Kerala Antimicrobial Resistance Surveillance Network

(KARS-Net)

Annual Report 2024

(Data from January to December 2023)

HANDLE ANTIMICROBIALS WITH CARE

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Smt VEENA GEORGE
Hon'ble Minister for Health & Family Welfare
Govt. of Kerala

FOREWORD

Antimicrobial Resistance (AMR) is a serious global public health threat which can be tackled only by a "One Health" approach. Kerala became the first state in India to draft and implement an AMR strategic action plan , KARSAP (Kerala Antimicrobial Resistance Strategic Action Plan) which was launched on 25 October 2018. KARSAP is the flagship project of the state in its fight against the growing threat of AMR. Lord Kelvin had stated that " If you cannot measure it, you cannot improve it". Hence inorder to understand the magnitude of AMR in the State, Kerala Antimicrobial Resistance Surveillance Network (KARS-NET) was established in 2019. In 2022 , Kerala became the first State in India to release its own antibiogram. KARSNET antibiograms of 2021 and 2022 for State of Kerala showed that the resistance trends among priority pathogens varied from centre to centre. KARSNET data is reflective of susceptibility trends in tertiary care institutions only. Hence with the aim of capturing the susceptibility trends among priority pathogens at all tiers of health care system, for the first time in India, hub and spoke model of AMR surveillance was initiated in almost all districts in Kerala . First District antibiogram in India was compiled and released by Ernakulam last year. Such stratified antibiograms at district level help in planning customized interventions at various levels of healthcare.

KARSNET over the years has expanded from 21 labs in 9 districts to 52 labs across13 districts in a phased manner. KARSNET annual report of 2024 depicts AMR trends from 34 surveillance centres across the state. This annual report reflects the dedication and hardwork of the nodal officers from the different KARSNET surveillance centres. I wholeheartedly congratulate the nodal officers and the entire KARSAP team for their exemplary work and wish them all the success in their unending fight against AMR.

Smt Veena George
Hon'ble Minister for Health & Family Welfare
Govt. of Kerala

Dr. Rajan N Khobragade IAS
Additional Chief Secretary,
Health & Family Welfare, Govt. of Kerala

FOREWORD

The Government of Kerala in collaboration with Ministry of Health and Family Welfare and World Health Organization India launched the Kerala Antimicrobial Resistance Strategic Action Plan in 2018.

The Health sector is grappling with the issues of antimicrobial resistance, as it has reached to catastrophic proportion. The other disease epidemic / pandemic are detected and lived through and managed but anti-microbial resistance is now reached to the level of '*the silent pandemic*'. In the Global context, prevalence of AMR, the World Health Organization estimates that antimicrobial resistance contributes to around 700,000 deaths worldwide. This number could rise to 10 million by 2050 if current trend continues. Common resistant pathogens include methicillin resistant Staphylococcus aureus, multi drug resistant tuberculosis and resistant strains of E coli.

Global antibiotic consumption has risen by nearly 40% since 2000.With significant increase in low- and middle-income countries. India has some of the highest rate of AMR globally, with studies indicating resistance rates of over 50% for common pathogens such as E. coli and Klebsiella pneumoniae India is one of the largest consumers of antibiotics, with a reported consumption rate of approximately 13.3 defined daily doses per 1000 inhabitants per day. If the antibiotic use is continuing without any interventions, these numbers will reach to catastrophic levels very soon. Realising this situation, Kerala Health has been taking serious efforts in tackling the AMR problem in the state with a multi prong approach. The key strategies are

1. Antimicrobial stewardship by implementing programs that promote the appropriate use of antimicrobial to reduce resistance.
2. Infection control practices to strengthen protocols in healthcare setting to prevent the spread of infection. This includes hand hygiene, sterilization of equipment, and isolation procedures for infected patients.
3. Education and training healthcare providers and the public about the responsible use of antimicrobials, the risk of misuse, and the importance of completing prescribed courses.
4. Research and development support for the development of new anti microbials and alternative therapies, as well as rapid diagnostic tools to improve treatment precision.
5. Regulatory measures policies that regulate the sale and distribution of antimicrobials, to reduce the use of these agents.
6. Public Awareness campaign to increase awareness about antimicrobial resistance through campaigns that highlight its consequences and encourage preventive measures.

   Effective management requires a collaborative approach involving healthcare providers, policymakers, researchers, and the public.

The KARS – NET report 2023 reflect the collective actions by all the stakeholders and people at the field level. It reflects institutional strengthening and through them collective actions. The pathogens and specimens included in surveillance and resistance profile will be of immense help to adjust the treatment protocols and to work out corrective measures.

I appreciate the scientific work done by the state level multi-disciplinary experts as well as by the field workers. Such coordinated programmatic actions will definitely assist Kerala Health to contain Anti-Microbial Resistance.

I also take this opportunity to thank World Health Organization and Ministry of Health and Family Welfare Govt of India for their continued encouragement and support.

Dr Rajan Khobragade
Addl. Chief Secretary.
Health & Family Welfare, Govt. of Kerala

Dr. Thomas Mathew
Director of Medical Education
Government of Kerala

FOREWORD

Antimicrobial resistance (AMR) has emerged as one of the most pressing global health threats of our time. AMR is often referred to as a silent tsunami, which if left unaddressed is predicted to lead to one crore deaths across the globe by 2050.The set back to the world economy by 2050 is expected to be to the tune of 100 trillion dollars. The rise of AMR poses significant risks to public health, making infections harder to treat and increasing the likelihood of severe outcomes and mortality. The AMR situation in Kerala is also alarming with more and more cases of infections due to XDR and PDR bacteria being reported from tertiary care centers across the State.

KARSAP is Kerala states decisive action plan to tackle the scourge of AMR. Addressing AMR requires comprehensive surveillance to monitor trends, guide treatment practices, and inform public health strategies. KARS-NET [Kerala antimicrobial resistance surveillance network] was established in 2019 for comprehensive AMR surveillance among priority human pathogens in Kerala.KARSNET antibiograms helps in tracking resistance patterns and this information is vital for clinicians to make informed treatment decisions and for public health authorities to design targeted interventions. Surveillance data informs the development of treatment guidelines and protocols. By understanding the local prevalence of resistant strains, healthcare providers can adjust their prescribing practices to avoid using drugs that are ineffective against prevalent resistant pathogens. AMR Surveillance also allows for the assessment of the effectiveness of infection control measures and antimicrobial stewardship programs. By tracking changes in resistance patterns over time, public health officials can evaluate whether interventions are having the desired impact or if new strategies are needed. Comprehensive AMR surveillance data also supports policy development and research efforts aimed at combating AMR. It provides evidence for policymakers to enact regulations on antimicrobial use and promotes research into new drugs and alternative treatments.

KARSNET annual report 2024 shows that concerted efforts at all levels including in infection prevention and control and antimicrobial stewardship is essential to tackle AMR.

Dr. Thomas Mathew
Director,
DME, GoK

Dr. Reena K.J.
Director of Health Services
Government of Kerala

MESSAGE

AMR is a critical issue in public health that requires our immediate and unwavering attention. This growing crisis poses a significant threat to our ability to treat infections effectively and safeguard public health. As the Director of Health Services, it is my responsibility to underscore the gravity of this issue and highlight the indispensable role of antimicrobial resistance surveillance in combating this challenge. The consequences of AMR are far-reaching and dire. Infections caused by resistant organisms result in longer hospital stays, higher medical costs, and increased mortality rates. Common procedures and treatments, such as surgeries, chemotherapy, and organ transplants, become riskier when effective antibiotics are no longer available. Moreover, AMR undermines progress made in modern medicine and public health. Diseases that were once manageable have become formidable challenges, and the benefits of medical advancements are getting diminished. This erosion of medical efficacy is not just a local issue but a global crisis that transcends borders.

Effective surveillance of antimicrobial resistance is a cornerstone of our response to this crisis. Surveillance involves the systematic collection, analysis, and interpretation of data on resistance patterns and trends. I would like to congratulate entire KARSAP team for expanding KARSNET surveillance network to all most all districts in Kerala. District level antibiograms have been made possible by the unique hub and spoke model of AMR.

The threat of antimicrobial resistance is real and immediate, and our response must be equally resolute. By enhancing our surveillance efforts, promoting responsible antimicrobial use, and fostering multi-stakeholder collaboration, we can address this challenge effectively and safeguard the future of public health.

Dr. Reena K.J.
Director of Health Services
Government of Kerala

Dr S Manjusree
Nodal Officer KARSAP
Professor and Head, Microbiology Department
Government Medical College,
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FOREWORD

Antimicrobial resistance (AMR) is a complex and multifaceted public health crisis that poses a significant threat to human health, food security, and economic development. The consequences of AMR are far-reaching. Patients with resistant infections may require more intensive treatment, longer hospital stays, and more expensive medications. In some cases, infections may become untreatable, leading to death. Additionally, AMR can complicate common medical procedures, such as surgery and chemotherapy, as the risk of infection increases.

To combat AMR, it is essential to implement effective surveillance systems, which involves the systematic collection, analysis, and interpretation of data on antimicrobial resistance. By monitoring the prevalence of resistant microorganisms and tracking their spread, public health officials can identify emerging threats and implement timely interventions. Surveillance systems like KARSNET provide valuable information for decision-makers. KARSNET was established to foster standardization, strengthen and expand AMR surveillance in Kerala; Analyse and report KARS-Net data to State Government and NCDC on regular basis and to contribute towards the estimation of extent, burden and monitoring of AMR in Kerala.

Antibiograms generated helps to identify areas with high rates of AMR, guide the development of appropriate prevention and control measures, and assess the effectiveness of interventions. Over the years KARSNET has expanded to 52 nodal AMR surveillance centres from across 13 districts in Kerala. I am extremely proud to say that currently KARSNET has become the largest state level AMR surveillance network in India. Through concerted efforts from all nodal centres, the number of priority pathogen isolates for which sntimicrobial susceptibility (AST) data is available has increased to 45397 . Hub and spoke model of AMR surveillance initiated in the state will help in the development of stratified tier specific antibiograms from 2024 onwards. I take this opportunity to thank all the KARSNET nodal centres, NCDC and WHO for their wholehearted co-operation without which, generation of this report would not have been possible.

Dr S Manjusree
Nodal Officer, KARSAP

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Abbreviations

AMR	Antimicrobial resistance
AST	Antimicrobial susceptibility testing
BMD	Broth microdilution
CLSI	Clinical and Laboratory Standards Institute
CRE	Carbapenem resistant Enterobacteriaceae
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 *Enterococci*
WHO	World Health Organization

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1. 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 49 labs across 12 districts in a phased manner (Figure 1). Priority pathogens under surveillance currently include nine 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 for the period 1 January to 31 December 2023 from a total of 34 surveillance laboratories from 11 districts. Antimicrobial susceptibility (AST) data of 45,397 priority pathogens, along with the demographic information of the patients from whom these pathogens were isolated, were reported under KARS-Net during 2023. After data deduplication, data from 40,323 unique patient isolates were analysed; 47% (18,825) of reported isolates were from males; 53% (21,414) were from females. Gender data was not available for a small number of isolates.

Urine was the most commonly reported specimen 54% (21,790), followed by pus aspirate 34.5% (13,904), blood 8.8% (3,538), other sterile body fluids 2.5% (1042) and stool 0.1% (49). The most frequently reported priority pathogen from all specimens was *E. coli* (40%), followed by *Klebsiella* species (23.5%), *S. aureus* (11.9%), *Pseudomonas* species (10.8%), *Enterococcus* species (8.1%), *Acinetobacter* species (5.2%), *Salmonella enterica* serotype Typhi and Paratyphi A & B (0.3%) and *Shigella* species (0.1%). No *Vibrio cholerae* cases were reported during this time period.

Among the reported *Staphylococcus aureus* isolates, 29.8% were Methicillin resistant *Staphylococcus aureus* (MRSA). Among the Enterococcus isolates from blood, vancomycin resistance was 3% but linezolid resistance was not reported.

