ANNUAL REPORT

Surveillance of Priority Bacterial Pathogens under National Antimicrobial Resistance Surveillance Network

2018

National Programme on Antimicrobial Resistance Containment

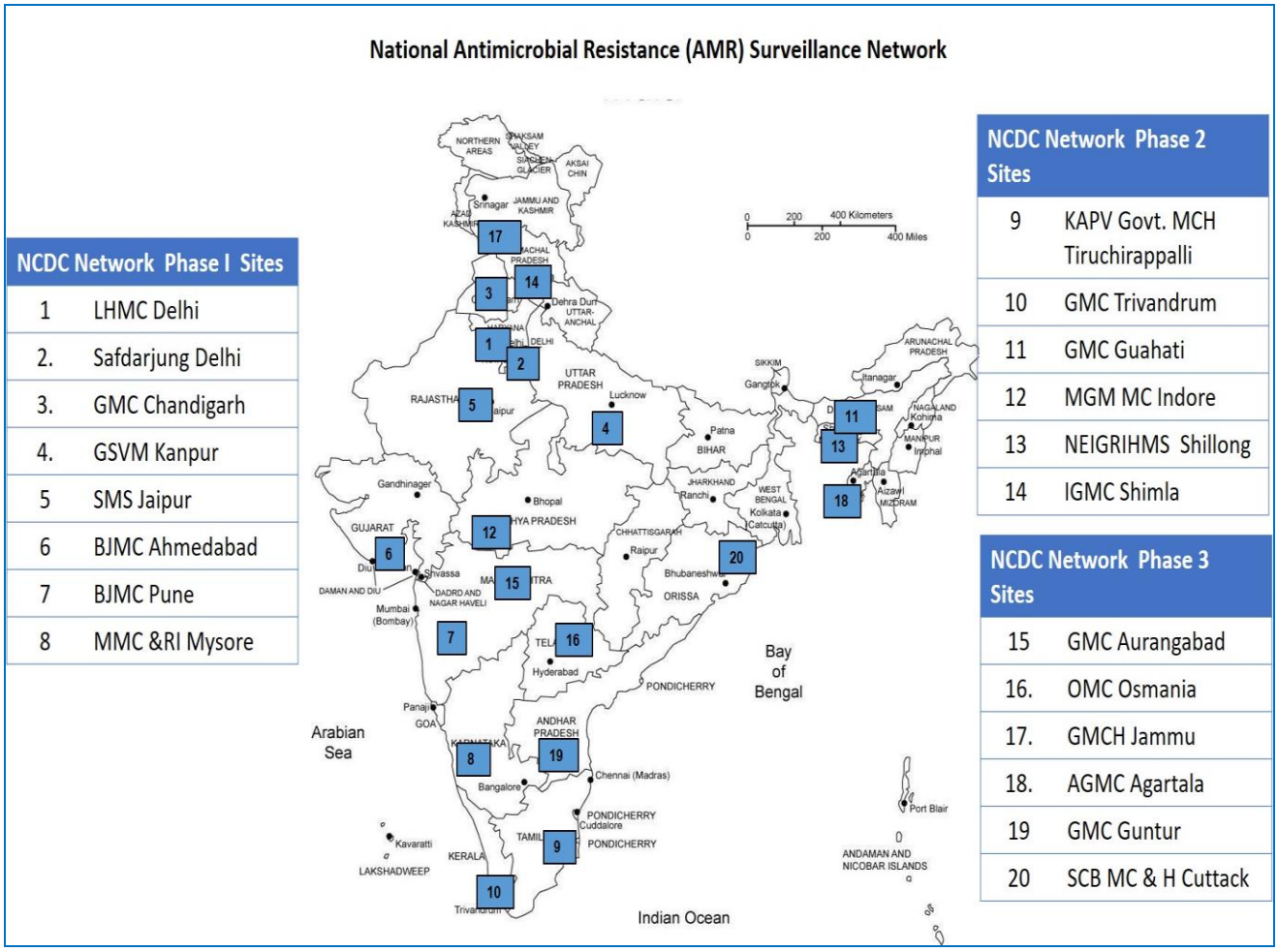
National Centre for Disease Control, Delhi, India

National Centre for Disease Control (NCDC) is coordinating the "National Programme on Antimicrobial Resistance Containment" initiated during the 12th five year plan. Under the programme a network of state medical college laboratories across the country are being strengthened in a phased manner for generating quality Antimicrobial Resistance (AMR) surveillance data in order to understand the AMR trends in various geographical regions through a sentinel surveillance platform. Currently under this network AMR surveillance for seven high priority pathogens and identified emerging AMR alerts are to be reported to the national AMR surveillance coordinating center at NCDC. NCDC being the national coordinating center for Global AMR Surveillance System (GLASS), has also been submitting the annual data to GLASS since 2017.

A standardized approach has been undertaken by NCDC for collection, analysis, and reporting of laboratory-based AMR surveillance data using WHONET, a microbiology data management software. Standard operating procedures (SOPs) and guidance documents have been developed for sentinel surveillance sites for AMR surveillance and the sites are trained to use them. Various measures are undertaken on a regular basis to improve the quality of culture, identification of pathogens and antimicrobial susceptibility testing (AST) with strict quality control. The officers and staff at the AMR surveillance network sites are provided regular hands on training and onsite support for streamlining AMR data management. Regular feedback is also provided to network sites to improve data quality.

As on 31st March 2019, the National AMR surveillance network includes 20 medical college laboratories located in 18 states (Figure 1 & Annexure-I). In the year 2018 (01 January 2018 to 31 December 2018), laboratories from 16 sentinel sites located in 14 states reported 50,724 priority pathogen isolates from unique patients and their antimicrobial sensitivity data. The data was validated and analyzed at NCDC for preparation of the AMR annual report for 2018.

