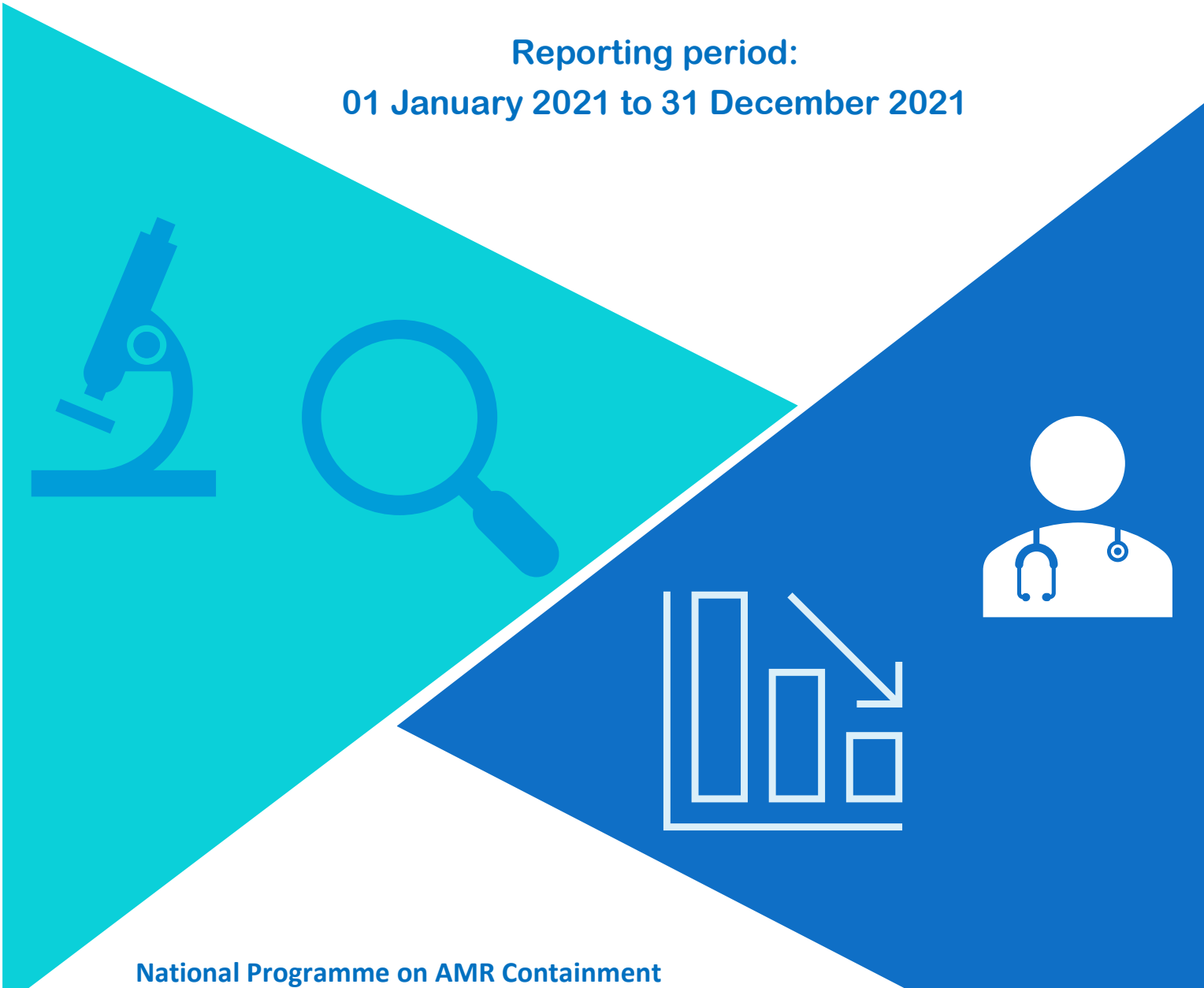
MINISTRY OF HEALTH & FAMILY WELFARE
GOVERNMENT OF INDIA

ANNUAL REPORT

NATIONAL ANTIMICROBIAL RESISTANCE SURVEILLANCE NETWORK (NARS-NET)

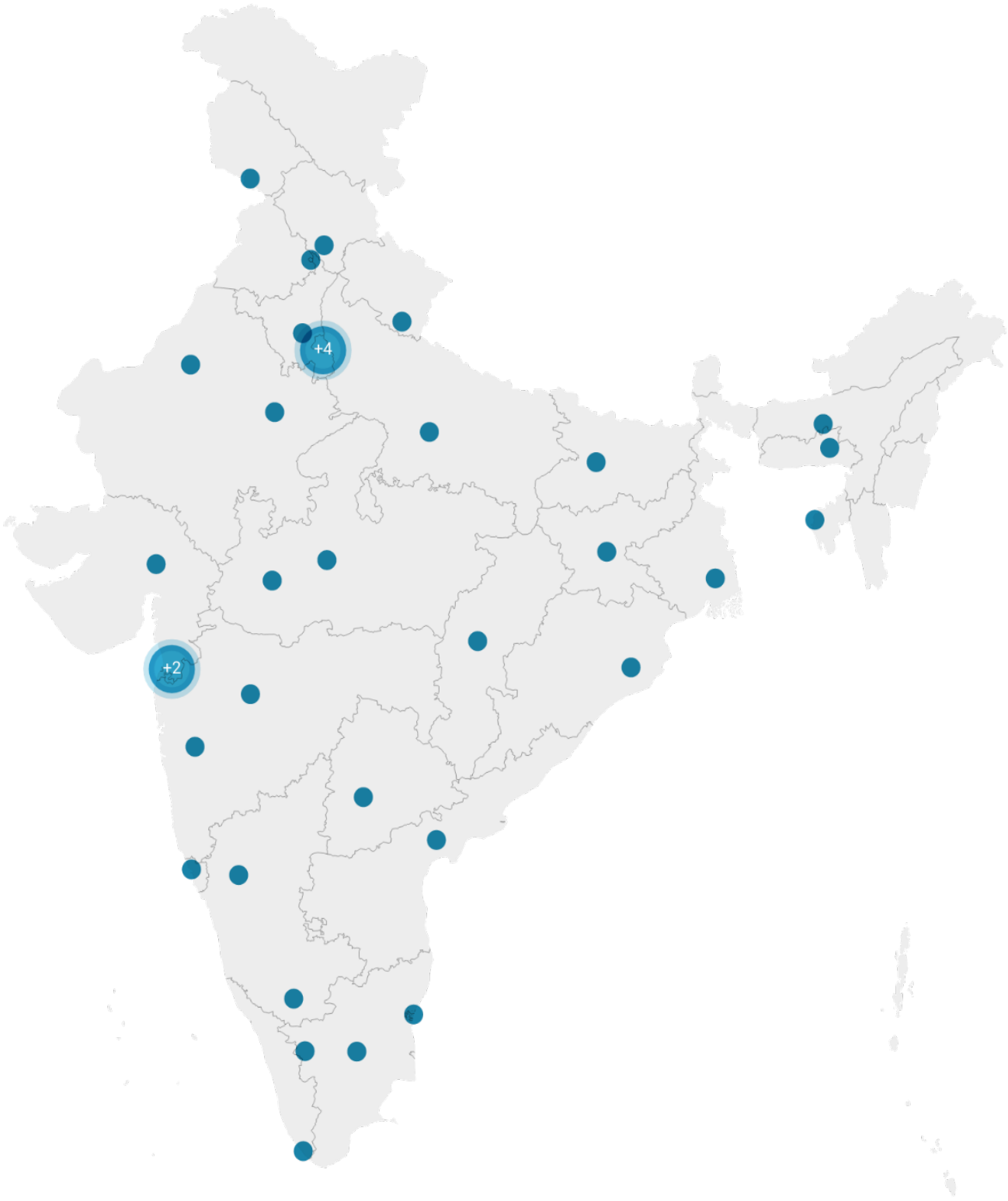
Reporting period:
01 January 2021 to 31 December 2021



National Programme on AMR Containment
National Centre for Disease Control (NCDC)
Directorate General of Health Services,
Ministry of Health and Family Welfare
Government of India

July 2022

National Antimicrobial Resistance Surveillance Network (NARS-Net India)



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Acronyms

AMR	Antimicrobial Resistance
AST	Antimicrobial Susceptibility Testing
BMD	Broth Microdilution
CLSI	Clinical & Laboratory Standards Institute
CSV	Comma-delimited
EQAS	External Quality Assessment Scheme
GLASS	Global Antimicrobial Resistance Surveillance System
IPD	In-patient
ICU	Intensive Care Unit
ID	Identification
IQC	Internal Quality Control
LIMS	Laboratory Information Management System
MRSA	Methicillin-Resistant S. aureus
NARS-Net	National AMR Surveillance Network
NFGNB	Non-fermenting Gram-negative bacilli
NCDC	National Centre for Disease Control
NRL	National Reference Laboratory
OPD	Outpatient
OSBF	Other Sterile Body Fluids
PA	Pus aspirate
R I S	Resistant Intermediate Sensitive
TMP-SMX	Trimethoprim-Sulfamethoxazole
SOP	Standard Operating Procedure
VBA	Virtual Basic Application
VRE	Vancomycin-Resistant Enterococcus species
WHO	World Health Organization

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I. EXECUTIVE SUMMARY

Antimicrobial resistance has emerged as a significant public health threat that requires urgent attention. To generate evidence of AMR Government of India initiated National Programme on AMR Containment in 2013. One of the key objectives of this program is to strengthen the laboratory capacity in state medical colleges for AMR surveillance. The network of labs over the years has been expanded from 10 in 8 states to 36 labs in 26 states in a phased manner (Fig 1). Priority pathogens under surveillance currently include seven 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 01 January 2021 to 31 December 2021. A total of 35 medical college laboratories from 25 states and UTs submitted their AMR data during this period. Under NARS-Net during 2021, antimicrobial susceptibility (AST) data of 96,370 priority pathogens, along with the demographic information of the patients from whom these pathogens were isolated, was reported from 35 sites in 25 states/UTs. After data deduplication, 87,996 unique patient isolate data were analysed; 55% (48398) of reported isolates were from male patients; 58% were from inpatients.

Urine was the most reported specimen 39% (34509), followed by pus aspirate 35% (30366), blood 22% (19097), and Other sterile body fluids 5% (4023). The frequently reported priority pathogen from all specimens was *E. coli* 29.8 %, followed by *Klebsiella* species 21.2 %, *S. aureus* 16.7%, *Pseudomonas* species 12.6 %, *Acinetobacter* species 10% *Enterococcus* species 9.5% and *Salmonella* enterica serovar Typhi and Paratyphi 0.2 %.

Among the reported Staphylococcus isolates 59% were Methicillin Resistant Staph aureus (MRSA) and 1% were Linezolid resistant. Linezolid resistance in *Enterococcus* spp. from blood culture was found to be 8.4%. ESBL was observed in 76% of *E. coli* and 81% of *Klebsiella* spp. isolated from blood specimens. With respect to Carbapenem Resistant Enterobacterales (CRE) in blood, 33% resistance was observed in *E. coli* and 50% in *Klebsiella* spp. *Salmonella* Typhi isolated from blood cultures showed 34% resistance to Ciprofloxacin.

56% resistance to Imipenem was observed in blood isolates of *Acinetobacter* spp. Carbapenem-resistance was observed in 26% of *Pseudomonas* spp. from blood. Resistance to colistin was observed to be < 1% among the gram-negative bacterial isolates.

II. National AMR Surveillance Network (NARS-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 initiatives is the launch "National Programme on Antimicrobial Resistance (AMR) Containment" in 2013, during the 12th five-year plan (2012-2017). This programme is being coordinated by National Centre for Disease Control (NCDC) 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 the problem. For this a network of laboratories called the National AMR Surveillance Laboratory network (NARS-Net) has been established under the programme. At the outset, NARS-Net included eight state medical college laboratories which have over the years increased in a phased manner to include 36 laboratories in 26 states/UTs as of March 2022. NCDC has been designated by MoHFW as the National Coordinating Centre for WHO-Global Antimicrobial Resistance Surveillance System (GLASS). The data generated by the network sites under the programme is submitted onto GLASS annually since 2018 every year. The seven priority pathogens included under the NARS-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 and Paratyphi

The clinical specimens currently included under NARS-Net are:

- Blood
- Urine
- Aspirated pus aspirate
- Other sterile body fluids
- Stool (only for *Salmonella* Typhi and Paratyphi)

Table 1- Pathogens and specimens included under surveillance

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

All the participating network sites quarterly report AMR data of the seven priority pathogens from the above-mentioned specimen types to the programme unit at NCDC. 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). On a quarterly basis, the network sites are to submit a pre-defined number of isolates for EQA to the AMR National Reference Laboratory (NRL) at NCDC. It is also mandatory for the sites to report and send all the emerging AMR alert isolates, as defined under the programme, for confirmation to AMR NRL at NCDC.