Extended spectrum beta-lactamase (ESBL) was observed in 71% of *E. coli* and 74% of *Klebsiella spp*. isolated from blood. With respect to carbapenem resistant Enterobacterales (CRE) in blood, 11% resistance was observed in *E. coli* and 43% in *Klebsiella spp*. Resistance to ciprofloxacin in *Salmonella Typhi* isolated from blood cultures was 61%.

Resistance to carbapenem was observed in 53% blood isolates of *Acinetobacter spp*. and 20% of *Pseudomonas spp*. Despite the relatively high resistance levels amongst Gram-negatives isolates in general, the overall resistance to colistin in gram negative isolates was only 0.3%.

2. 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 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 coordinated by National Centre for Disease Control (NCDC), New Delhi, aims to capture quality AMR surveillance data from sentinel surveillance sites to generate evidence of AMR prevalence in the country to guide the National Action Plan on AMR.

Kerala Antimicrobial Resistance Strategic Action Plan (KARSAP) was the first subnational State Action Plan on AMR conceptualised in India. It was launched 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) and National Centre for Disease Control (NCDC), the network has now expanded to 49 laboratories from both public and private sectors. The data generated by KARS-Net is shared with NCDC for submission to WHO's 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 uses WHONET software to collate, analyse and share AMR data on a monthly basis. KARS-Net currently includes surveillance of AMR in nine key priority pathogens responsible for high antibiotic resistance rates among bacteria that commonly cause human infections. The nine priority pathogens monitored by KARS-NET are:

1. *Staphylococcus aureus*
2. *Enterococcus* species
3. *Klebsiella* species
4. *Escherichia coli*
5. *Acinetobacter* species
6. *Pseudomonas* species
7. *Salmonella enterica* serovar Typhi and Paratyphi
8. *Shigella* species
9. *Vibrio cholerae*

KARS-Net includes 11 government medical college hospitals and 12 government hospitals under Directorate of Health Services, 3 semi-autonomous institutions, 16 private medical colleges, 7 private hospitals/laboratories (Figure 1). Of these 49 sites, AMR surveillance data was received for the period of one year from 1 January to 31 December 2023 from 34 network centres from 11 districts in Kerala. Fifteen more centres became part of KARS-Net after the above period of data collection.

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, *Shigella* spp and *Vibrio cholerae*)

Table 1: Pathogens and specimens included under surveillance

	Staph. aureus	*Enterococcus* spp.	*Klebsiella* spp.	*E. coli*	*Acinetobacter* spp.	*Pseudo-monas* spp.	*Salmonella Typhi/ Paratyphi*	*Shigella* spp.	*Vibrio cholerae*
Blood	✓	✓	✓	✓	✓	✓	✓	x	x
Urine	X	✓	✓	✓	✓	✓	x	x	x
PA	✓	✓	✓	✓	✓	✓	x	x	x
OSBF	✓	✓	✓	✓	✓	✓	x	x	x
Stool	x	x	x	x	x	x	✓	✓	✓

(x: specimen not relevant)

All the participating network sites report the monthly AMR data of the nine priority pathogens from the above-mentioned specimen types to the Department of Microbiology, Government Medical College, Thiruvananthapuram. The feedback regarding the quality and completeness of 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.

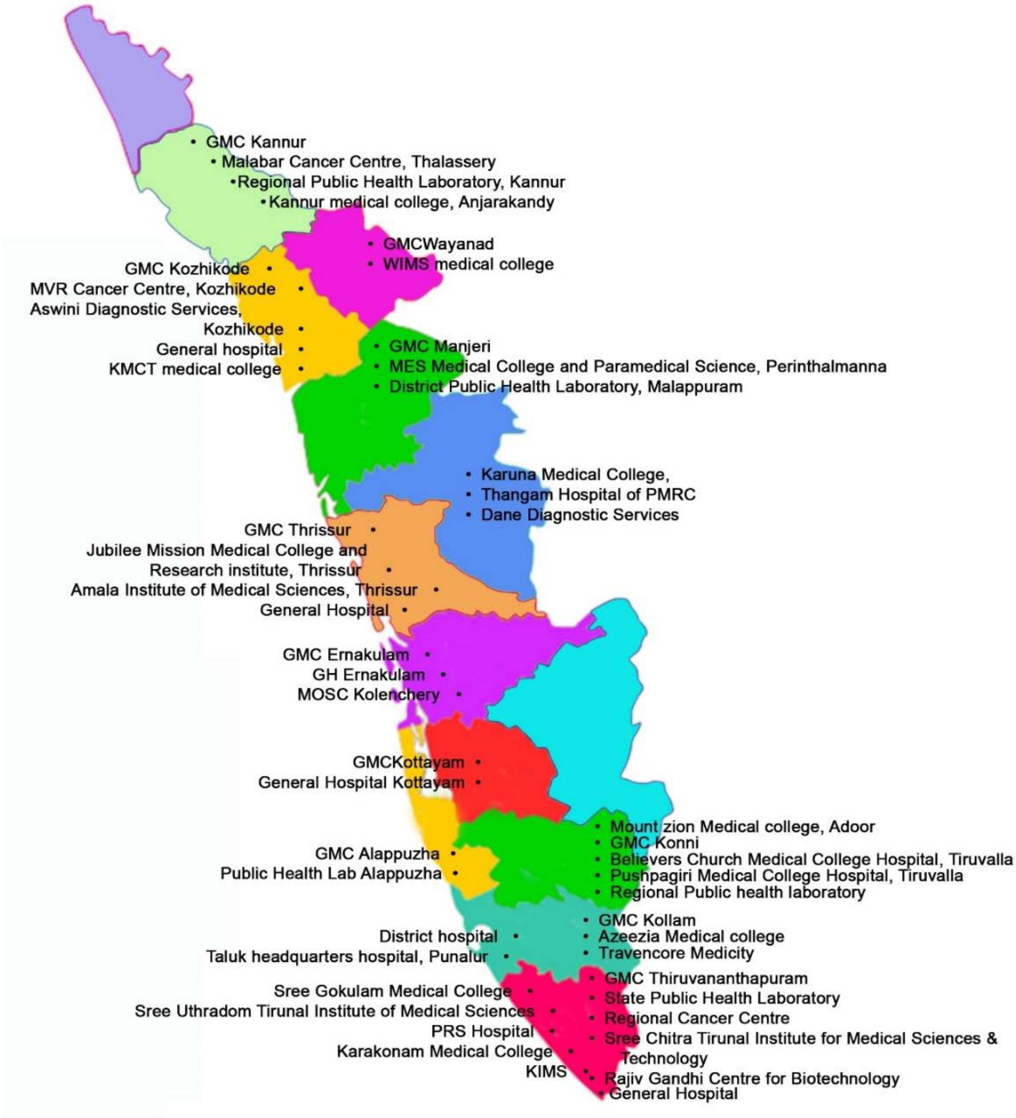

Figure 1: Institutions in the Kerala AMR Surveillance Network (KARS-Net)

The laboratories enrolled in KARS-Net follow a standardised approach for AMR data collection, analysis, and reporting using WHONET software. Trainings are provided on using WHONET for AMR data management. 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. Hands on training on antimicrobial susceptibility testing with emphasis on broth micro dilution (BMD) method and WHONET training was conducted at Government Medical College, Thiruvananthapuram for the new member sites in December 2023. 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 were adopted from NARS-Net for strengthening the network sites on routine AST techniques and for improving internal quality control for AST testing in laboratories, which are reviewed on a regular basis.

3. Data collection

The WHONET software is used for the collection, collation and analysis of the antimicrobial susceptibility (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 local, national, regional and global surveillance efforts worldwide.

The classification of the isolates as susceptible, intermediate or resistant is based on the Clinical & Laboratory Standards Institute (CLSI) guidelines. During 2023, AST data of 45,397 priority pathogens, along with the demographic information of the patients from whom these pathogens were isolated, was reported from 34 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 were screened and analysed and the detailed feedback was provided to them for each month. Based on feedback the corrected WHONET files were received.

4. Data analysis

The analysis of cumulative data for the year 2023 has been performed by the Department of Microbiology, Government Medical College Thiruvananthapuram, based on which this annual report was prepared. The AST data includes data of conventional disk diffusion method, broth-micro dilution (BMD) and automated antimicrobial susceptibility testing systems.

a. Data de-duplication

As a first step for data analysis, a single file was created by collating all the cumulative AMR data files. During this step, duplicate isolates (from 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) was 40,323 (Figure 2).

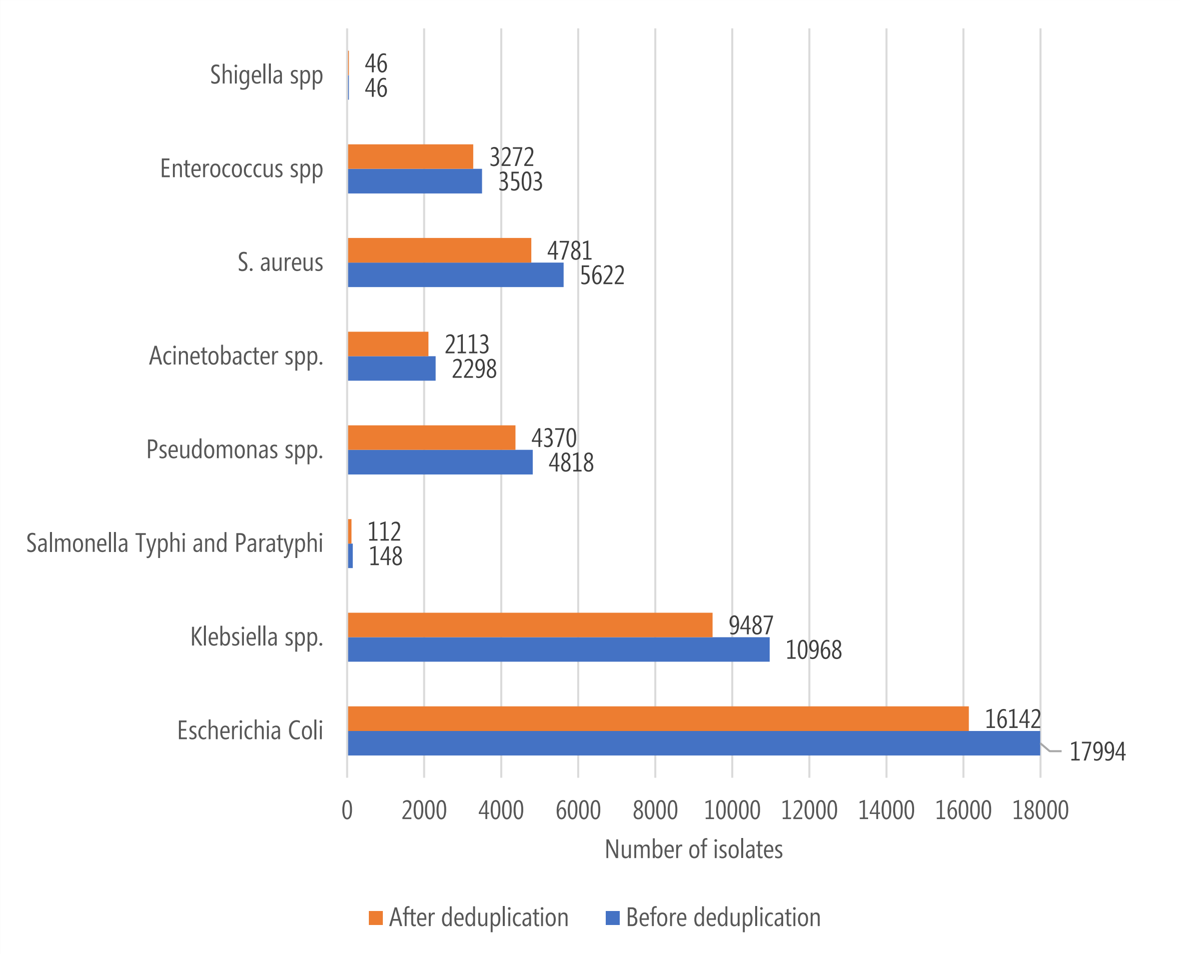

Figure 2: Priority pathogens before and after de-duplication

b. Demography and distribution of priority pathogens

Among the total of 40,323 unique patients, 47% pathogens were from males as compared to females (53%). Age data was available for 99.9% 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 (2.65%) were reported from age group of 85-100 years (Figure 3).

