report. MRSA was observed in blood this year (27%). *Enterococcus spp.* isolated from blood cultures showed 2% resistance to vancomycin. Upto 10% of *E. coli* and up to 43% of *Klebsiella spp.* isolated from blood were found to be CREs.

AMR surveillance through the KARS-NET plays a pivotal role in determining the burden and trends of AMR in Kerala, providing valuable information for evidence based policy making and implementation for containment of AMR.

Acknowledgements

This annual report is based on surveillance conducted on antimicrobial resistance priority pathogens by Kerala Antimicrobial Resistance Surveillance Network sites in the year 2022.

Thanks to the effort taken by all the sentinel surveillance network centers for submitting the monthly WHONET data to the State AMR Surveillance nodal center, Department of Microbiology, Government Medical College, Thiruvananthapuram.

Special thanks to the KARS-NET AMR Surveillance project team, GMC Thiruvananthapuram for the immense effort for preparing the annual report.

Sincere thanks and gratitude to NCDC and WHO team for the constant support and guidance for publishing the annual report.

Nodal Officer
State AMR Surveillance
Kerala

Annexure

List of AMR surveillance sites under KARS-NET

1. Government Medical College (GMC) Manjeri
2. Government Medical College (GMC) Kozhikode
3. Government Medical College (GMC) Thrissur
4. Government Medical College (GMC) Ernakulam
5. Government Medical College (GMC) Kottayam
6. Government Medical College (GMC) Alappuzha
7. Government Medical College (GMC) Kollam
8. Government Medical College (GMC) Thiruvananthapuram
9 Government Medical College Kannur
10. General Hospital (GH) Ernakulam
11. General Hospital (GH) Thiruvananthapuram
12. General Hospital (GH) Kottayam
13. State Public Health Laboratory, Thiruvananthapuram
14. Regional Cancer Centre, Thiruvananthapuram
15. Sree Chitra Tirunal Institute for Medical Sciences &Technology, Thiruvananthapuram
16. Rajiv Gandhi Centre for Biotechnology, Thiruvananthapuram
17. Believers Church Medical College Hospital, Tiruvalla
18. Jubilee Mission Medical College and Research institute, Thrissur
19. Amala Institute of Medical Sciences, Thrissur
20. Karuna Medical College, Palakkad
21. MES Medical College and Paramedical Science, Perinthalmanna
22. Pushpagiri Medical College Hospital, Tiruvalla
23. Thankam Hospital of PMRC, Palakkad
24. Malabar Cancer Centre, Thalassery
25. MVR Cancer Centre, Kozhikode
26. Aswini Diagnostic Services, Kozhikode
27. Dane Diagnostic Services, Palakkad
28. Sree Uthradom Tirunal Institute of Medical Sciences, Thiruvananthapuram
29. Regional Public Health Laboratory, Kannur
30. Regional Public Health Laboratory, Pathanamthitta
31. District Public Health Laboratory, Malappuram

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