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, NCDC regularly organizes trainings and workshops on WHONET software, the software used for AMR data management, to streamline AMR surveillance data flow from network sites to NCDC. Numerous one on one online trainings provided for the development of antibiograms for sharing the AMR data with clinicians for local use and broth microdilution lab testing techniques have helped in improving implementation of programme activities at the network sites.

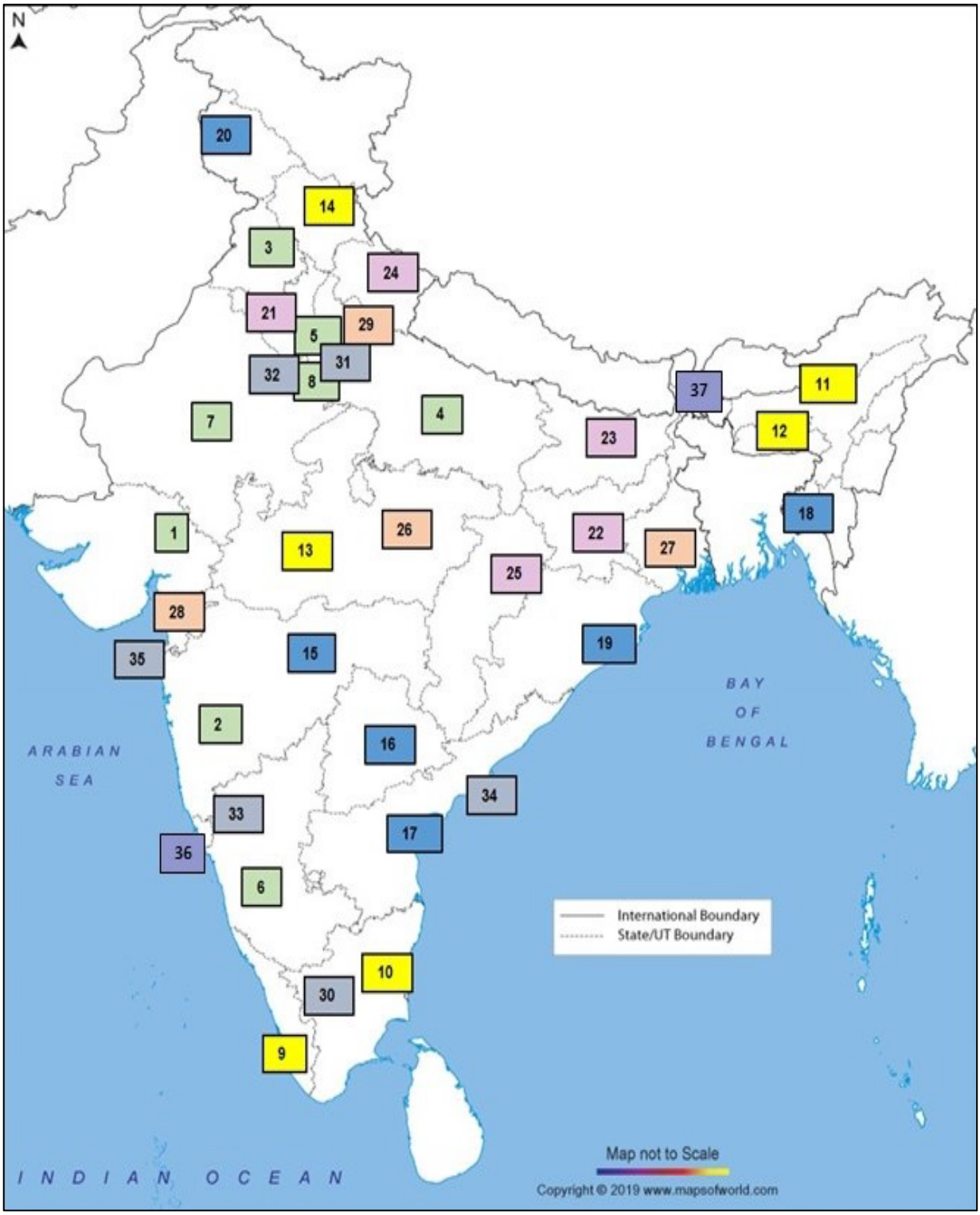


Fig. 1 – National AMR Surveillance Network (NARS-Net): Institutions under NARS-Net from serial no. 1-35 reported AMR Surveillance data of 2021 to NCDC (List of Institutions at Annexure)

III. DATA COLLECTION

The WHONET software is used for the collection and analysis of the antimicrobial susceptibility (AST) data generated by the manual testing methods and the automated systems at the programme sites. The classification of the isolates as susceptible, intermediate or resistant is based on the Clinical & Laboratory Standards Institute (CLSI) guidelines. During 2021 antimicrobial susceptibility (AST) data of 96,370 priority pathogens, along with the demographic information of the patients from whom these pathogens were isolated, was reported from 35 sites in 25 states/UTs.

All sentinel sites submitted the data quarterly after validation by the AMR nodal officer at the sites. The data as per programme guidelines is to be submitted by the network sites within 15 days after each quarter:

- Data from January 1 to March 31 of the current year sent by 15th April
- Data from April 1 to June 30 of the current year sent by 15th July
- Data from July 1 to September 30 of the current year sent by 15th October
- Data from October 1 to December 31 of the previous year sent by 15th January

The quarterly data submitted by the sites was screened and analyzed and the detailed feedback was provided to them for each quarter. In addition to AMR data, as per programme requirements, representative isolates were submitted by the sites to AMR NRL at NCDC as a part of the External Quality Assessment (EQA). The NRL at NCDC performed identification and susceptibility testing by strictly following the standard operating protocols (SoPs) and after confirmation results were informed to the sites. Antibiotic-resistant alert isolates of public health concern as specified under the programme were also submitted to NCDC, along with the duly filled form, for confirmation.

IV. DATA ANALYSIS

The analysis of cumulative data for the year 2021 has been performed by the programme unit at NCDC and the National AMR surveillance Annual Report has been prepared. This annual report covers the AMR data from 1st January 2021 to 31st December 2021. A total of 35 medical college laboratories from 25 states and UTs submitted their AMR data during 2021. The antimicrobial susceptibility testing 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.

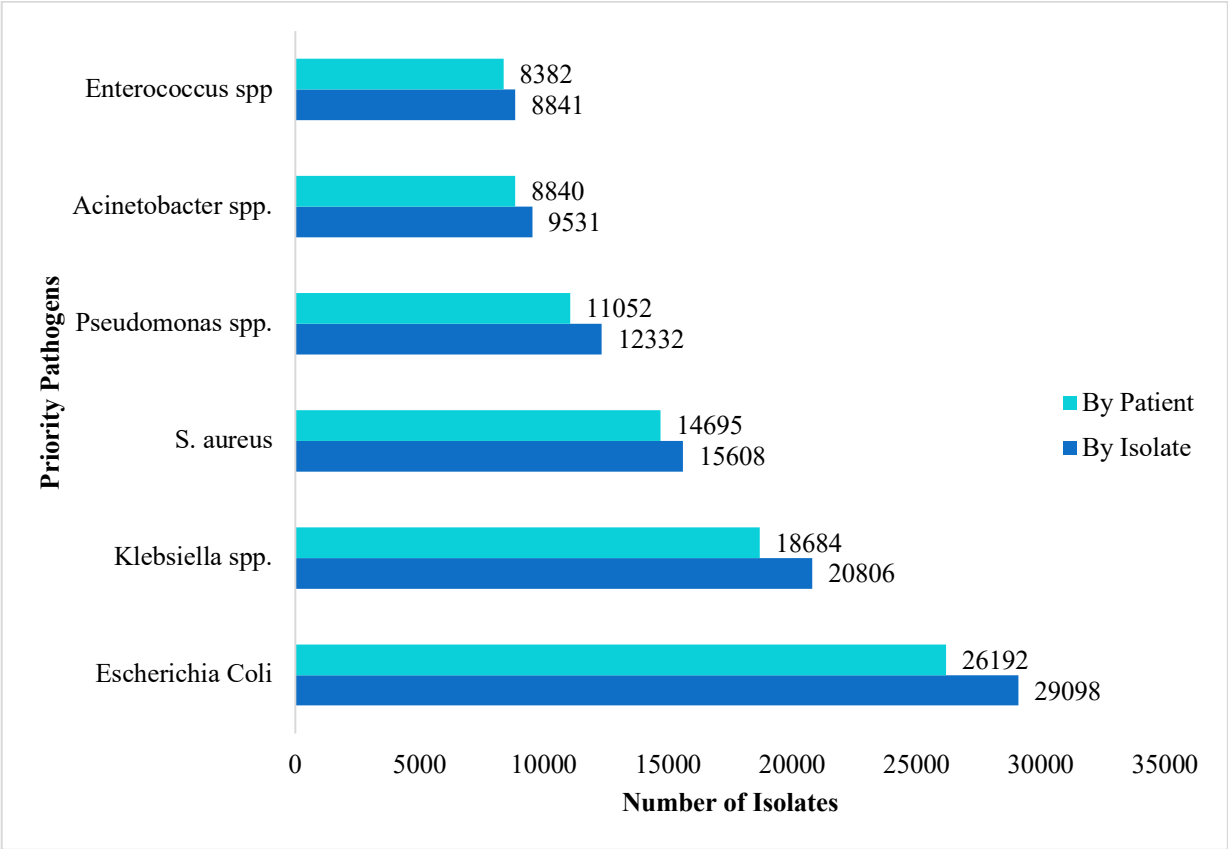


Fig. 2- Priority pathogens before and after de-duplication

b. Demography and distribution of priority pathogens

Among the total of 87, 996 unique patients, 55% pathogens were isolated from male patients as compared to female patients (45%). Age data was available for 95% of unique patient isolates. The highest proportion of unique patients contributing to the AST data belong to economically productive age group that is 15-54 years whereas the lowest number of pathogens are reported from age group of 85 years and above (1%).