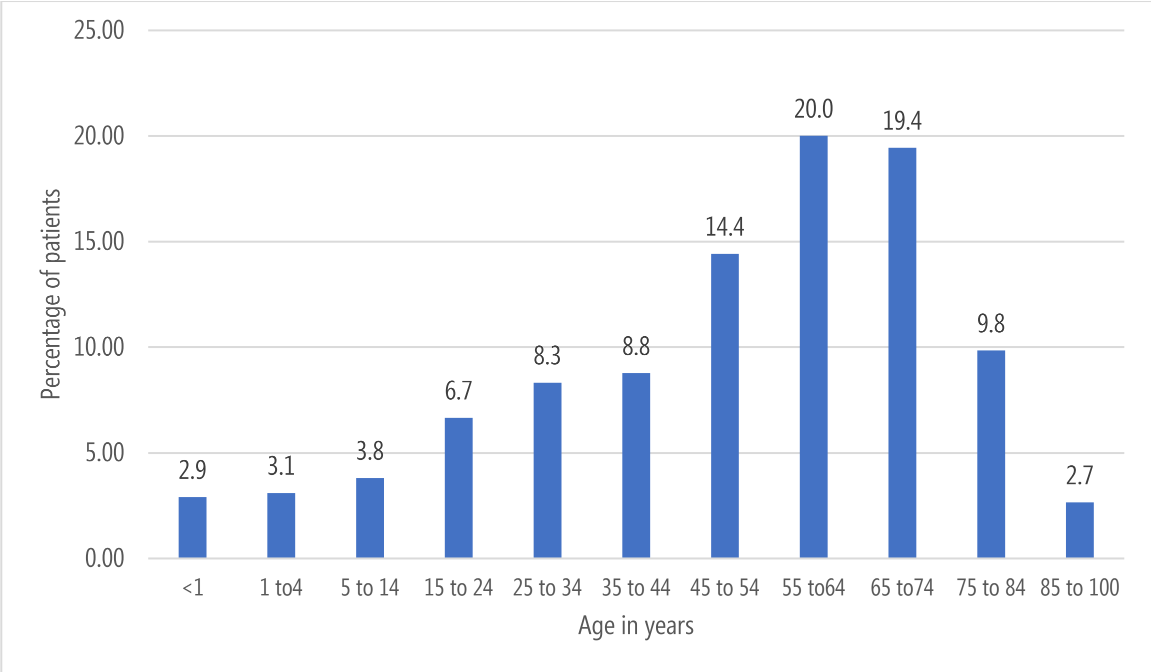

Figure 3: Distribution of isolates based on age

Of the total unique isolates (after de-duplication; 40,323) the following was the specimen distribution:

- Urine – 21,790 (54%)
- Blood – 3,538 (8.8%)
- Pus aspirate (PA) – 13,904 (34.5%)
- Other sterile body fluids (OSBF) – 1,042 (2.6%)
- Stool – 49 (0.1%)

The total number of isolates reported in the year 2023 has increased over those reported last year, probably due to the increase in reporting sites. In 2023 AMR surveillance data, the most commonly isolated priority pathogen was *E. coli* (40%), followed by *Klebsiella* species (23.5%), *Staph. aureus* (11.9%), *Pseudomonas* species (10.8%), *Enterococcus* species (8.1%), *Acinetobacter* species (5.2%), *Salmonella enterica* serovar Typhi & Paratyphi A & B (0.3%) and *Shigella* species (0.1%). (Figure 4).

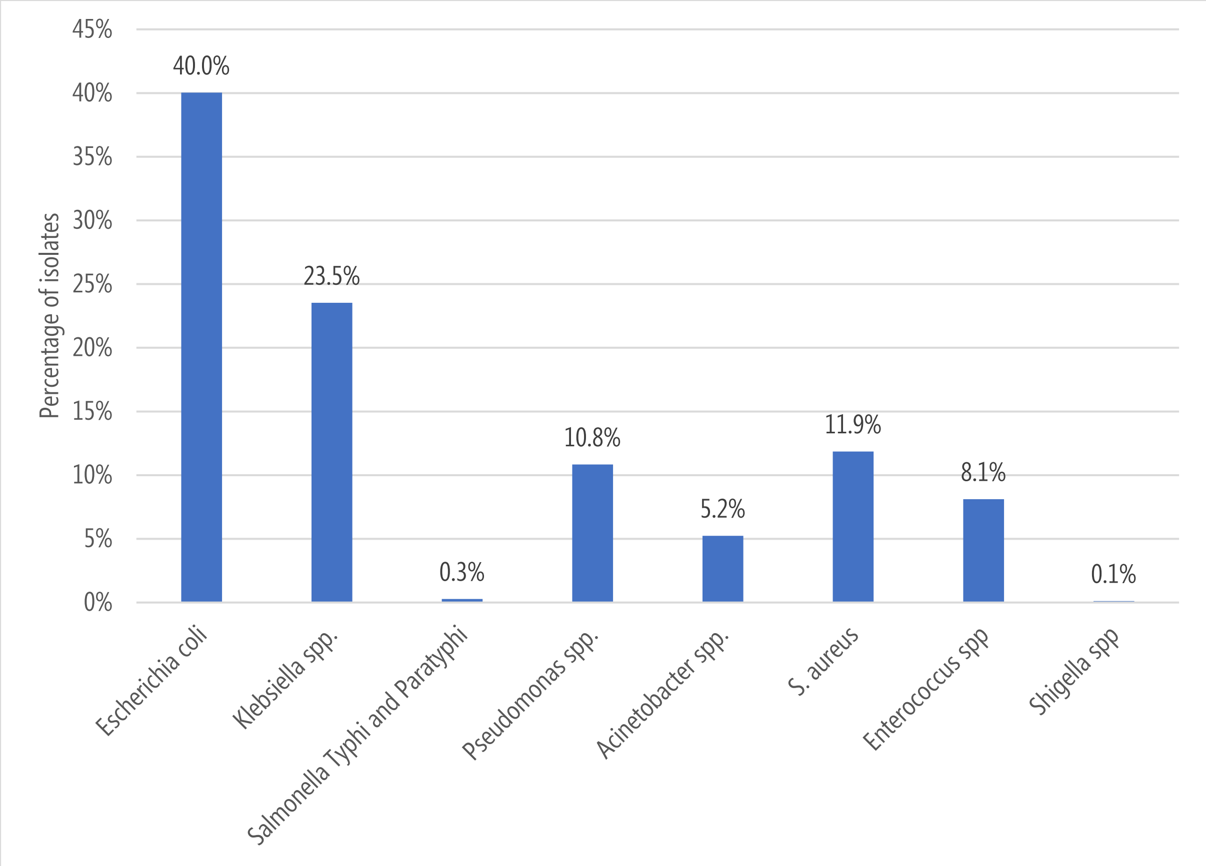

Figure 4: Distribution of AMR surveillance priority pathogens

Among all specimen types, highest number of *E. coli* (78.8%) were isolated from urine samples. From blood specimen the highest percentage of priority pathogen isolated was *Klebsiella* spp. (26%) and in pus aspirate it was *Staphylococcus aureus* (30%), while the lowest percentage of pathogens isolated from blood was *Salmonella enterica* serovar Typhi and Paratyphi A and B (3%). The most common pathogen isolated from OSBF was *Klebsiella* spp. (32%). Lowest percentage of pathogen isolated from PA was *Acinetobacter* spp. (6%) whereas from OSBF it was *Staphylococcus aureus* (8%) and *Enterococcus* species (8%); (Table 2, Figure 5). *Vibrio cholerae* was not reported from any of the centres.

Table 2: Specimen-wise isolation of priority pathogens

Priority pathogens	Blood (%)	PA (%)	OSBF (%)	Urine (%)	Stool (%)
Escherichia coli	717 (20%)	2490 (18%)	211 (20%)	12724 (58%)	
Klebsiella spp.	911 (26%)	2808 (20%)	329 (32%)	5439 (25%)	
Salmonella Typhi & Paratyphi	109 (3%)				3 (6%)
Shigella spp.					46 (94%)
Pseudomonas spp.	299 (8%)	2401 (17%)	190 (18%)	1480 (7%)	
Acinetobacter spp.	659 (19%)	873 (6%)	140 (13%)	441 (2%)	
Staph. aureus	574 (16%)	4123 (30%)	84 (8%)		
Enterococcus spp.	269 (8%)	1209 (9%)	88 (9%)	1706 (8%)	
Total	**3538**	**13904**	**1042**	**21790**	**49**