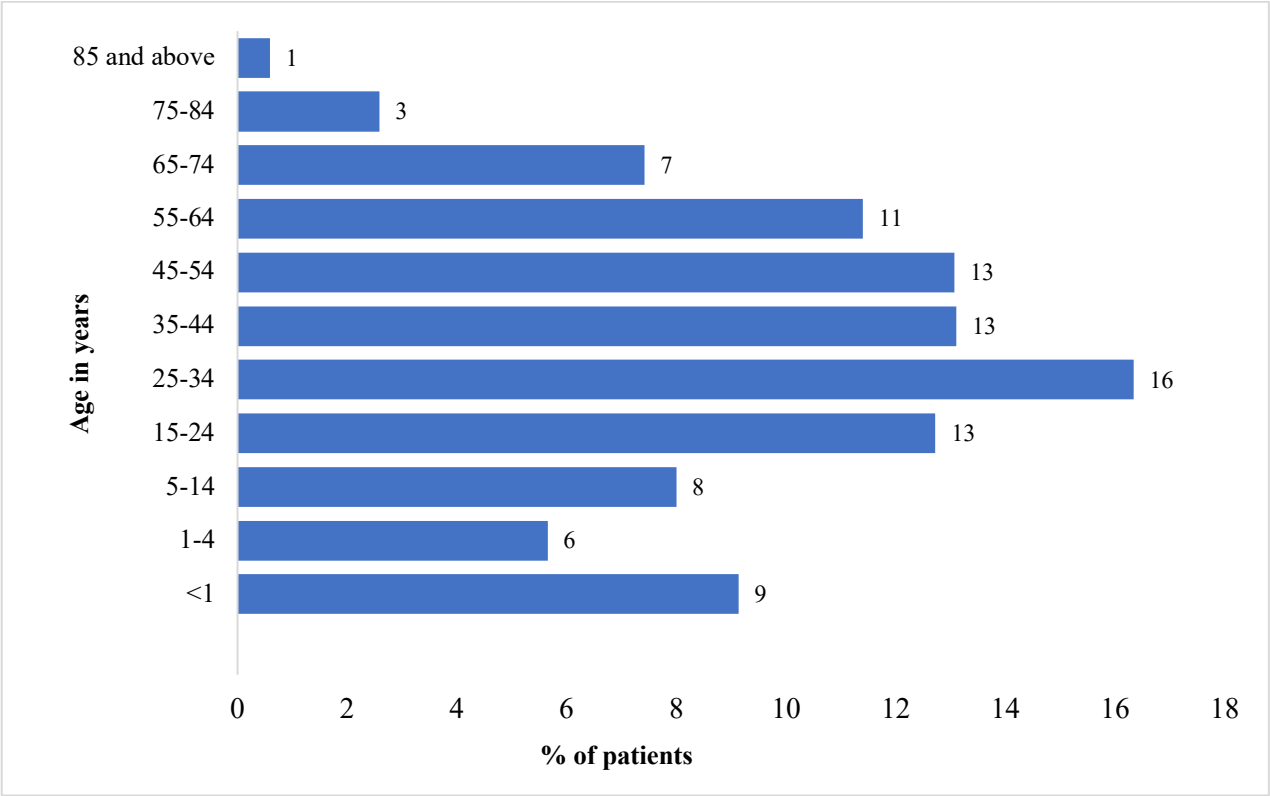


Fig. 3 - Distribution of isolates based on age

The total number of isolates from unique patients (after de-duplication) = 87,996

Urine- 34509 (39.21%)

Blood-19097 (21.70%)

Pus aspirate (PA)- 30366 (34.50%)

Other Sterile body fluids (OSBF)- 4023 (4.57%)

Stool- 1

The number of isolates reported in the year 2021 has increased over that reported annually in the past four years. In 2021 AMR surveillance data, the most commonly isolated priority pathogen is *E. coli* (29.8 %), which is similar to previous four years data, followed by *Klebsiella* species (21.2 %), *S. aureus* (16.7%), *Pseudomonas* species (12.6 %), *Acinetobacter* species (10 %) *Enterococcus* species (9.5%) and *Salmonella* enterica serovar Typhi and Paratyphi (0.2 %).

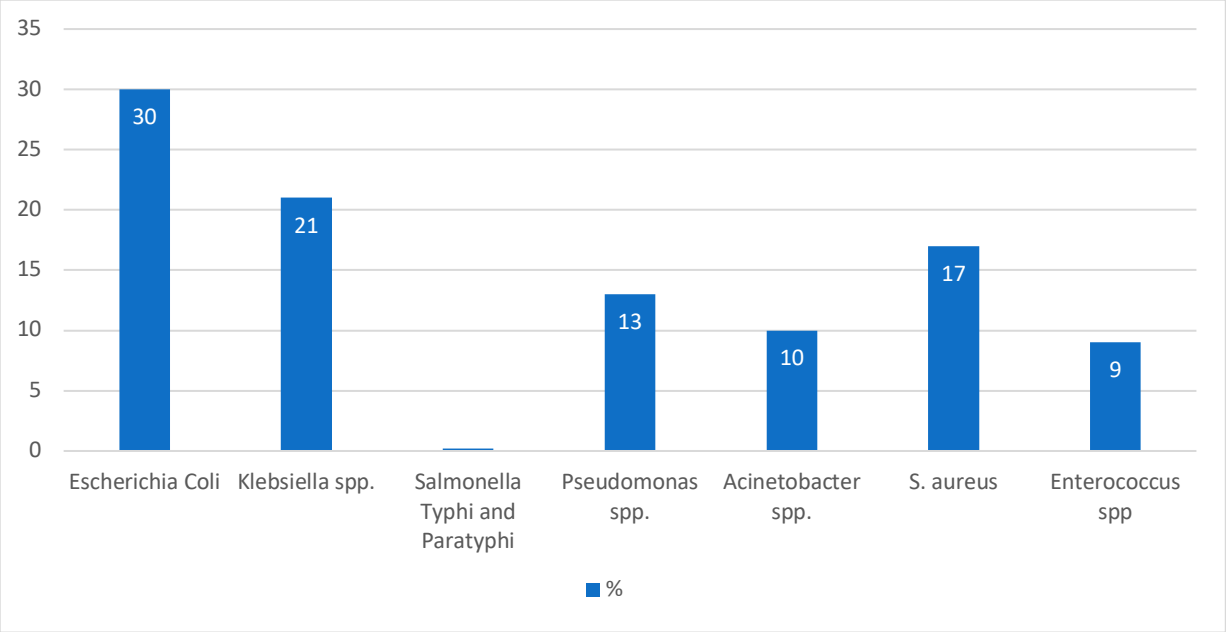


Fig. 4- Distribution of AMR surveillance priority pathogens

Similar to the previous four-year annual reports among all specimen types highest number of *E. coli* are isolated from urine samples. Both from blood and pus aspirate specimen types the highest number of priority pathogen isolated is *S. aureus* (32% & 26% respectively) followed by *Klebsiella* spp. (19% & 22% respectively). While the lowest number of pathogen isolated from blood is *Salmonella* enterica serovar Typhi and Paratyphi (1%). The majority of pathogens isolated from OSBF are *Pseudomonas* species and *Acinetobacter* species (20% each respectively). Both from pus aspirate and OSBF, lowest percentage of pathogen isolated is *Enterococcus* species (4% & 8% respectively).

Table 2- Specimen-wise isolation of Priority Pathogens

Priority Pathogen	Blood (%)		Pus aspirate (%)		OSBF (%)		Urine (%)	
S. aureus	6119	(32%)	7946	(26%)	630	(16%)		
Enterococcus spp.	1842	(10%)	1121	(4%)	332	(8%)	5087	(15%)
Escherichia coli	1806	(9%)	6434	(21%)	675	(17%)	17277	(50%)
Klebsiella spp.	3662	(19%)	6688	(22%)	792	(20%)	7542	(22%)
Salmonella Typhi and Paratyphi	150	(1%)						
Pseudomonas spp.	1859	(10%)	5406	(18%)	800	(20%)	2987	(9%)
Acinetobacter spp.	3659	(19%)	2771	(9%)	794	(20%)	1616	(5%)
Total	**19097**		**30366**		**4023**		**34509**	

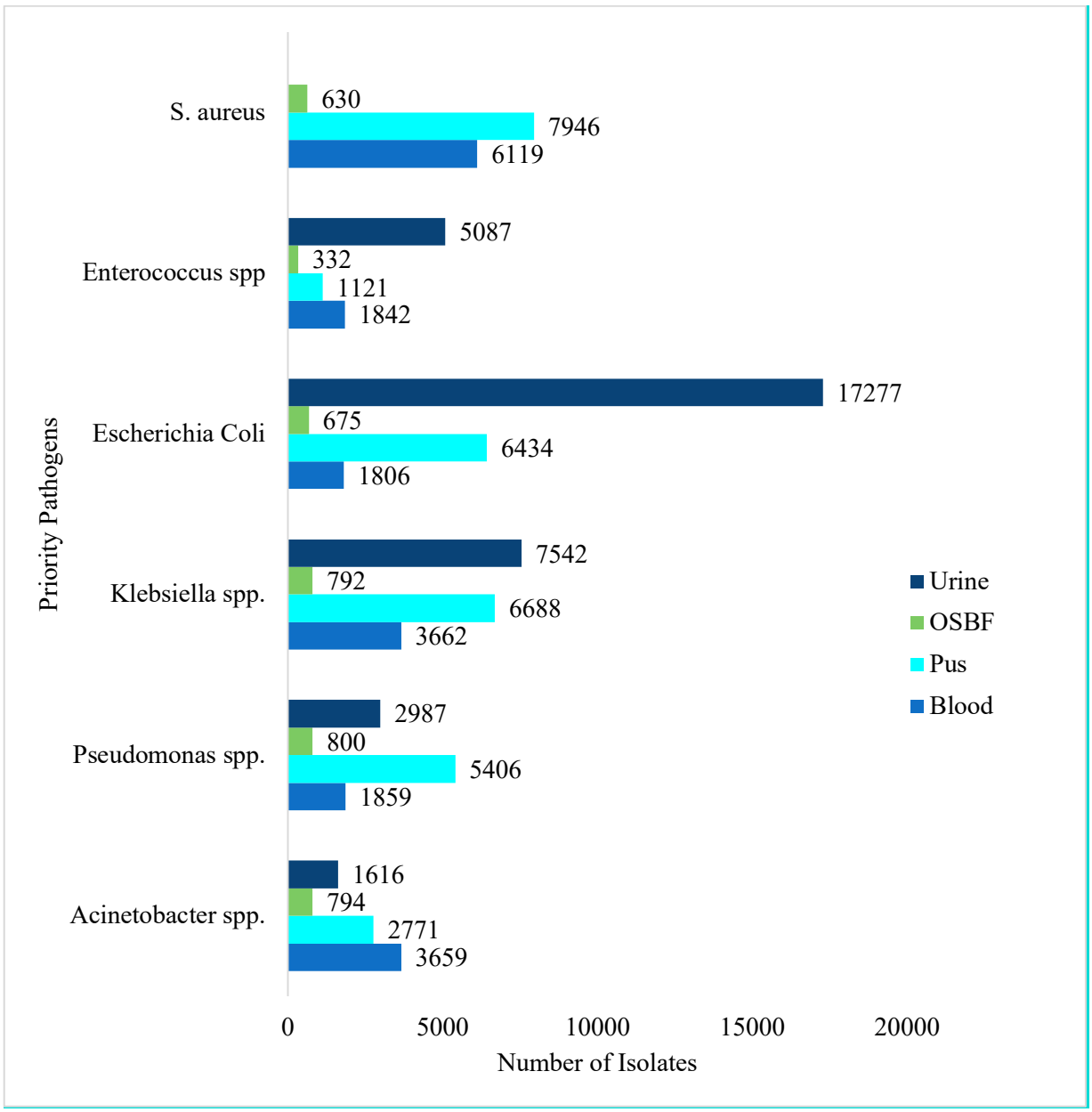


Fig. 5- Specimen wise distribution of priority pathogens

Of the 87,996 isolates included in the 2021 AMR surveillance data, 58% are from IN patients (IPD), 26% from Outpatient (OPD), 12% from ICU patients and 4% from the Emergency location of hospital settings (Fig- 9). The most commonly isolated pathogen from all four location types is *E. coli* except in ICU. In ICU facilities most *Klebsiella* spp. (24%) is the most commonly isolated pathogen, followed by *Acinetobacter* spp. (19%) and *Pseudomonas* spp. (12%). In IPD patients' maximum isolates are of *E. coli* (28%) followed by *Klebsiella* spp. (22%), *S. aureus* (17%), *Pseudomonas* spp. (13%), *Acinetobacter* spp. (10%) and *Enterococcus* spp. (10%).

Among isolates from OPD patients, after *E. coli* (39%) second highest pathogen isolated is *Klebsiella* spp. (19%). In Emergency highest isolation is of *E. coli* (30%), the second-highest pathogen isolated is *S. aureus* (24%).