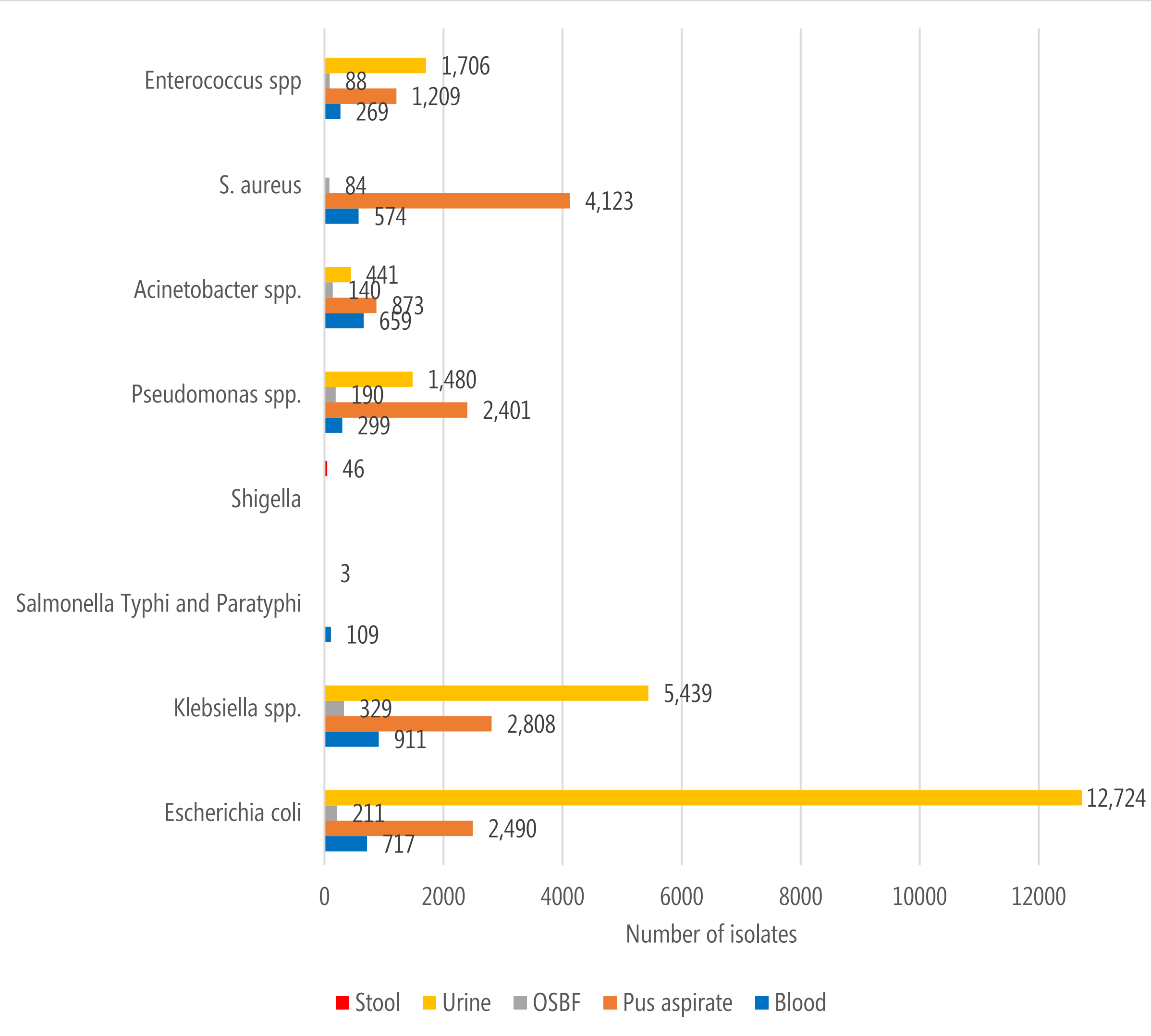

Figure 5: Specimen wise distribution of AMR surveillance priority pathogens

Out of the 40,323 isolates, 49% were from in-patients (IPD), 38% from out-patients (OPD) and 13% from patients in Intensive care units (ICU); (Figure 6). The most common pathogen isolated from IPD and OPD was *E. coli*. In IPD patients, maximum isolates were *E. coli* (38%) followed by *Klebsiella* spp. (24%), *Pseudomonas* spp. (11%), *Staph. aureus* (11%), *Enterococcus* spp. (9%) and *Acinetobacter* spp. (5%). Among OPD patients, the most common pathogen was *E. coli* (46%) followed by *Klebsiella* spp. (21%). In ICU facilities, *Klebsiella* spp. (29%) and *E. coli* (29%) were the most common pathogens isolated, followed by *Pseudomonas* spp *(12%)* and *Acinetobacter* spp. (12%); (Table 3, Figure 6). No *Vibrio cholerae* cases were reported.

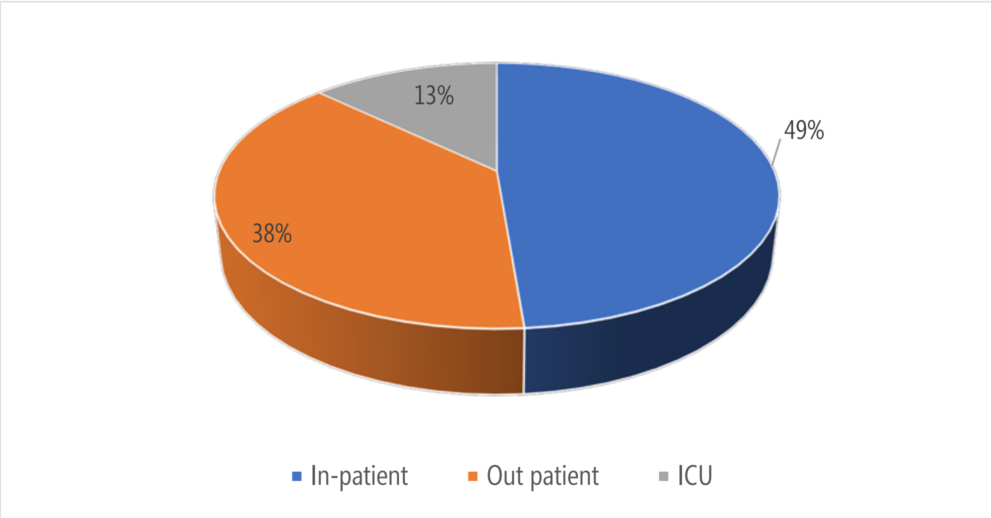

Figure 6: Location-wise distribution of isolates

Table 3: Location-wise distribution of priority pathogens

Priority Pathogens	ICU (%)	IPD (%)	OPD (%)
Escherichia coli	1,496 (29%)	7,531 (38%)	7,115 (46%)
Klebsiella spp.	1,504 (29%)	4,704 (24%)	3,279 (21%)
Salmonella Typhi and Paratyphi	2 (0.04%)	94 (0.48%)	16 (0.1%)
Pseudomonas spp.	598 (12%)	2,230 (11%)	1,542 (10%)
Acinetobacter spp.	597 (12%)	1,076 (5%)	440 (3%)
S. aureus	448 (9%)	2,162 (11%)	2,171 (14%)
Enterococcus spp.	543 (10%)	1,810 (9%)	919 (6%)
Shigella spp	1 (0.02%)	31 (0.16%)	14 (0.09%)
Total (N)	5,189	19,638	15,496

5. AMR profile of priority pathogens

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

a. Gram positive cocci

AMR surveillance under KARS-Net covers two important globally prevalent gram-positive bacterial pathogens i.e., *Staphylococcus aureus* and *Enterococcus* species. The AST data of 9,125 Gram positive cocci have been submitted by KARS-Net sites, of which 8,053 isolates are from unique patients.

Staphylococcus aureus

Staphylococcus aureus constituted 12% of all the isolates (Figure 4). Data of a total of 5,622 *S. aureus* isolates were submitted by the KARS-Net sites of which 4,781 isolates were from unique patients. Of the 4,781 isolates, 12% were from blood, 86% from PA and 1.8% from OSBF. Methicillin resistance was reported as 30% overall. Methicillin resistance was 33% in blood isolates, 29% in PA and 33% in OSBF (Table 4). Erythromycin resistance was observed in 64% of *S. aureus* isolated from blood; 53% from PA and 61% from OSBF (Table 4). Distribution of *S. aureus* isolates reported under the AMR programme in 2023 is from 9% of ICU patients, 11% of IPD patients and 14% of OPD patients (Table 3). Resistance profile of *S. aureus* isolated from blood from different location types is depicted in Figure 7.

Table 4: Resistance profile of *Staphylococcus aureus*

Antibiotic tested	**Blood** (N = 574)			**PA** (N = 4123)			**OSBF** (N = 84)		
	Number tested	Number Resistant	**Resistance** (%)	Number tested	Number Resistant	**Resistance** (%)	Number tested	Number Resistant	**Resistance** (%)
Cefoxitin	499	166	33	3596	1050	29	72	24	33
Gentamicin	516	96	19	3480	443	13	52	12	23
Ciprofloxacin	359	166	46	3296	1547	47	44	20	45
Co-trimoxazole	498	72	14	3656	292	8	81	4	5
Clindamycin	479	130	27	3846	702	18	72	19	26
Erythromycin	532	342	64	4057	2137	53	82	50	61
Linezolid	431	0	0	3464	0	0	62	0	0
Teicoplanin	110	1	1	790	4	1	18*	0	-
Doxycycline	185	6	3	1780	26	1	16*	0	-
Vancomycin	331	0	0	1985	0	0	46	0	0

* Percentage not computed due to numbers being < 30

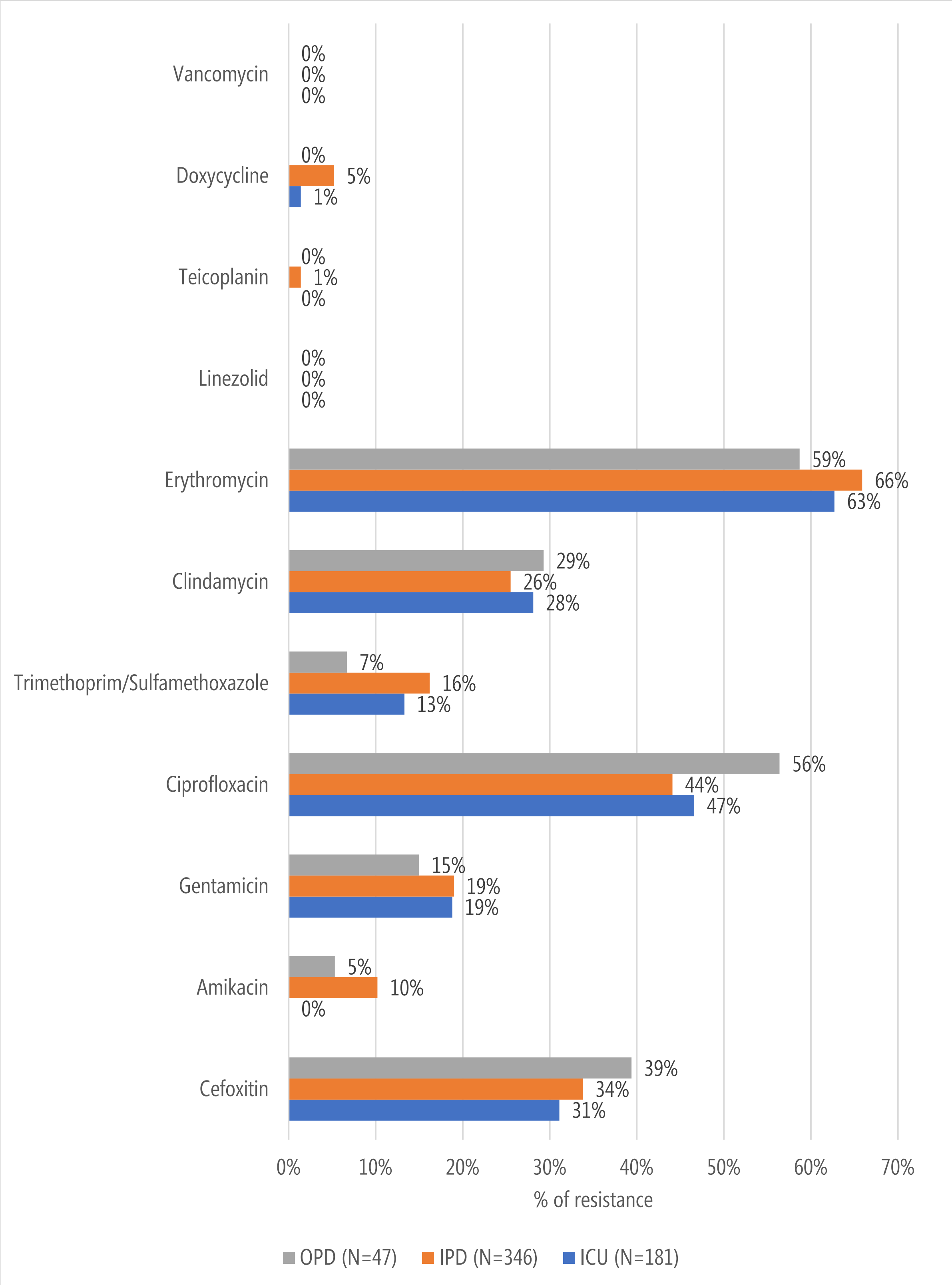

Figure 7: Resistance profile of S. aureus isolated from blood from different location types

Enterococcus species

During the reporting period, *Enterococcus* species constituted 8% of all isolates (Figure 4). The data of 3,503 isolates of *Enterococcus* species were submitted by KARS-Net sites of which 3,272 isolates were from unique patients. Reported *Enterococcus species* represent 8% of blood culture isolates, 9% of OSBF isolates and PA each, and 8% of urine isolates (Table 2).

Vancomycin resistance among urinary isolates was 2%, blood isolates was 3% and pus aspirates was 1%. No VRE was reported from OSBF. Two isolates (one from urine and another from pus aspirate) showed linezolid resistance. An overall 1.8% vancomycin resistance was observed. Resistance profile of *Enterococcus* species is given in Table 5.

Table 5: Resistance profile of *Enterococcus* species

Antibiotic tested	**Blood** (N=269)			**PA** (N=1209)			**OSBF**(N=88)			**Urine** (N=1706)		
	Number tested	No. Resistant	**Resistance %**	Number tested	No. Resistant	**Resistance %**	Number tested	No. Resistant	**Resistance %**	Number tested	No. Resistant	**Resistance %**
Ampicillin	220	83	38	1,105	213	19	69	32	46	1,342	559	42
Gentamicin HLAR	214	64	30	1,068	233	22	66	22	33	1,286	446	35
Ciprofloxacin										1,268	906	71
Erythromycin	190	149	78	932	667	72	73	50	68			
Linezolid	217	0	0	1,042	1	0.1	78	0	0	1,329	1	0.1
Vancomycin	235	7	3	1,046	12	1	84	0	0	1,485	32	2
Teicoplanin	75	4	5	275	5	2	29*	0	-	452	8	2
Doxycycline	71	33	46	200	45	23	32	16	50			
Fosfomycin										418	115	28
Tetracycline	19*	13	-	46	34	74	10*	5	-	1,087	762	70
Nitrofurantoin										1,232	375	30

* Percentage not computed due to numbers being less than 30

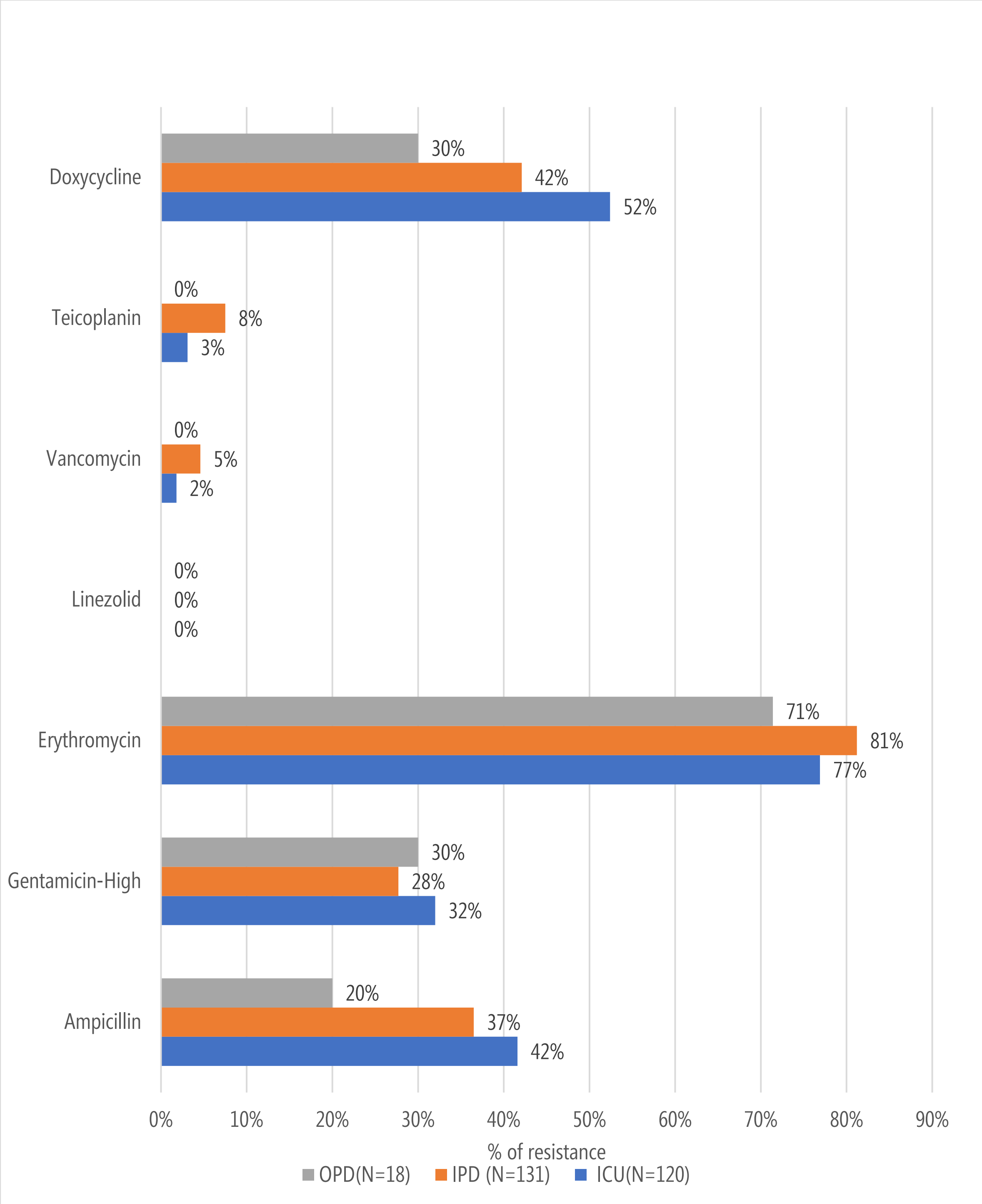

Figure 8: Resistance profile of Enterococcus species isolated from blood

b. Gram negative bacilli

Under KARS-Net, seven commonly isolated gram-negative bacilli of public health importance are included for AMR surveillance. These are *E. coli*, *Klebsiella* species, *Pseudomonas* species, *Acinetobacter* species, *Salmonella enterica* serovar Typhi and Paratyphi, *Shigella* species and *Vibrio cholerae*.

AST data of 36,272 isolates of Gram-negative bacilli have been reported from 32,270 unique patients during the reporting period. No *Vibrio cholerae* cases were reported during this period.

1) Enterobacteriaceae

During January to December 2023, *E. coli*, *Klebsiella* species, *Salmonella enterica* serovar Typhi, Paratyphi and *Shigella* spp AST data submitted by network sites accounted for 29,156 (64%) isolates from 25,787 (64%) unique patients. In concordance to KARS-Net report 2023 (data from 2022), this year also maximum isolates belonged to Enterobacteriaceae.

Escherichia coli

A total of 17,994 *E. coli* isolates were reported from 16,142 unique patients. *E. coli* constituted 40% of data reported from unique patients for the year 2023. 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 85% in all specimen types. Cefotaxime resistance was observed in >60% from *E. coli* isolated from all specimen types. Among blood isolates of *E. coli*, 71% were ESBL producers. Carbapenem resistance observed in *E. coli* isolates from blood was 11%. For non-beta-lactam antibiotics, 66% resistance was observed to ciprofloxacin and 47% to trimethoprim-sulfamethoxazole (TMP/SMX). Twenty one per cent blood isolates showed resistance to piperacillin tazobactam. Around 10% resistance to nitrofurantoin was seen in urinary isolates (Table 6). The colistin susceptibility testing was done using the broth microdilution method as per CLSI M02 and M100, though for a limited number of isolates. Only two *E.coli* isolates were resistant to colistin (Table 6, Figure 9).

Table 6: Resistance profile of *Escherichia coli*

Antibiotic tested	Blood (N=717)			PA (N=2,490)			OSBF (N=211)			Urine (N=12,724)		
	Number tested	Number resistant	Resistance %	Number tested	Number resistant	Resistance %	Number tested	Number resistant	Resistance %	Number tested	Number resistant	Resistance %
Ampicillin	373	330	88	1993	1765	89	159	138	87	9973	8500	85
Co-amoxyclav	337	110	33	1116	424	38	81	30	37	6054	1675	28
Piperacillin-Tazobactam	681	141	21	2351	503	21	203	50	25	10575	1621	15
Cefuroxime	401	289	72	1103	755	68	78	50	64	8230	5043	61
Ceftriaxone	526	360	68	1647	1086	66	128	82	64	6589	4232	64
Cefotaxime	411	290	71	1514	981	65	153	97	63	7596	4631	61
Cefepime	473	252	53	1650	761	46	131	57	44	9349	4201	45
Ertapenem	202	24	12	644	77	12	39	8	21	4605	270	6
Imipenem	584	65	11	1911	219	11	142	29	20	9840	723	7
Meropenem	638	70	11	2084	196	9	167	26	16	9358	567	6
Amikacin	693	106	15	2303	368	16	203	38	19	11007	1347	12
Gentamicin	677	201	30	2355	617	26	205	63	31	11647	2320	20
Ciprofloxacin	688	457	66	2390	1427	60	201	124	62	10906	5905	54
Co-trimoxazole	620	294	47	1913	849	44	162	63	39	11499	4504	39
Colistin	320	1	0.31	916	0	0	86	0	0	2554	1	0.04
Doxycycline				201	54	27	16*	6	-			
Fosfomycin										2094	36	2
Nitrofurantoin										11989	1231	10

* Percentage not computed due to numbers being less than 30

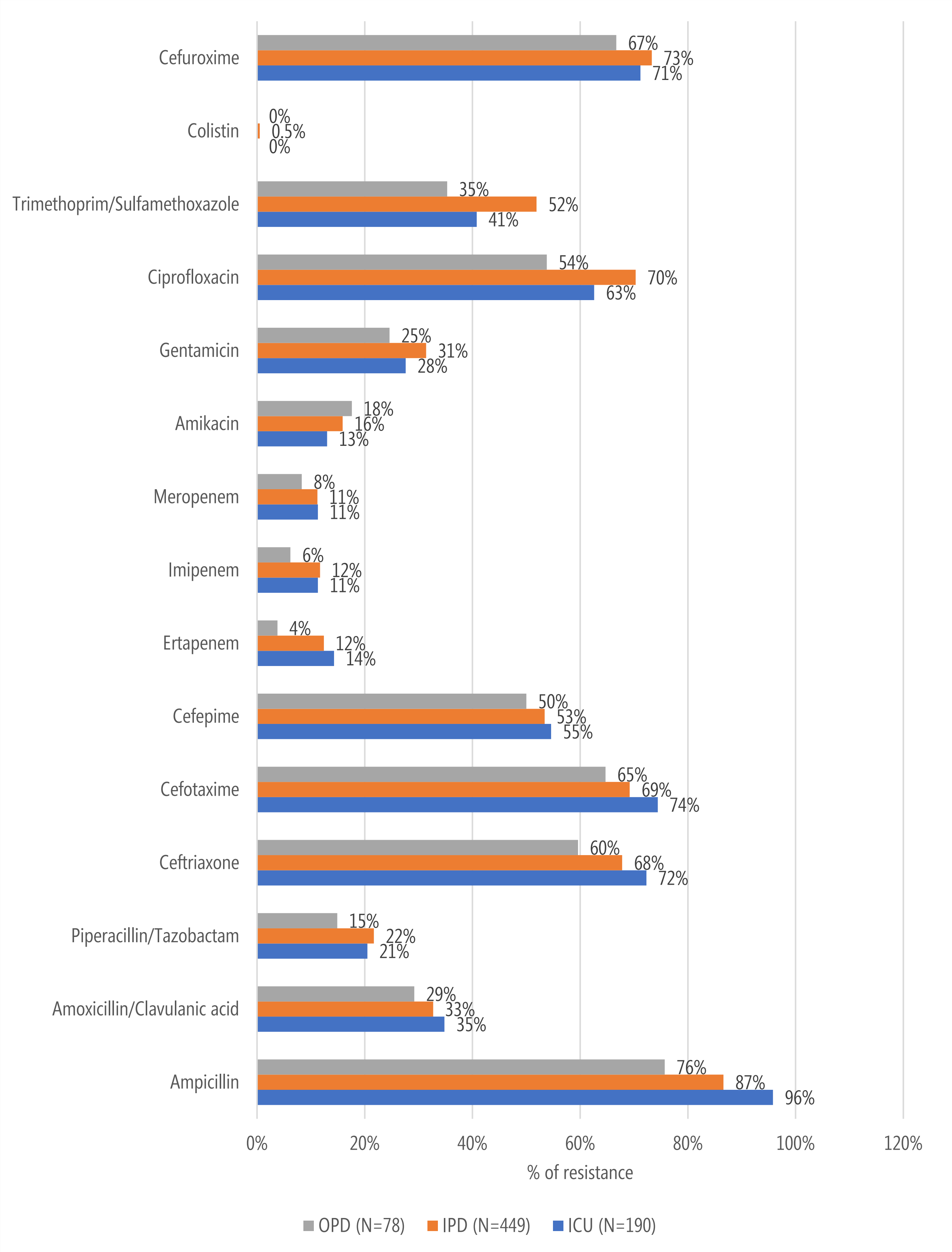

Figure 9: Resistance profile of Escherichia coli isolated from blood

Klebsiella species

High level of resistance was observed in *Klebsiella* spp. isolated from all specimen types and for all antibiotics, except colistin. Total of 5,439 *Klebsiella species* were isolated from urine specimens. Cefotaxime resistance in the blood isolates was 74% followed by 64% in PA isolates, 66% in OSBF isolates and 56% in urinary isolates. Highest resistance to carbapenems was observed in isolates of *Klebsiella* spp. from blood i.e., 43% compared to the other specimen types (Table 7). ESBL production was observed in 74% of blood isolates. Colistin resistance of *Klebsiella* spp from blood was 2%.