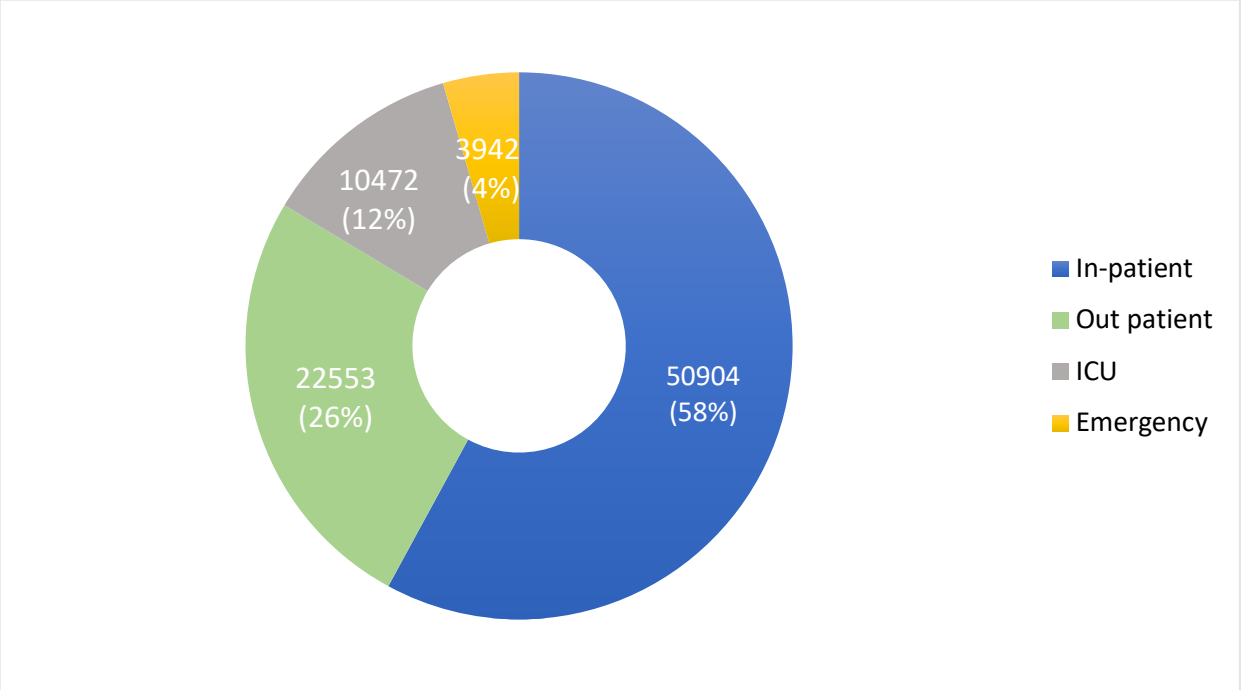


Fig. 6 - Location-wise distribution of isolates

Table 3- Location-wise distribution of priority pathogens

Priority Pathogen	ICU (%)	IPD (%)	OPD (%)	Emergency (%)
Escherichia coli	1947 (19%)	14160 (28%)	8848 (39%)	1188 (30%)
Klebsiella spp.	2477 (24%)	11206 (22%)	4382 (19%)	585 (15%)
Salmonella Typhi and Paratyphi**	14	68	35	34
Pseudomonas spp.	1265 (12%)	6413 (13%)	2985 (13%)	384 (10%)
Acinetobacter spp.	1952 (19%)	5217 (10%)	1202 (5%)	454 (12%)
S. aureus	1673 (16%)	8809 (17%)	3274 (15%)	931 (24%)
Enterococcus spp.	1144 (11%)	5031 (10%)	1827 (8%)	366 (9%)
Total (N)	**10472**	**50904**	**22553**	**3942**

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

V. AMR PROFILE OF PRIORITY PATHOGENS

The data collected under National AMR Surveillance Network (NARS-Net) is for selected antibiotics only as per the NCDC AMR surveillance data management Standard Operating procedure (SoP). This AMR surveillance data is from patients visiting the emergency and out-patient departments of the hospitals and from patients admitted to the in-patient departments & intensive care units.

a. Gram positive cocci

The AMR Surveillance under NARS-Net covers 2 important globally prevalent gram-positive bacterial pathogens i.e. *Staphylococcus aureus* and *Enterococcus* species. The AST data of 24,449 Gram positive cocci have been submitted to NCDC, of which 23077 isolates are from unique patients.

Staphylococcus aureus

Staphylococcus aureus constituted 17% of all the isolates (Fig. 4). Data of a total of 15,608 *S. aureus* isolates was submitted by the NARS-Net sites of which 14,695 isolates are from unique patients. AST analysis of 14,695 isolates indicated that the *S. aureus* isolation rate from blood is 32%, 26% from pus aspirate and 16% from OSBF.

59% resistance to methicillin is observed in *S. aureus* isolates from blood, and resistance to methicillin in isolates from aspirated pus and other sterile body fluids is found to be 49% and 48% respectively (Table 4). The linear trend Analysis for MRSA in blood over last 4 years was done using Chi-square for trend (Extended Mantel Haenszel) and it is found that there is significant decrease in the proportion of MRSA in blood from the year 2018 to 2021 (Chi-square value for Linear trend-18.9, p value - <0.0001). The last five-year MRSA trend in blood isolates is given below.

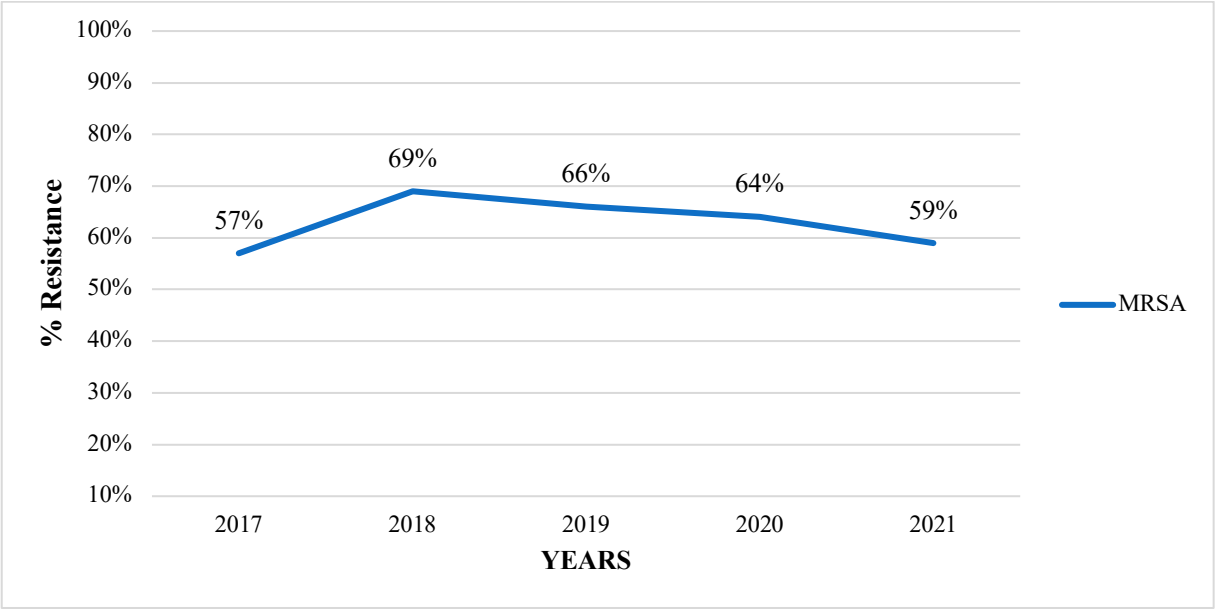


Fig. 7- Trends of MRSA from 2017 to 2021 in blood isolates

Erythromycin resistance is observed in 63% of *S. aureus* isolated from blood, 51% from pus aspirates and 54% from OSBF (Table 4). Similar to the last four years linezolid resistance to *S. aureus* is 1%.

S. aureus is the more commonly isolated gram-positive bacteria from each location type. Distribution of *S. aureus* isolates reported under the programme in 2021 is from 16% of ICU patients, 17% of IPD patients, 24% of patients in emergency units and 15% of OPD patients. (Table 3) 64% MRSA are isolated from ICU patients followed by IN and OPD patients (upto 58%).

Table 4: Resistance profile observed in *Staphylococcus aureus*

Antibiotic tested	Blood (N=6119)			Pus aspirate (N=7946)			Other Sterile Body Fluids (N=630)		
	Number Tested	Number Resistant	Resistance (%)	Number Tested	Number Resistant	Resistance (%)	Number Tested	Number Resistant	Resistance (%)
Cefoxitin	5805	3441	59	7602	3703	49	608	294	48
Ciprofloxacin	5357	2695	50	6607	3884	59	524	209	40
Clindamycin	5755	1960	34	7295	1630	22	588	160	27
Doxycycline	5419	863	16	6215	796	13	533	50	9
Erythromycin	5911	3730	63	7430	3807	51	626	341	54
Gentamicin	5437	1396	26	7258	1698	23	584	121	21
Linezolid	5761	36	1	7452	49	1	629	9	1
TMP / SMX	4656	2015	43	6680	1803	27	514	191	37
Teicoplanin	1206	14	1	1662	30	2	96	1	1

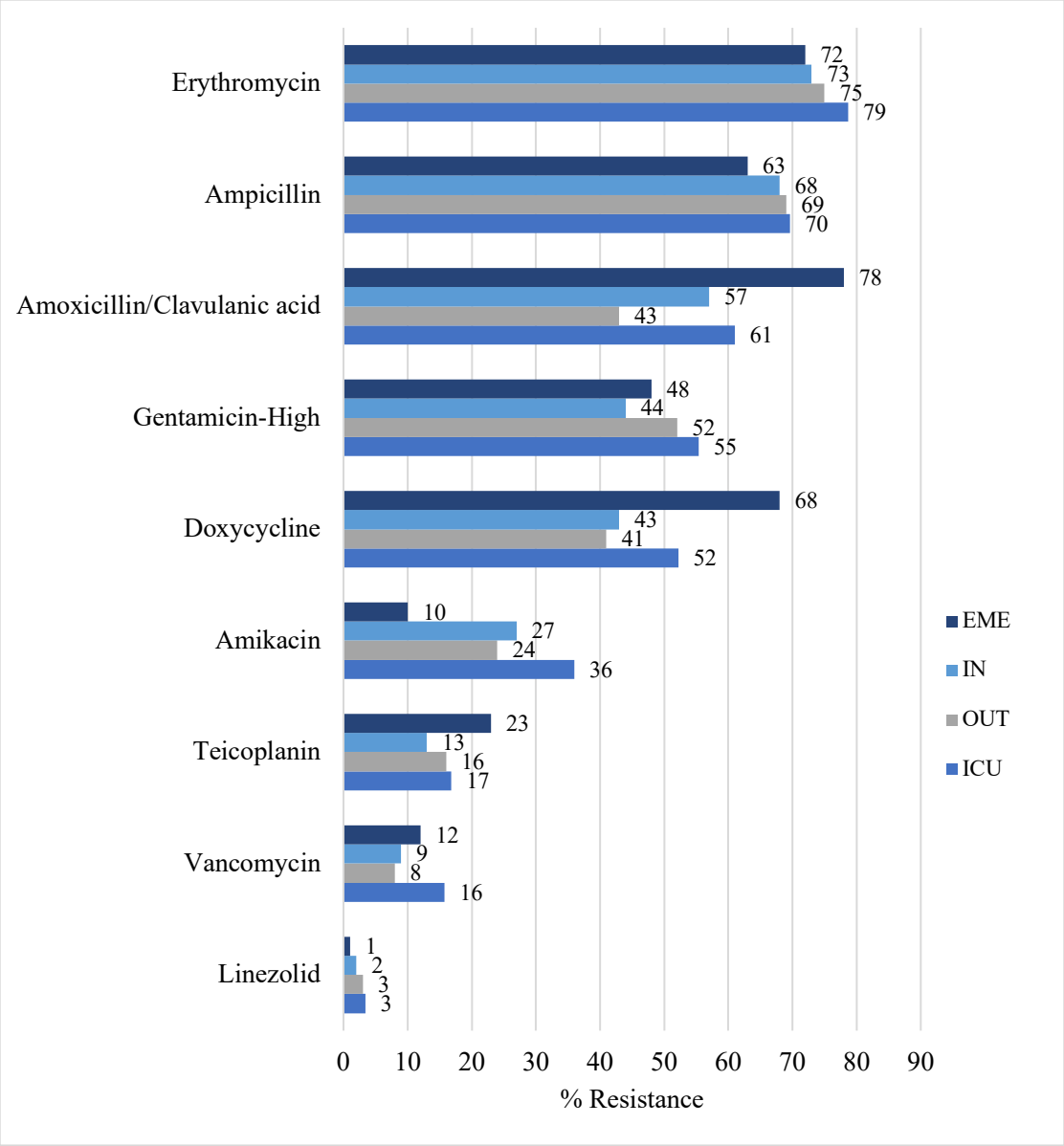


Fig. 8- Resistance profile of *S. aureus* isolated from blood from different location types

Enterococcus species

Enterococcus species constitutes 9% of all isolates (Fig 4). A total of 8,841 *Enterococcus* species isolate data was submitted by the NARS-Net sites during 2021 of which 8,382 isolates are from unique patients. *Enterococcus* species reported in 2021 NARS-Net data represent 10% of blood culture isolates, 8% of OSBF isolates, 15% of urine isolates and 4% of isolates from pus aspirates. (Table 2)

Among the *Enterococcus* species isolated from blood, pus aspirate and OSBF specimens, the highest resistance is observed to Erythromycin i.e., 75%, 66%, 71% respectively. Next highest resistance is observed to ampicillin in all four specimen types i.e. blood, pus aspirate, OSBF and

urine which is 68%, 51%, 59% and 61% respectively (Table 5). Among urinary isolates, 77% are resistant to ciprofloxacin, 7% to vancomycin and 2% to linezolid respectively.

Enterococcus species reported during 2021 under NARS-Net are from 11% of ICU patients, 10% of IPD patients, 9% of patients in Emergency department and 8% of OPD patients. (Table 3) Isolates from blood cultures of ICU patients show a high percentage of vancomycin-resistant enterococcus (VRE) i.e. 16% and 3% are resistant to linezolid. (Fig. 9) Blood isolates from all location types show high level resistance to Erythromycin and Ampicillin i.e. > 70 % and > 60% respectively (Fig. 9). Linezolid-resistant VRE isolates from blood have increased from 5% in year 2019 to 8.4% in year 2021. High level resistance observed in *Enterococcus* species isolated from blood is a matter of concern in ICU patients. (Fig. 9)

Table 5- Resistance profile of *Enterococcus* species

Antibiotic Tested	Blood (N=1842)			Pus aspirate (N=1121)			OSBF (N=332)			Urine (N=5087)		
	Number Tested	Number Resistant	Resistance %	Number Tested	Number Resistant	Resistance %	Number Tested	Number Resistant	Resistance %	Number Tested	Number Resistant	Resistance %
Ampicillin	1462	994	68	956	488	51	286	168	59	4604	2790	61
Doxycycline	1185	548	46	786	399	51	258	126	49			
Erythromycin	1493	1118	75	965	640	66	312	221	71			
Gentamicin-High	1427	675	47	955	300	31	298	138	46	4495	2267	50
Linezolid	1582	40	3	1021	24	2	315	6	2	4880	118	2
Teicoplanin	572	80	14	326	21	6	94	14	15	1574	196	12
Vancomycin	1563	177	11	944	27	3	327	30	9	4581	332	7
Ciprofloxacin										4233	3268	77
Tetracycline										3356	1986	59
Fosfomycin										888	122	14

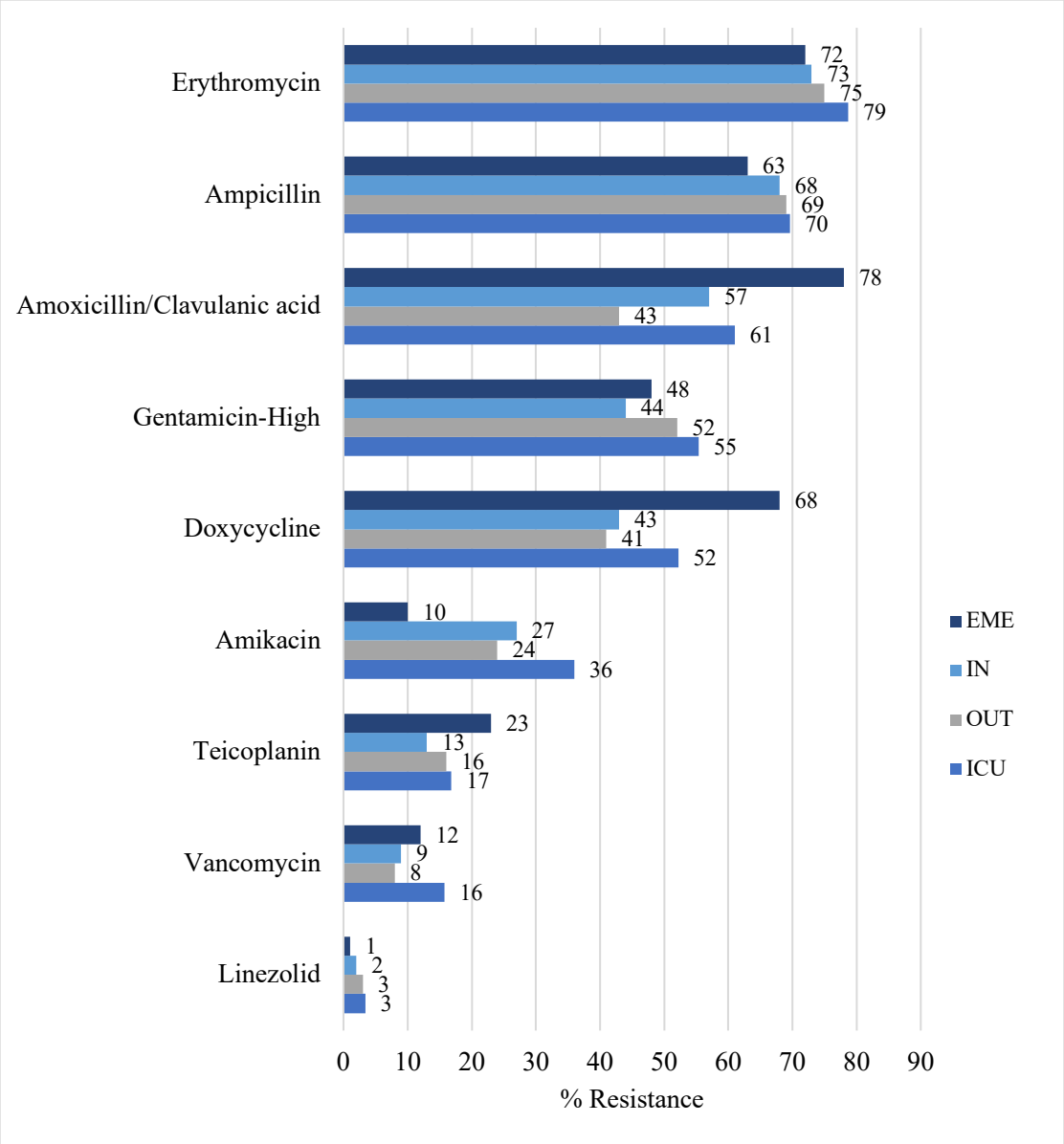


Fig. 9- Resistance profile of *Enterococcus* species isolated from blood from different location types

b. Gram negative bacilli

Under NARS-Net, five 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 71,921 isolates of gram-negative bacilli have been reported from 64,919 unique patients during the period of January 2021 to December 2021 from 35 sentinel sites. The colistin resistant isolates included in the annual data for 2021 are those that have been confirmed at AMR-NRL at NCDC.

i. Enterobacteriaceae

E. coli, Klebsiella species and *Salmonella enterica* serovar Typhi and Paratyphi AST data submitted by network sites accounts for 50,058 (52%) isolates from 45,027 (51%) unique patients. Thus, in concordance to previous annual reports this year also maximum isolates belong to the Enterobacteriaceae family.

Escherichia coli

A total of 29,098 *E. coli* isolate AST data has been reported from 26,192 unique patients. *E. coli* constituted 30% of data reported from unique patients for the year 2021. The highest number of *E coli* has been reported from urine samples, followed by PA, blood & OSBF. (Table 2) Ampicillin resistance in *E. coli* is observed to be more than 80% in all specimen types. For third generations cephalosporin cefotaxime, resistance is observed in > 70 % *E. coli* isolated from all specimen types. Among blood isolates of *E. coli*, 76% are ESBL positive. Carbapenem resistance observed in *E. coli* isolates from blood is up to 33%. For non-beta-lactam antibiotics, 73% resistance is observed to ciprofloxacin, 59% to Trimethoprim-Sulfamethoxazole (TMP/SMX) and 11% to nitrofurantoin in urinary isolates. (Table 6) Similarly, in *E. coli* isolates from blood, percentage resistance to non-beta-lactam antibiotics observed is 63% to ciprofloxacin, 54% to TMP/SMX. 43% isolates from blood show 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 resistance profile of *E. coli* isolates from blood, urine, PA & OSBF from different location types is shown in Fig. 10.

Table 6: Resistance profile of *Escherichia coli*

Antibiotic Tested	Blood (N=1806)			Pus Aspirate (N=6434)			OSBF (N=675)			Urine (N=17277)		
	Number Tested	Number Resistant	Resistance %	Number Tested	Number Resistant	Resistance %	Number Tested	Number Resistant	Resistance %	Number Tested	Number Resistant	Resistance %
Amikacin	1510	1088	29	5399	1280	24	565	121	21	12006	2323	19
Amoxicillin/ Clavulanic acid	680	390	57	2848	1660	58	262	151	58	6565	3435	52
Ampicillin	1294	584	84	4986	4281	86	501	417	83	13371	11357	85
Cefepime	1286	1056	62	4999	3014	60	548	327	60	12699	6862	54
Cefotaxime	1380	797	77	5302	4045	76	577	447	77	14485	10377	72
Ciprofloxacin	1551	135	63	5820	4266	73	644	454	70	15064	11037	73
Colistin	914	0	0	1847	0	0	337	0	0	4293	1	
Ertapenem	406	211	33	1186	283	24	186	46	25	3931	814	21
Gentamicin	1260	431	39	4775	1696	36	421	132	31	7885	2323	29
Imipenem	1593	491	29	5810	1193	21	646	161	25	15254	2350	15
Meropenem	854	981	25	3605	592	16	302	58	19	5938	895	15
Piperacillin/ Tazobactam	1350	701	43	5293	2268	43	547	257	47	2937	2937	29
Trimethoprim/ Sulfamethoxazole	1289	14	54	4971	2872	58	516	308	60	8918	8918	59
Nitrofurantoin										16229	1725	11
Fosfomycin										855	58	7
Cefuroxime										3257	2581	79
Doxycycline				762	398	52	111	49	44			

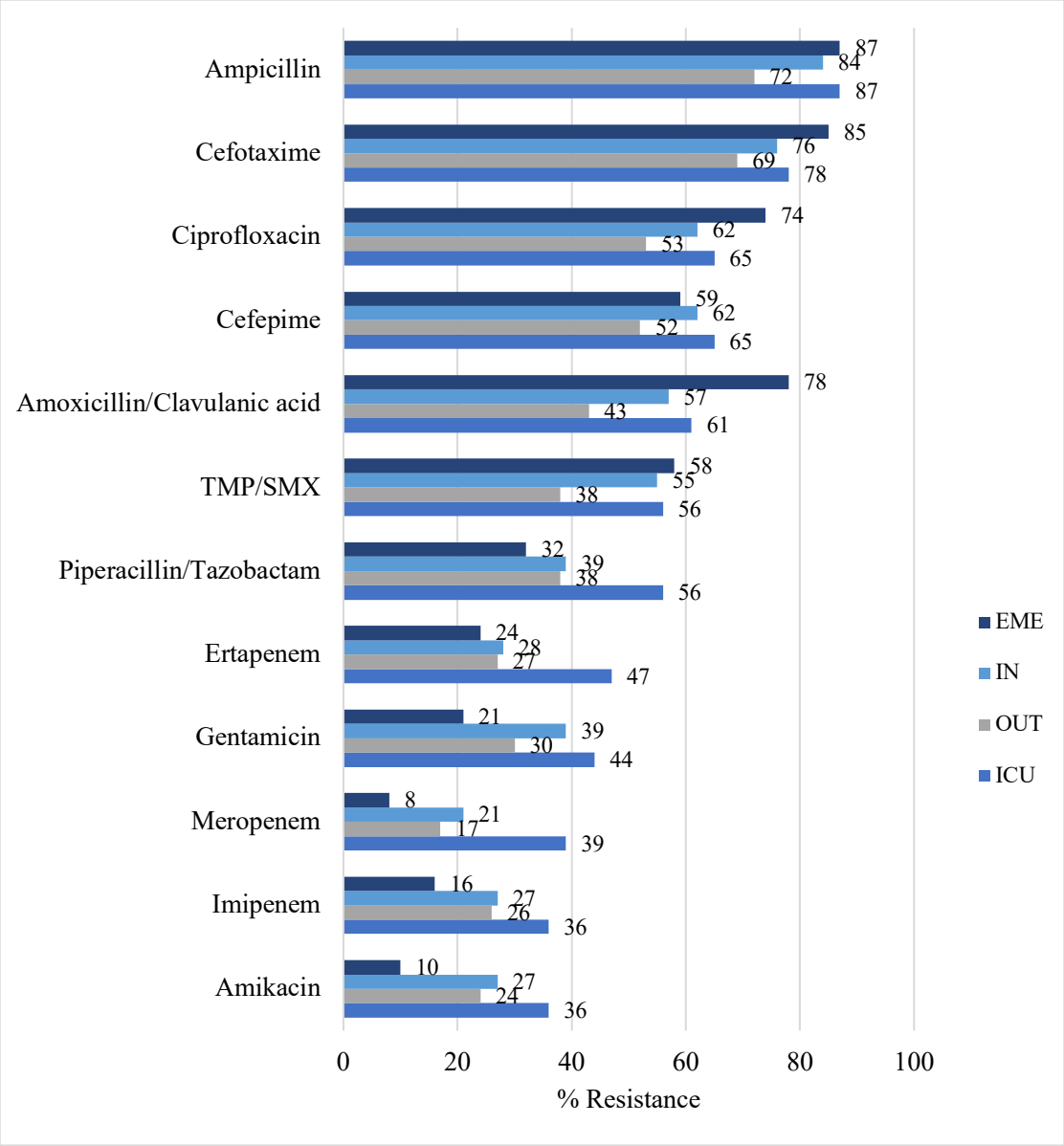


Fig. 10: Resistance profile of *Escherichia coli* isolated from blood from different location types