Table 7: Resistance profile of *Klebsiella species*

Antibiotic tested	**Blood** (N=911)			**PA** (N=2,808)			**OSBF** (N=329)			**Urine** (N=5439)		
	Number tested	Number resistant	Resistance %	Number tested	Number resistant	Resistance %	Number tested	Number resistant	Resistance %	Number tested	Number resistant	Resistance%
Co-amoxyclav	366	197	54	1247	651	52	117	45	38	2519	1008	40
Piperacillin/ Tazobactam	853	480	56	2669	1214	45	315	150	48	4731	1658	35
Cefuroxime	427	296	69	1282	860	67	158	112	71	3663	2077	57
Ceftriaxone	366	197	69	1933	1198	62	241	155	64	3049	1677	55
Cefotaxime	741	143	74	1820	1172	64	261	171	66	3454	1932	56
Cefepime	853	480	64	2032	1143	56	183	97	53	4178	1896	45
Ertapenem	227	96	42	795	305	38	76	24	32	2155	523	24
Imipenem	670	275	41	2242	785	35	240	99	41	4444	1044	23
Meropenem	841	361	43	2487	855	34	282	106	38	4386	1035	24
Amikacin	871	411	47	2622	940	36	319	104	33	4866	1350	28
Gentamicin	850	416	49	2678	1095	41	313	124	40	5070	1493	29
Ciprofloxacin	865	572	66	2710	1686	62	325	190	58	4706	2481	53
Trimethoprim/ Sulfamethoxazole	726	382	53	2309	1142	49	278	133	48	4966	2015	41
Colistin	423	7	2	1226	3	0.24	146	1	0.68	1864	6	0.32
Doxycycline				148	26	18	18*	7	-			
Nitrofurantoin										5029	2377	47

* Percentage not computed due to numbers being less than 30

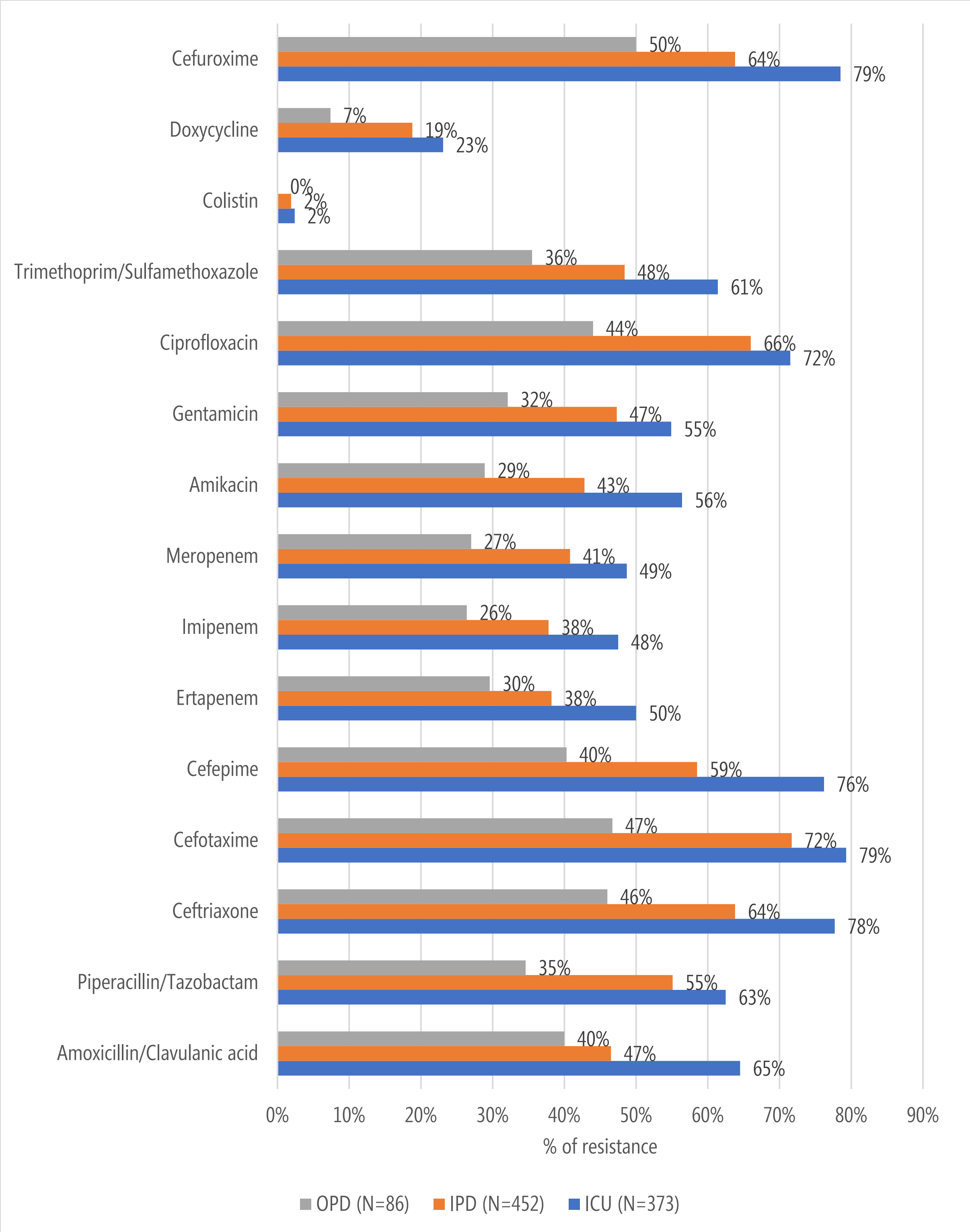

Figure 10: Resistance profile of Klebsiella species isolated from blood

Salmonella enterica serovar Typhi and Paratyphi

AMR surveillance data of 148 *Salmonella* enterica serovar Typhi and Paratyphi isolates showed that 112 isolates were from unique patients. Low resistance to first-line antibiotics (3% for ampicillin) was observed compared to ciprofloxacin (61%) in *S. Typhi*.

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

Antibiotic tested	*S. Typhi* (N=95)			*S. Paratyphi* (N=17)	
	Number tested	Number Resistant	% Resistant	Number tested	Number Resistant
Ampicillin	62	2	3	12*	1
Ceftriaxone	87	0	0	13*	0
Imipenem	51	0	0	7*	0
Ciprofloxacin	95	58	61	17*	9
Azithromycin	31	0	0	6*	0
Chloramphenicol	45	0	0	8*	0
Trimethoprim/Sulfamethoxazole	86	0	0	13	0

* Percentage not computed due to numbers being less than 30

Shigella species

The resistance profile of 46 *Shigella* isolates (from 46 unique patients) showed that resistance to ciprofloxacin was 91% and an alarming resistance rate was observed for azithromycin (25%).

Table 9: Resistance profile of *Shigella* spp

Antibiotic tested	***Shigella* spp** (N=46)		
	Number tested	Number Resistant	% Resistant
Ampicillin	45	19	42
Ceftriaxone	14*	3	-
Ciprofloxacin	45	41	91
Azithromycin	44	11	25
Chloramphenicol	14*	1	-
Trimethoprim/Sulfamethoxazole	44	11	25

* Percentage not computed due to numbers being less than 30

2) Non-fermenting Gram-negative bacilli

Among the non-fermenting Gram-negative bacilli (NFGNB) collected during Jan-Dec 2023 across all KARS-Net sites, *Pseudomonas* species (4,370) was the most common pathogen isolated followed by *Acinetobacter* species (2,113). Similar isolation rates of NFGNB were observed as last year.

Pseudomonas species

Pseudomonas species isolated from blood showed 20% resistance to meropenem as well as piperacillin-tazobactam. Isolates from blood in ICU, IPD and OPD patients showed high resistance to ceftazidime i.e., 46%, 30% and 17%, respectively. Carbapenem-resistance was observed in 26% of *Pseudomonas* spp. isolated from urine. (Table 10, Figure 11).

Table 10: Resistance profile of *Pseudomonas species*

Antibiotic tested	**Blood** (N=299)			**PA** (N=2,401)			**OSBF** (N=190)			**Urine** (N=1,480)		
	Number tested	Number resistant	Resistance %	Number tested	Number resistant	Resistance %	Number tested	Number resistant	Resistance %	Number tested	Number resistant	Resistance %
Piperacillin-Tazobactam	283	57	20	2260	505	22	187	60	32	1375	363	26
Ceftazidime	291	94	32	2334	759	33	186	71	38	1391	526	38
Aztreonam	89	18	20	533	108	20	30	8	27	440	147	33
Imipenem	204	39	19	2001	297	15	113	46	41	1130	328	29
Meropenem	257	51	20	2080	268	13	144	41	28	1245	323	26
Amikacin	247	53	21	1367	250	18	120	29	24	1272	327	26
Gentamicin	226	60	27	1522	347	23	131	33	25	962	264	27
Ciprofloxacin	255	60	24	2249	663	29	174	56	32	1269	418	33
Colistin	98	0	0	753	3	0.4	48	0	0	413	1	0.24
Netilmicin	9*	4	-	243	59	24	8*	4	-	197	80	41