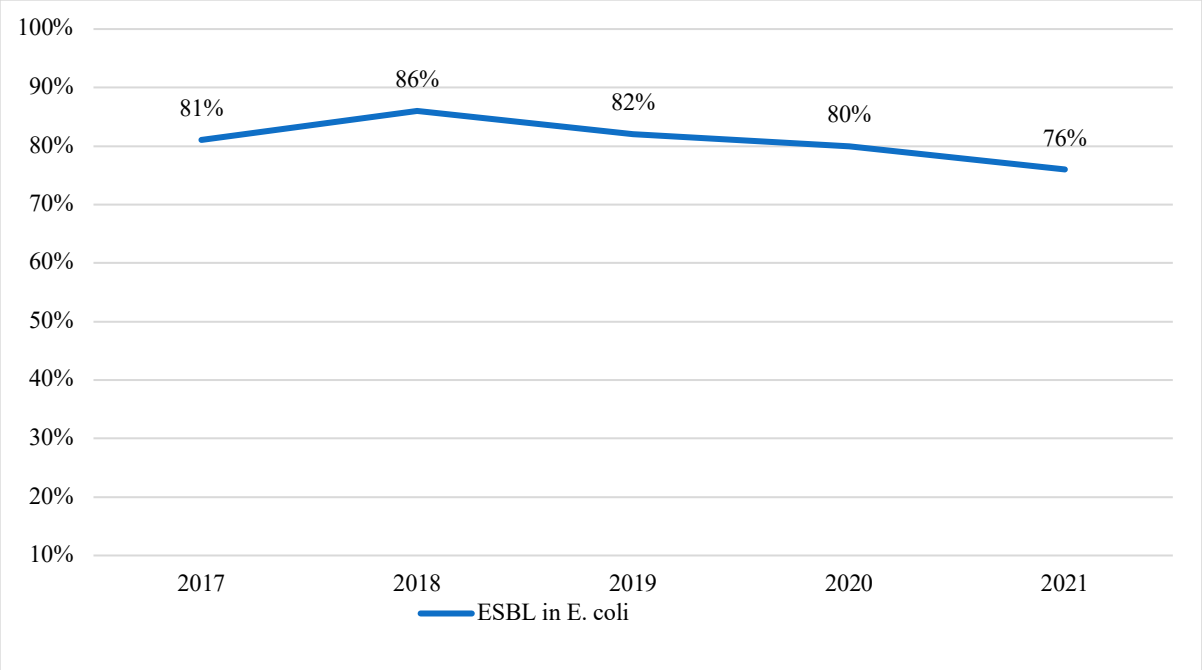


Fig. 11: Trends of ESBL producing *Escherichia coli* isolated from blood in last 5 years

The linear trend Analysis for ESBL producing *E. coli* (blood) was done using Chi-square (Extended Mantel Haenszel) and it was found that there is significant decrease in the proportion of ESBL producing *E. coli* isolates from the year 2018 to 2021 (Chi-square value for Linear trend- 17.56, p value - <0.0001) [Fig. 11]

Klebsiella species

High level of resistance was observed in *Klebsiella* spp. isolates from all specimen types and for all antibiotics except colistin. Total of 7,542 *Klebsiella* species were isolated from urine specimens. ESBL positivity was observed in 81% of blood isolates of *Klebsiella* species. Cefotaxime resistance in the blood isolates is 82% followed by 79% in OSBF isolates, 77% in pus aspirate isolates and 69% in urine isolates. Ciprofloxacin resistance in isolates from all four specimen types ranges from 62% to 65% and the amikacin resistance ranges from 32% to 52%. Highest resistance to ertapenem was observed in isolates of *Klebsiella* spp. from blood i.e. 50% compared to the other specimen types. (Fig. 12)

Table 7: Resistance profile of *Klebsiella* species

Antibiotic Tested	Blood (N=3662)			Pus Aspirate (N=6688)			OSBF (N=792)			Urine (N=7542)		
	Number Tested	Number Resistant	Resistance %	Number Tested	Number Resistant	Resistance %	Number Tested	Number Resistant	Resistance %	Number Tested	Number Resistant	Resistance %
Amikacin	2859	1473	52	5688	2471	43	606	268	44	5549	1751	32
Amoxicillin/ Clavulanic acid	1451	988	68	2815	1887	67	300	197	66	3042	1754	58
Cefepime	2658	1863	70	5241	3433	66	655	421	64	5655	3115	55
Cefotaxime	2774	2273	82	5537	4238	77	668	527	79	6392	4423	69
Ciprofloxacin	3172	2064	65	6130	4035	66	734	462	63	6634	4091	62
Colistin	1868	9		2026	2		381	0		2002	7	
Ertapenem	692	345	50	1040	342	33	173	79	46	1550	527	34
Gentamicin	2625	1453	55	5352	2637	49	545	254	47	3691	1289	35
Imipenem	3287	1290	39	6039	1982	33	753	313	42	6681	1684	25
Meropenem	1808	696	38	3942	1052	27	409	172	42	2710	697	26
Piperacillin/ Tazobactam	2809	1677	60	5646	3169	56	613	344	56	4809	1833	38
Trimethoprim/ Sulfamethoxazole	2633	1529	58	5229	3131	60	631	381	60	6629	3775	57
Cefuroxime										1661	1337	80
Nitrofurantoin										6468	2448	38
Doxycycline				718	353	49	111	45	41			

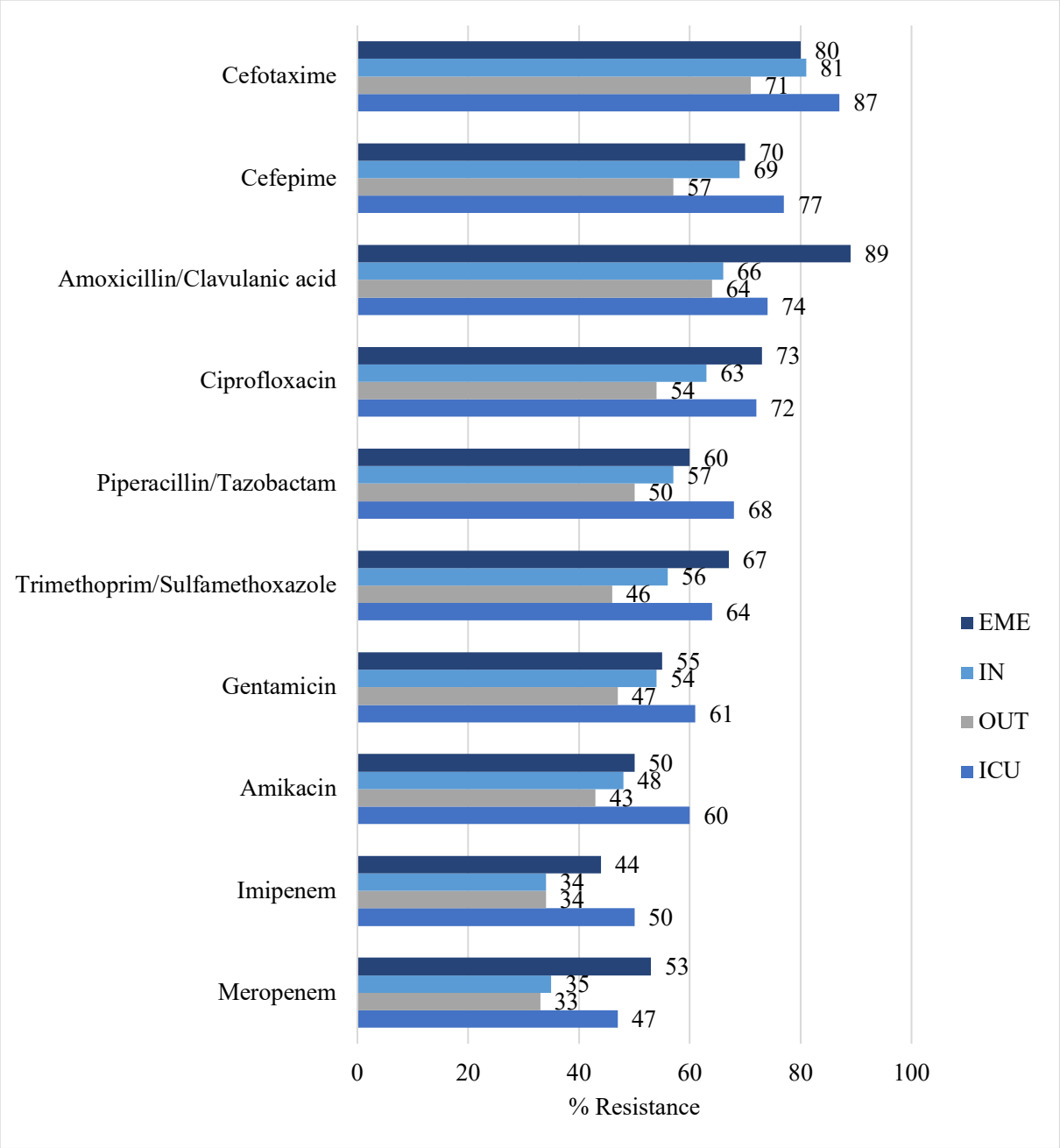


Fig. 12: Resistance profile of *Klebsiella* species isolated from blood specimens

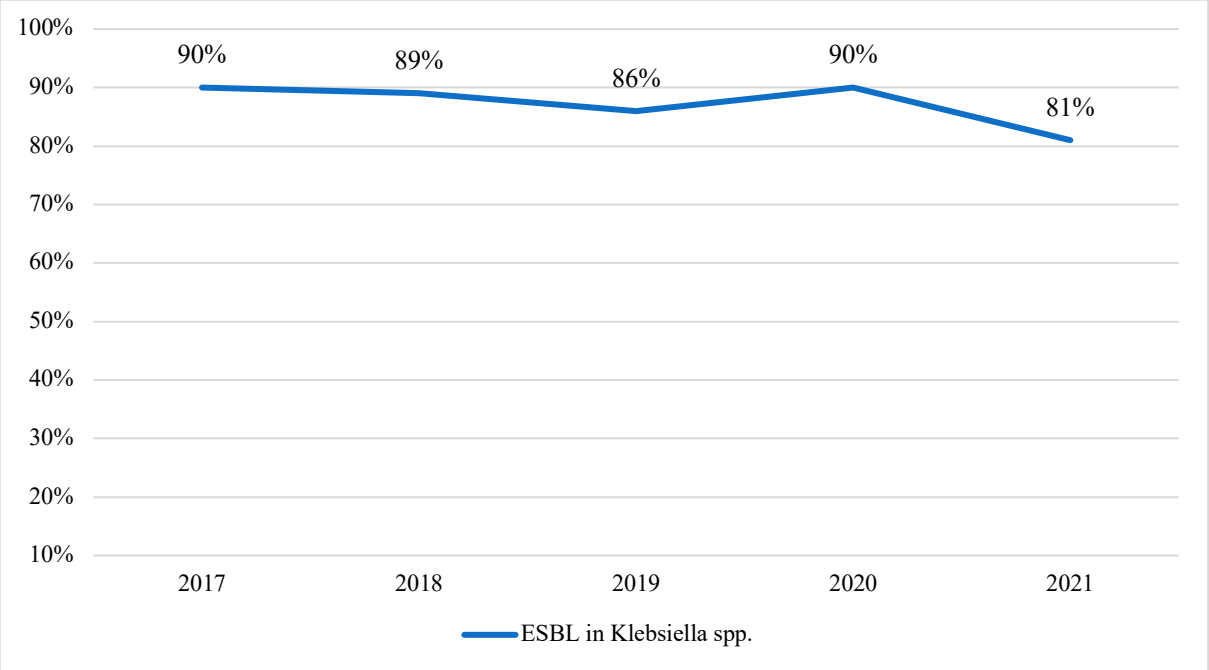


Fig. 13: Trends of ESBL producing blood isolates of *Klebsiella* spp. in the last 5 years