* Percentage not computed due to numbers being less than 30

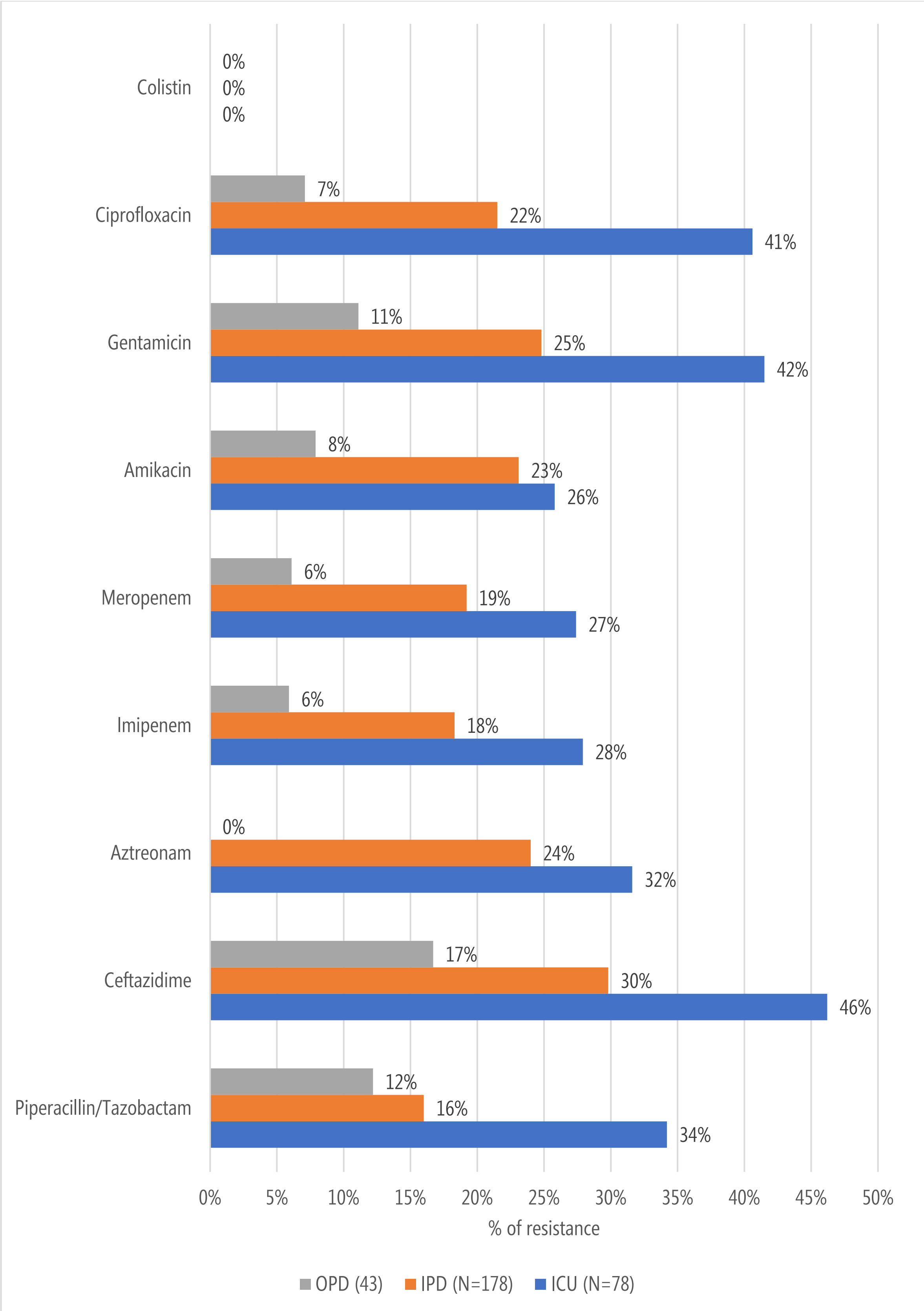

Figure 11: Resistance profile of Pseudomonas species isolated from blood

Acinetobacter species

Data from a total of 2,298 *Acinetobacter* species isolates was submitted by network sites, of which 2,113 were from unique patients. Majority of *Acinetobacter* spp. were from pus aspirate (41.3%), unlike the previous year where maximum number of isolates were obtained from blood. Sixty one per cent resistance to imipenem was observed in blood isolates. *Acinetobacter spp*. isolated from all specimen types showed highest resistance to ceftazidime (Table 11, Figure 12).

Table 11: Resistance profile of *Acinetobacter species*

Antibiotic tested	**Blood** (N=659)			**PA** (N=873)			**OSBF** (N= 140)			**Urine** (N=441)		
	Number tested	Number resistant	Resistance %	Number tested	Number resistant	Resistance %	Number tested	Number resistant	Resistance %	Number tested	Number resistant	Resistance %
Ampicillin/ Sulbactam	94	42	45	186	101	54	41	30	73	92	26	28
Piperacillin/ Tazobactam	609	339	56	818	582	71	132	89	67	393	131	33
Ceftazidime	404	264	65	634	476	75	60	40	67	228	106	46
Imipenem	443	268	60	756	509	67	108	82	76	325	112	34
Meropenem	537	285	53	703	453	**64**	115	79	69	311	100	32
Amikacin	613	298	49	792	479	60	138	79	57	386	110	28
Gentamicin	619	317	51	817	550	67	132	87	66	397	120	30
Ciprofloxacin	546	283	52	784	580	74	123	80	65	385	136	35
Cotrimoxazole	527	255	48	751	452	60	123	67	54	376	89	24
Colistin	290	1	0.34	422	1	0.24	75	1	1	144	0	0
Minocycline	289	97	34	424	170	40	78	20	26	124	11	9
Tetracycline										118	30	25

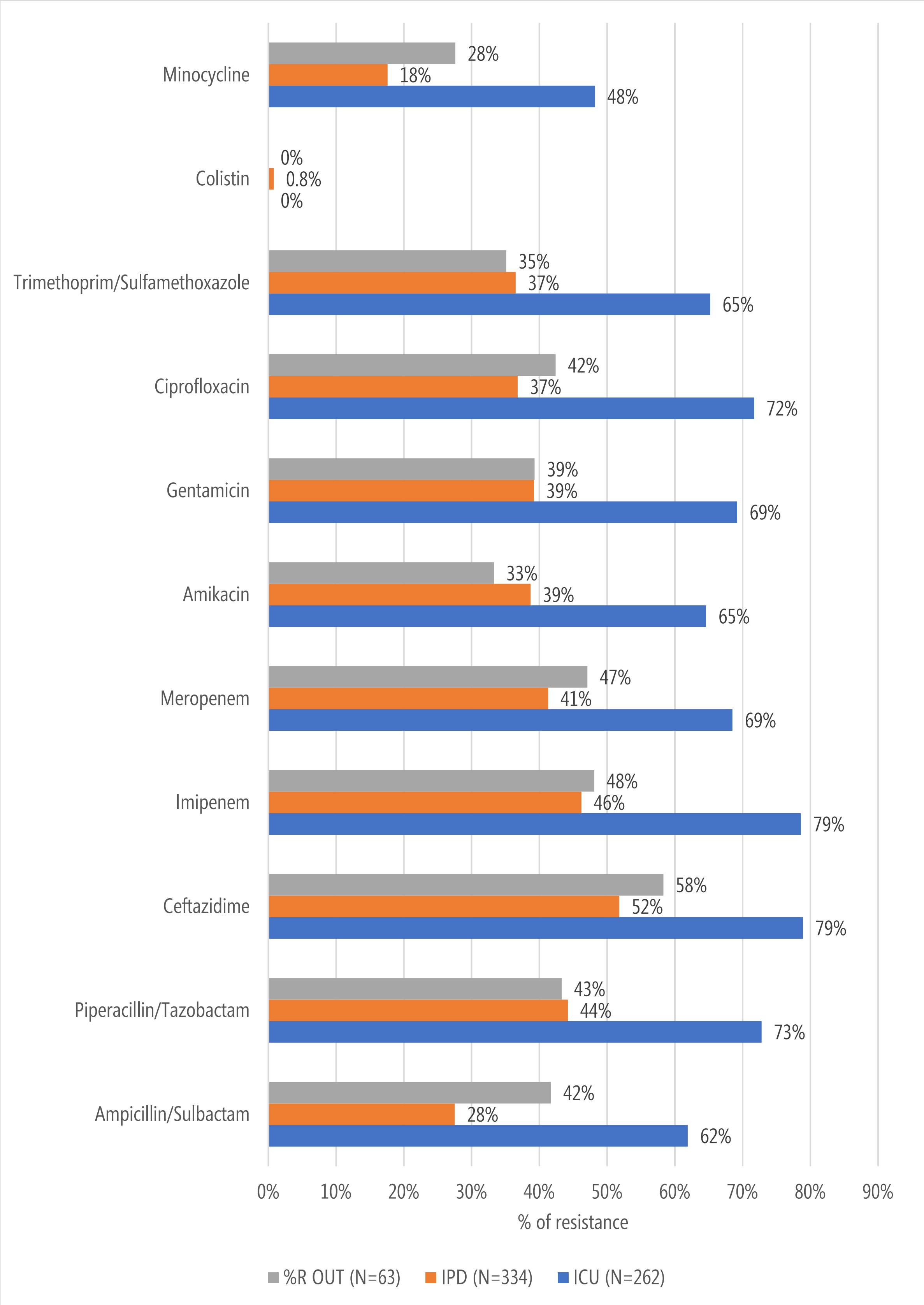

Figure 82: Resistance profile of Acinetobacter species isolated from blood

6. Trends of AMR in Kerala over 5 years

The trends of AMR in Kerala over five years (2018, 2019, 2021, 2022 and 2023) 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 COVID pandemic. It was observed that ESBL production as well as carbapenem resistance has been increasing over the years except for *E. coli* (Figures 13 and 14). 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 the pandemic and majority of centres being COVID care centres. Slight increase in MRSA rates were observed during the past year. But the VRE rates have shown a decreasing trend (Figure 15).