The linear trend Analysis for ESBL producing *Klebsiella* spp. (for blood isolates) was done using Chi-square for trend (Extended Mantel Haenszel) and it was found that there is significant decrease in the proportion of ESBL producing *Klebsiella* spp. isolates from the year 2018 to 2019 followed by an upward trend in 2020 (90%). Further in 2021 the proportion of ESBL producing bacteria significantly decreased to 81% (Chi-square value for Linear trend-54.03, p value - <0.0001) [Fig. 13]

Salmonella enterica Typhi and Paratyphi

This year network sites submitted AMR surveillance data of 154 *Salmonella* enterica serovar Typhi and Paratyphi isolates of which 151 isolates are from unique patients. Only one isolate of Salmonella has been reported from stool specimen hence is not included in the analysis. Low resistance to first-line antibiotics (13% ampicillin, 4% chloramphenicol, 10% TMP/SMX) has been observed compared to ciprofloxacin which is 34 %. Also, the resistance for ceftriaxone in the year 2019, 2020 & 2021 is consistently observed as 2%.

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

Antibiotic tested	S. Typhi (N=148)			S. Paratyphi (N=2)	
	Number tested	Number Resistant	Resistance (%)	Number tested	Number Resistant
Ampicillin	123	16	13	2	0
Azithromycin	119	3	3	2	1
Ceftriaxone	125	2	2	0	0
Chloramphenicol	119	5	4	2	0
Ciprofloxacin	128	43	34	2	1
Imipenem	114	0	0	2	0
Trimethoprim/Sulfamethoxazole	126	13	10	2	1

ii. Non-Fermenting Gram-negative bacilli

Among the Non-fermenting Gram-negative bacilli (NF GNB) collected during Jan-Dec 2021 across all NARS-Net sites, *Pseudomonas* species (12,332) was the most commonly isolated pathogen followed by *Acinetobacter* species (9,531). Similar isolation rates of NF GNB have been observed in the last two years.

Pseudomonas species

Pseudomonas species isolated from blood showed 18% resistance to Meropenem and 19% to Piperacillin tazobactam. Isolates from blood in ICU, IN & OUT patient facilities showed high resistance to ceftazidime i.e., 35%, 46% & 36% respectively; in isolates from emergency department ceftazidime resistance is observed to be 28%. Carbapenem-resistance is observed in 26% of *Pseudomonas* spp. isolated from blood and 27% from urine.

Table 9: Resistance profile of *Pseudomonas* species

Antibiotic Tested	Blood (N=1859)			Pus aspirate (N=5406)			OSBF (N=800)			Urine (N=2987)		
	Number Tested	Number Resistant	Resistance %	Number Tested	Number Resistant	Resistance %	Number Tested	Number Resistant	Resistance %	Number Tested	Number Resistant	Resistance %
Amikacin	1650	362	22	5028	1544	31	728	132	18	2706	848	31
Aztreonam	683	242	35	2612	836	32	310	86	28	1215	437	36
Ceftazidime	1580	649	41	4937	2152	44	715	245	34	2742	1222	45
Ciprofloxacin	1467	432	29	4986	2079	42	751	191	25	2643	1230	47
Colistin	932	2		1702	1		427	1		751	1	
Gentamicin	1345	368	27	4686	1661	35	656	147	22	2435	858	35
Imipenem	1646	424	26	4990	1265	25	742	178	24	2776	753	27
Meropenem	779	137	18	2859	551	19	341	80	23	1219	293	24
Netilmicin	146	33	23	620	178	29	60	24	40	276	104	38
Piperacillin/Tazobactam	1574	293	19	4949	1317	27	707	142	20	2722	654	24

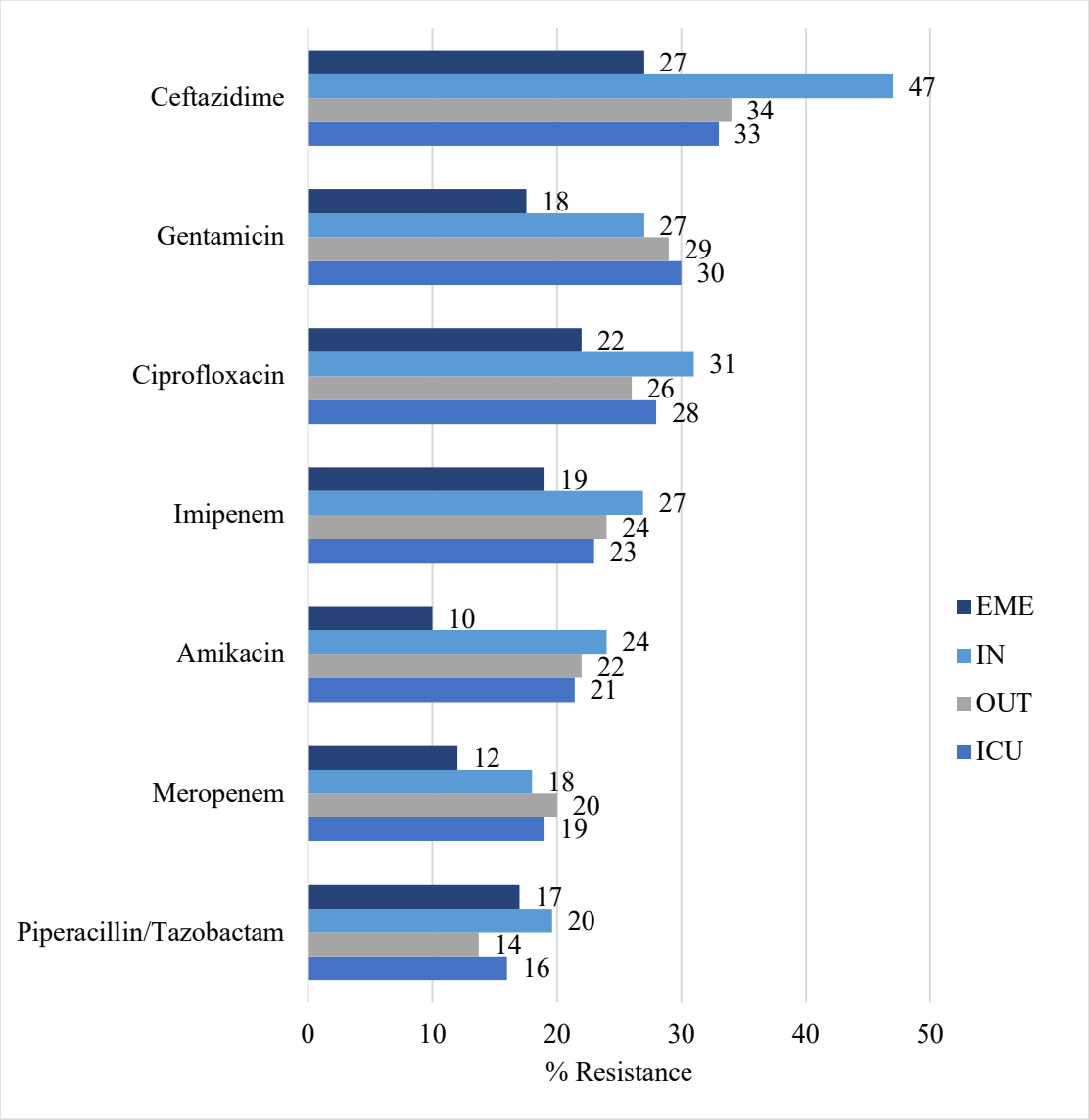


Fig. 14-Resistance profile of *Pseudomonas* species isolated from blood from different location types

Acinetobacter

Total of 9,531 *Acinetobacter* species isolate data was submitted by network sites of which 8,840 are from unique patients. Majority of *Acinetobacter* spp. reported under NARS-Net are from blood cultures (3659). 56% resistance to Imipenem was observed in blood isolates. *Acinetobacter* spp. isolated from all specimen types showed highest resistance to Ceftazidime. One isolate each from blood and plural fluid and two isolates from urine are resistant to colistin.

Table 10: Resistance profile of *Acinetobacter* species

Antibiotic Tested	Blood (N=3659)			Pus Aspirate (N=2771)			OSBF (N=794)			Urine (N=1616)		
	Number Tested	Number Resistant	Resistance %	Number Tested	Number Resistant	Resistance %	Number Tested	Number Resistant	Resistance %	Number Tested	Number Resistant	Resistance %
Amikacin	3128	1587	51	2568	1505	59	731	408	56	1393	464	33
Cefotaxime	1592	1144	72	1619	1188	73	447	322	72	860	491	57
Ceftazidime	2867	2036	71	2339	1790	77	692	495	72	1329	753	57
Ciprofloxacin	2999	1643	55	2483	1743	70	725	406	56	1359	603	44
Colistin	2070	1		940	0		489	1		441	2	
Gentamicin	2737	1396	51	2268	1330	59	634	322	51	1167	431	37
Imipenem	3172	1781	56	2538	1420	56	733	457	62	1501	467	31
Meropenem	1228	559	46	1299	638	49	348	192	55	521	121	23
Minocycline	2147	467	22	1379	346	25	556	117	21	736	161	22
Piperacillin/ Tazobactam	2994	1498	50	2438	1462	60	719	393	55	1451	458	32
Trimethoprim/ Sulfamethoxazole	1942	1004	52	1840	1162	63	486	258	53	1118	493	44

Minocycline and Colistin were the only antibiotics with low levels of resistance in *Acinetobacter* species isolates from blood cultures.

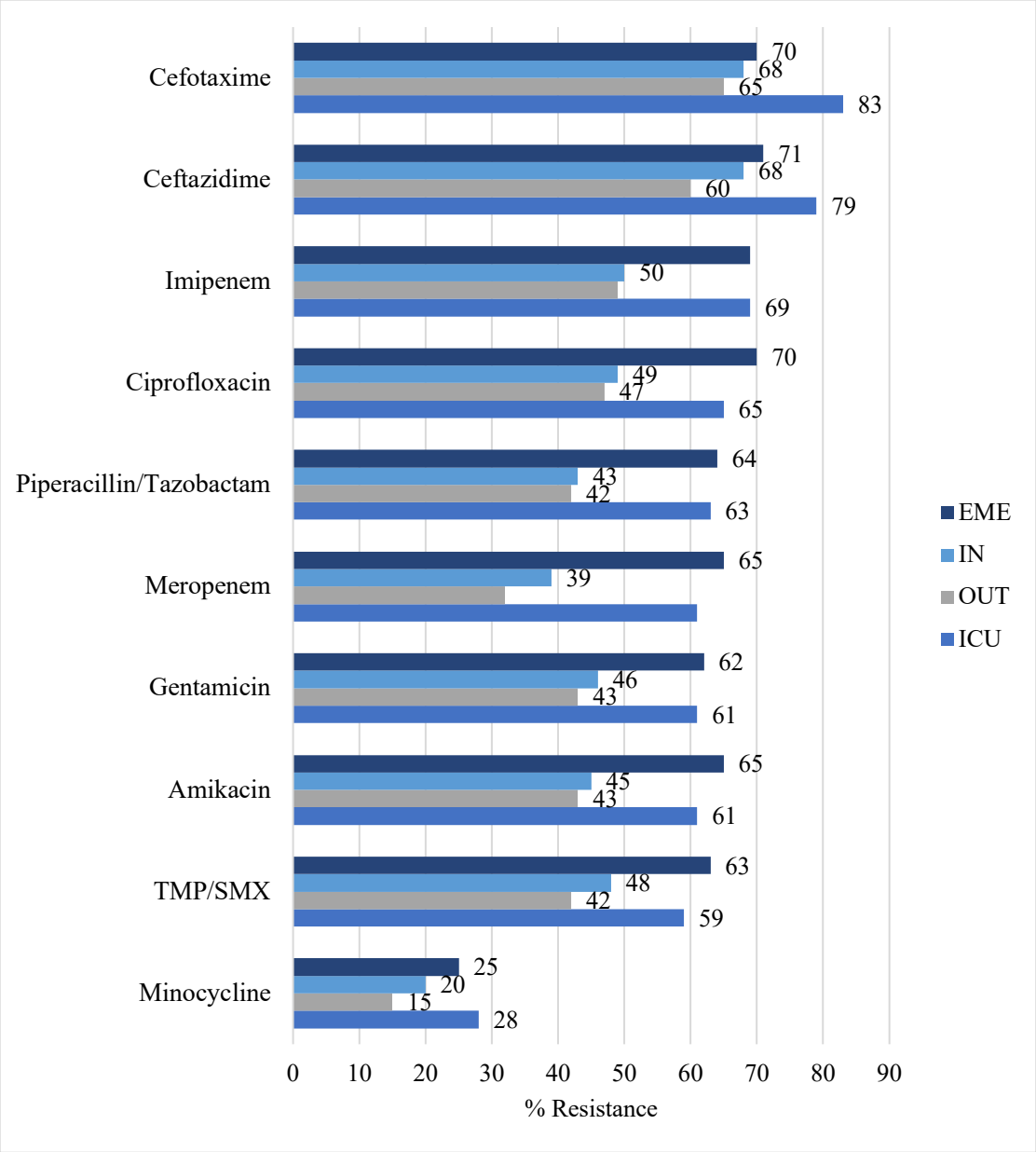


Figure 15- Resistance profile of *Acinetobacter* species isolated from blood specimens from different location types

VI. Discussion

Strengthening global, national and local AMR surveillance is critical for AMR containment as it is the basis for putting in place evidence-based strategies, monitoring the effectiveness of public health interventions and detecting new trends and threats.

Antimicrobial resistance (AMR) poses a significant global health challenge threatening the attainment of Sustainable Development Goals (SDGs) related to health. WHO has declared AMR as one of the top ten global public health threats. Under the National Programme on AMR Containment, NARS-Net annually generates the National AMR Surveillance report. The activities under NARS-Net include capacity building of a network of govt. medical college laboratories for AMR Surveillance. NARS-Net is being expanded in a phased manner to all states and UTs in the country. AMR surveillance under NARS-Net includes standardised collection, analysis and compilation of AMR data from all the network sites. The compiled data is used to generate the annual National AMR surveillance report which is shared with stakeholders at the National and state level and is also made available in the public domain (on NCDC website). For vancomycin resistant *S. aureus* and colistin resistant gram-negative bacteria, only the isolates for which identification and AST has been confirmed at the AMR-NLR at NCDC have been included in this data. This network data is also submitted annually to WHO's Global AMR Surveillance System (GLASS).

This report for the year 2021 presents analysed data from 35 sentinel sites located in 25 states/UTs of India. Compared to the previous year's National AMR Surveillance Report which included 2020 data from 29 network sites, the number of sites submitting the AMR data during 2021 has increased to 35 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 virtual capacity-building program initiated in 2020 to standardise bacteriology testing methods at the laboratories across the network using the ECHO platform has been continuously assisting the sites. In addition, quarterly feedbacks on AMR data are provided to the network sites using a customised VBA tool (developed with support from CDC-India). 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. Certain limitations that could

affect this data are lack of strict compliance to the internal quality control SoPs by some sites. Also, the small number of isolates from emergency settings may make that data less representative. Inclusion of data from more number of centres and from all states and UTs would make the data more representative for the country.

E. coli is the most commonly isolated pathogen (30%) in the AMR Surveillance data of 2021 which is found to be similar to the previous 4 years reports. Amongst urinary isolates, *E. coli* is the most commonly isolated pathogen (50%) while *S. aureus* is the most commonly isolated pathogen from pus aspirates and this finding corroborated with the previous year reports. In terms of location type, *E coli* is predominantly isolated from OPD patients (39%) and In -patient (28%) settings whereas *Klebsiella* spp. were more commonly isolated in the ICU setting (24%). Similar pathogen burden in respective location types was also seen in the previous year report.

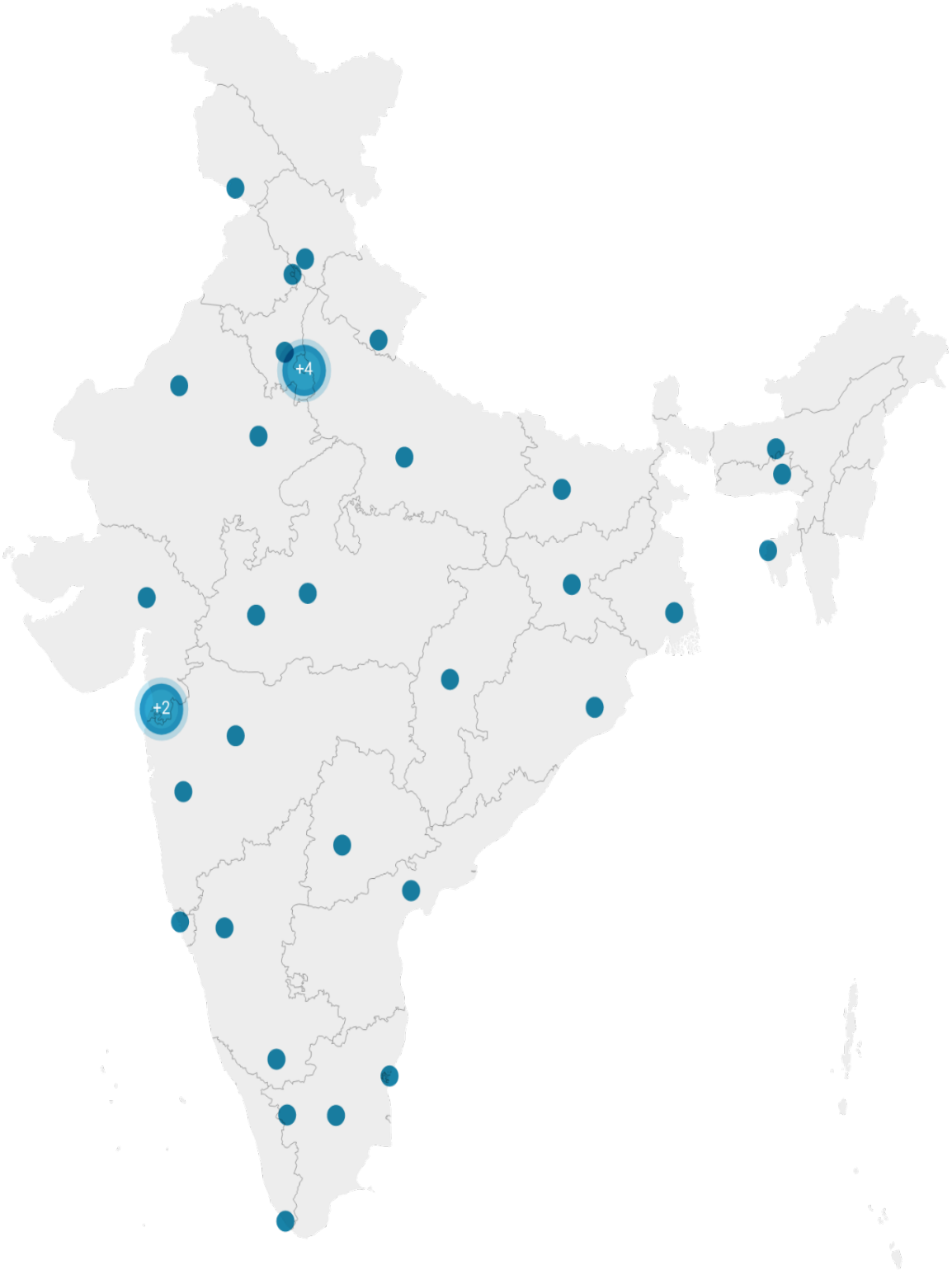
A significant reduction in Methicillin-resistant *S. aureus* (MRSA) in blood was observed this year (59%) in comparison to the previous years since 2018. Similar to the previous years, Linezolid resistance in *S. aureus* was found to be 0.7%. *Enterococcus* spp. isolated from blood cultures showed 11% resistance to Vancomycin.

The linear trend analysis for ESBL producing blood isolates of *E. coli* showed significant decrease in the proportion of ESBL producing *E. coli* isolates from the year 2018 (86%) to 2021(76%). Significant reduction may be due to stringent internal quality control of antibiotic discs and increase in the number of sentinel sites in NARS-Net. Upto 33% of *E. coli* and upto 50% of *Klebsiella* spp. isolated from blood were found to be CREs.

Currently, resistance to last-resort antibiotics has been significantly increasing which poses a serious challenge as there are no newer drugs in the pipeline. Strengthening local infection prevention, antimicrobial stewardship practices at healthcare facilities in the country and addressing the drivers of AMR requires an urgent multisectoral multipronged strategy to combat AMR.

VII. List of NARS-Net sites

1. Lady Hardinge Medical College and Associated hospitals, Delhi
2. Vardhman Mahavir Medical college and S.J Hospital, Delhi
3. SMS medical College, Jaipur, Rajasthan
4. B.J Medical College, Ahmedabad, Gujarat
5. B.J Medical college, Pune, Maharashtra
6. Government Medical college, Chandigarh
7. Mysore Medical college, Mysuru, Karnataka
8. GSVM Medical College, Kanpur, Uttar Pradesh
9. Gauhati Medical College and Hospital, Guwahati, Assam
10. K.A.P V. Government Medical College, Tiruchirappalli, Tamil Nadu
11. NEIGRIHMS, Shillong, Meghalaya
12. Govt. Medical College, Thiruvananthapuram, Kerala
13. M.G.M College and Hospital, Indore, Madhya Pradesh
14. IGMC, Shimla, Himachal Pradesh
15. Govt. Medical College and Hospital, Aurangabad, Maharashtra
16. Osmania Medical College, Hyderabad, Telangana
17. Govt. Medical College & Hospital, Jammu, Jammu and Kashmir
18. Agartala Govt. Medical College, Agartala, Tripura
19. Guntur Medical College, Guntur, Andhra Pradesh
20. SCB Medical College & Hospital, Cuttack, Odisha
21. Pt. Jawaharlal Nehru Memorial Medical College, Raipur, Chattisgarh
22. Rajendra Institute of Medical Sciences, Ranchi, Jharkhand
23. Pandit Bhagwat Dayal Sharma, Post Graduate Institute of Medical Sciences (PGIMS) Rohtak, Haryana
24. Indira Gandhi Institute of Medical Sciences, Sheikhpura, Patna, Bihar
25. Govt. Medical College, Haldwani, Uttarakhand
26. Gandhi Medical College, Bhopal, Madhya Pradesh
27. Calcutta School of Tropical Medicine, Kolkata, West Bengal
28. Lala Lajpat Rai Memorial (LLRM) Medical College, Meerut, Uttar Pradesh
29. GMERS Medical College and Civil Hospital, Valsad, Gujarat
30. Coimbatore Medical College & Hospital, Coimbatore, Tamil Nadu
31. Karnataka Institute of Medical Sciences (KIMS), Hubli, Karnataka
32. Indira Gandhi Medical College & Research Institute (IGMC & RI) Puducherry
33. NAMO Medical Education and Research Institute (MERI), Silvassa, Dadra & Nagar Haveli
34. Maulana Azad Medical College (MAMC) and Associated Hospitals, Delhi
35. Sardar Patel Medical College (SPMC) and Hospital, Bikaner, Rajasthan
36. Goa Medical College & Hospital, Bambolim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