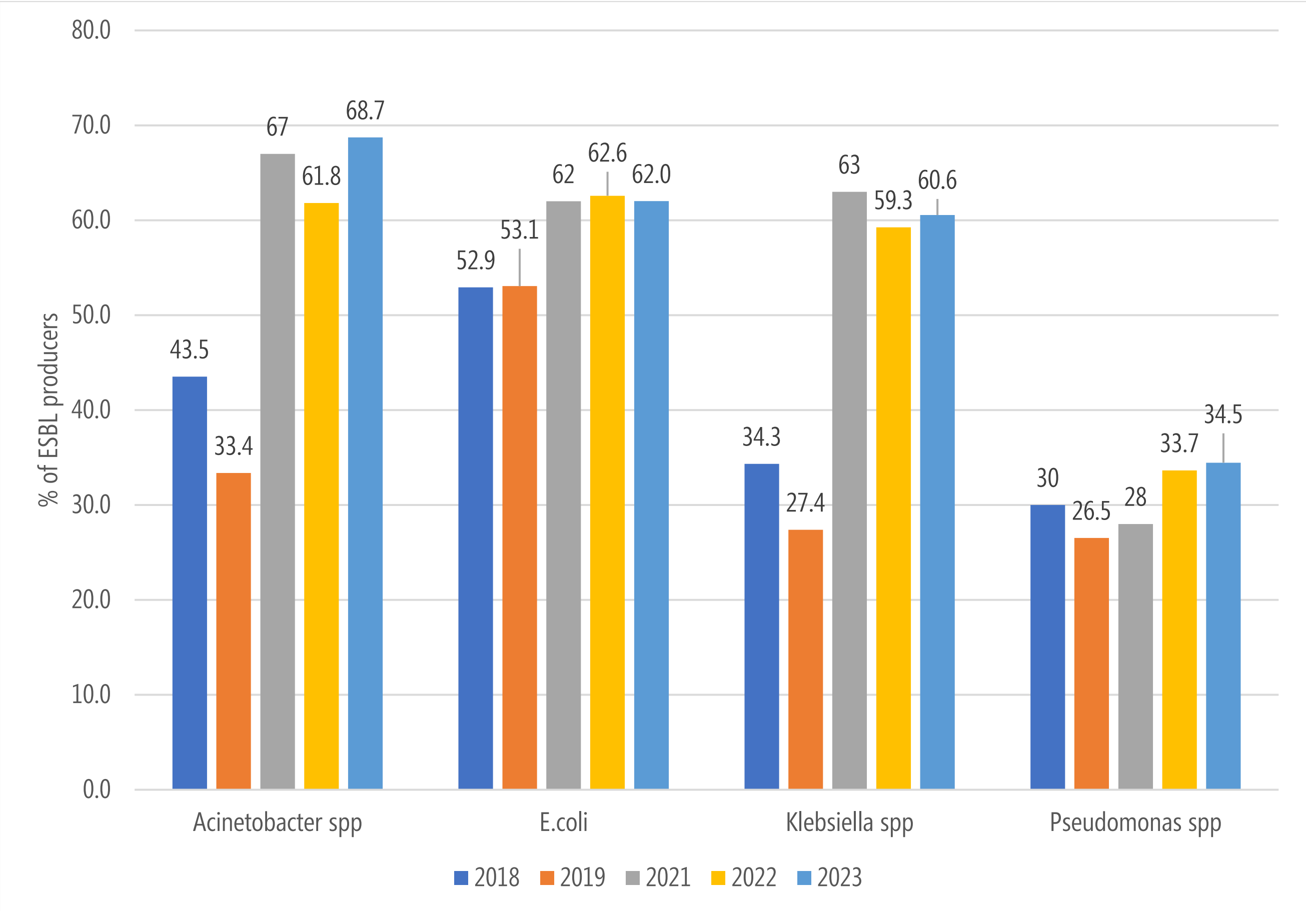

Figure 93: Evidence from KARS-Net – ESBL trends over 5 years

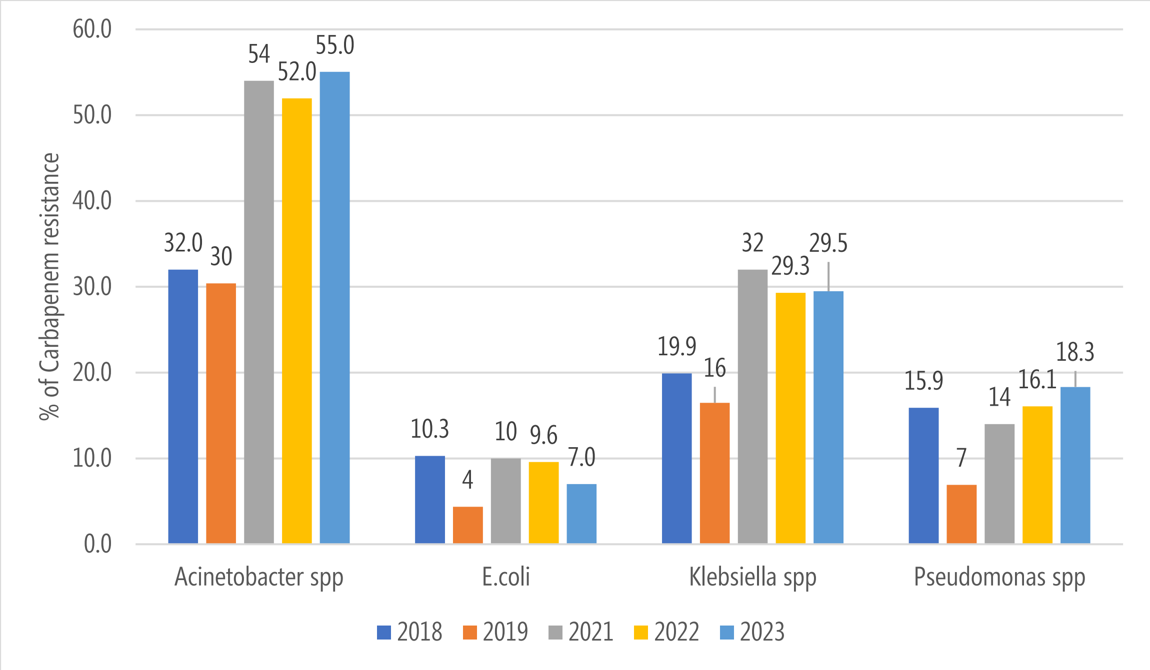

Figure 104: Evidence from KARS-Net – Carbapenem resistance trends over 5 years

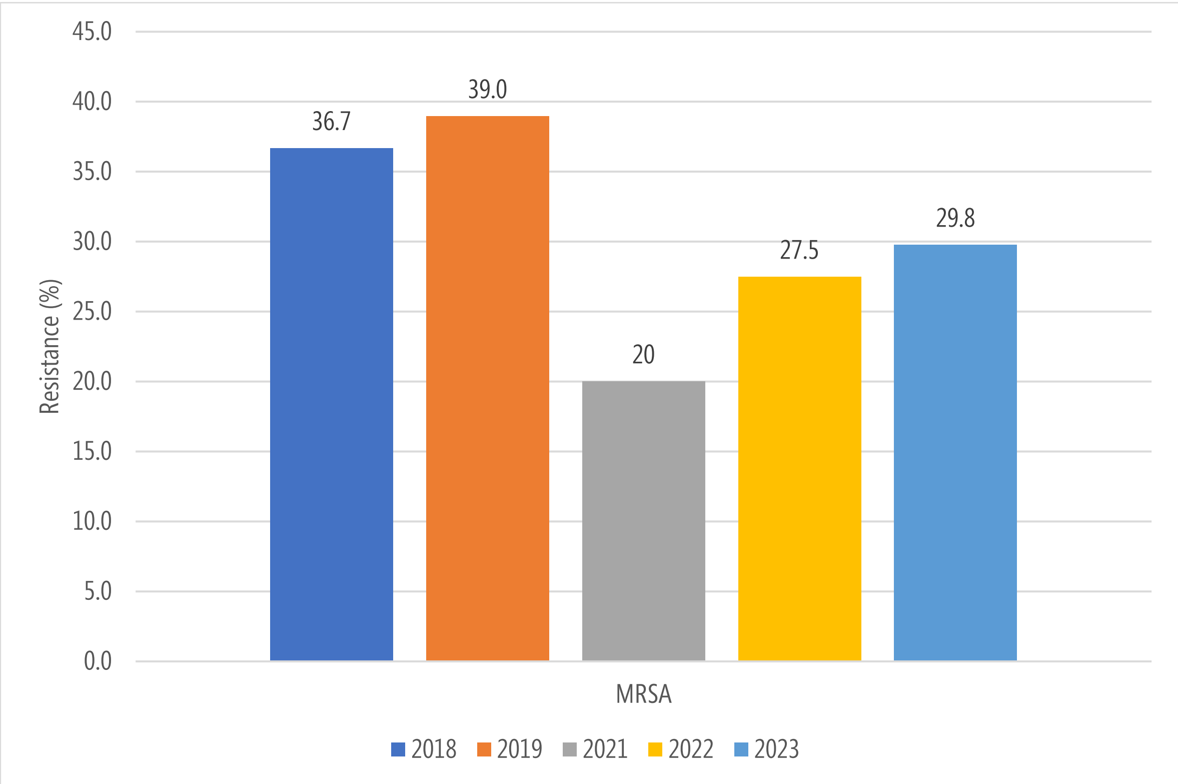

Figure 115: Evidence from KARS-Net – MRSA trends over 5 years

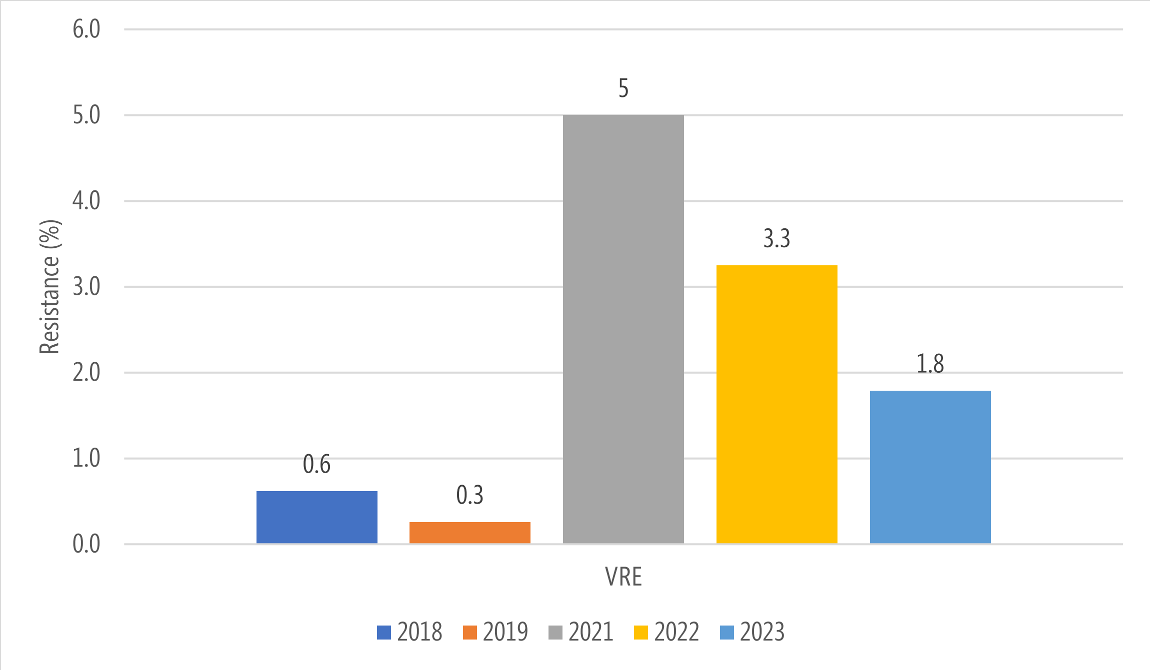

Figure 126: Evidence from KARS-Net – VRE trends over 5 years

7. 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 emerging 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 12 districts across the state. AMR surveillance under KARS-Net includes standardised collection, collation, 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 Global AMR Surveillance System (GLASS).

The 2024 report presents data analysed from 34 sentinel sites located in 11 districts of Kerala from January to December 2023. Compared to the previous years' Kerala AMR surveillance report which included 2021 data from 18 network sites, and 2022 data from 23 network sites, the number of sites submitting AMR data during 2023 has increased to 34 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 AMR programme.

E. coli was the most common pathogen isolated (40%) in the AMR surveillance data of 2023 which is similar to the previous year report. Amongst urinary isolates, *E. coli* was the most common pathogen isolated (58%) while *Klebsiella spp.* (26%) was the most common pathogen isolated from blood. This finding corroborated with the previous year's report. *Klebsiella* spp. was the predominant pathogen isolated from OSBF (32%), while *Staphylococcus aureus* was the predominant pathogen isolated from PA (30%). In terms of location type, *E coli* was the most common priority pathogen isolated from OPD (46%) and IPD (38%) settings. In the ICU setting, both *E.coli* and *Klebsiella* spp. were the common pathogens reported, each amounting to 29%. Similar pathogen burden in respective location types was also seen in the previous year report. An increase in the proportion of MRSA among the *S. aureus* isolates from blood was noted this year (33%), compared to the previous year (27%). *Enterococcus spp.* isolated from blood cultures showed 3% resistance to vancomycin, whereas it was 2% during the previous year. About 12% 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.

Annexure

List of KARS-Net surveillance sites

1. Government Medical College (GMC), Thiruvananthapuram
2. Government Medical College (GMC), Kozhikode
3. Government Medical College (GMC), Thrissur
4. Government Medical College (GMC), Kottayam
5. Government T.D Medical College (GMC), Alappuzha
6. Government Medical College (GMC), Manjeri
7. Government Medical College (GMC), Ernakulam
8. Government Medical College (GMC), Kollam
9. General Hospital (GH), Ernakulam
10. State Public Health Laboratory, Thiruvananthapuram
11. Believers Church Medical College Hospital, Tiruvalla
12. Aswini Diagnostic Services, Kozhikode
13. Dane Diagnostic Services, Palakkad
14. Karuna Medical College, Palakkad
15. Pushpagiri Medical College Hospital, Tiruvalla
16. Regional Cancer Centre, Thiruvananthapuram
17. Sree Chitra Tirunal Institute for Medical Sciences &Technology, Thiruvananthapuram
18. MVR Cancer Centre, Kozhikode
19. Thangam Hospital of PMRC, Palakkad
20. Rajiv Gandhi Centre for Biotechnology, Thiruvananthapuram
21. General Hospital, Thiruvananthapuram
22. General Hospital, Kottayam
23. Government Medical College (GMC), Kannur
24. Jubilee Mission Medical College and Research institute, Thrissur
25. Amala Institute of Medical Sciences, Thrissur
26. MES Medical College and Paramedical Science, Perinthalmanna
27. Malabar Cancer Centre, Thalassery
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
32. Government Medical College (GMC), Konni
33. Dr Somervell Memorial CSI Medical College, Karakonam
34. Mount Zion Medical College, Adoor
35. KMCT Medical College, Mukkam
36. MOSC Medical college, Kolenchery
37. Gokulam Medical College and Research Foundation, Venjarammoodu
38. PRS hospital, Thiruvananthapuram
39. KIMSHEALTH Hospital, Thiruvananthapuram
40. Government Medical College (GMC), Wayanad
41. Azeezia Medical College, Kollam
42. District Hospital Kollam
43. Taluk Head Quarters Hospital Punalur
44. Public Health Lab, Alappuzha
45. General Hospital, Thrissur
46. General Hospital, Kozhikode
47. Travancore Medical College Hospital, Kollam
48. Kannur Medical College, Anjarakkandy
49. Dr Moopen’s Medical College, Wayanad

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