Figure 1. National AMR Surveillance Network laboratories under National Programme on AMR Containment, National Centre for Disease Control, New Delhi



NCDC Network Phase I Sites	
1	LHMC Delhi
2.	Safdarjung Delhi
3.	GMC Chandigarh
4.	GSVM Kanpur
5	SMS Jaipur
6	BJMC Ahmedabad
7	BJMC Pune
8	MMC &RI Mysore

NCDC Network Phase 2 Sites	
9	KAPV Govt. MCH Tiruchirappalli
10	GMC Trivandrum
11	GMC Guahati
12	MGM MC Indore
13	NEIGRIHMS Shillong
14	IGMC Shimla

NCDC Network Phase 3 Sites	
15	GMC Aurangabad
16.	OMC Osmania
17.	GMCH Jammu
18.	AGMC Agartala
19	GMC Guntur
20	SCB MC & H Cuttack

List of seven priority pathogens included under surveillance

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

National AMR Surveillance data:

The AMR data collected under the National Programme on AMR Containment for the year 2018 is from 16 tertiary health care settings (medical colleges) in 14 states, s.no. 1 to 16 in the above list. AMR surveillance data of a total of 50,724 isolates submitted to NCDC has been analyzed and is summarized below:

Table 1. The pathogens and specimens included under surveillance

Specimen	*Staph. aureus*	*Enterococcus* species	*Klebsiella* species	*E. coli*	*Acinetobacter* species	*Pseudomonas* species	*Salmonella* Typhi/Paratyphi
Blood	●	●	●	●	●	●	●
Urine		●	●	●			
Pus Aspirates	●	●	●	●	●	●	
Other Sterile Body fluids	●	●	●	●	●	●	
Stool							●

Total number of isolates from unique patients after validation = 50,724

- Urine - 21,944 (43%)
- Blood - 10,787 (21%)
- Pus Aspirates (PA) and Other Sterile body fluids (OSBF) - 17,991 (36%)
- Stool - 2

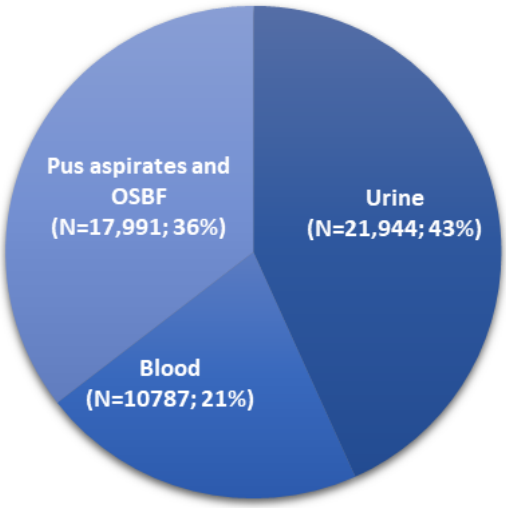


Figure 2. Specimen wise distribution of the priority pathogens reported under the programme

Of the 50,724 priority pathogen isolates submitted, the commonest is *E.coli* (36%) followed by *S. aureus* (22%), *Klebsiella* species (17%), *Enterococcus* species (10%), *Acinetobacter* species (8%) and *Pseudomonas* species (6%) (Table 2). From blood culture, *S. aureus* (38%) is the most common isolate followed by *Acinetobacter* species (19%) and *Klebsiella* species (18%) (Table 2).

Table 2. Specimen wise isolation of the Priority Pathogens under National AMR Surveillance Network

Priority Pathogens	Urine	Blood	Pus aspirates and OSBF	Stool	Total
Staph. aureus		4098	6968		11066 (22%)
***Enterococcus* spp.**	3643	801	715		5159 (10%)
Escherichia coli	14130	831	3148		18109 (36%)
***Klebsiella* spp.**	4171	1942	2737		8850 (17%)
***Pseudomonas* spp.**		777	2420		3197 (6%)
***Acinetobacter* spp.**		2036	2003		4039 (8%)
***Salmonella* Typhi and Paratyphi**		302		2	304 (1%)
Total	21944 (43%)	10787 (21%)	17991 (36%)	2	**50,724**

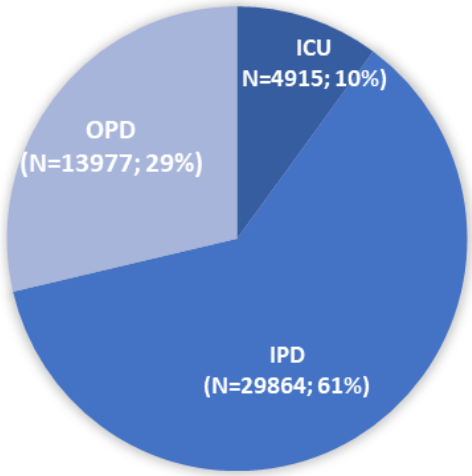


Figure 3. Patient location wise distribution of Priority pathogens reported in 2018

Table 3. Patient location wise isolation of the Priority Pathogens under National AMR Surveillance Network

Priority pathogens	Total	ICU	IPD	OPD
Staph. aureus	10839	896 (18%)	7173 (24%)	2770 (20%)
***Enterococcus* spp.**	4933	608 (12%)	2963 (10%)	1362 (10%)
Escherichia coli	17446	716 (15%)	10465 (35%)	6265 (45%)
***Klebsiella* spp.**	8358	1306 (27%)	4941 (16.5%)	2111 (15%)
***Pseudomonas* spp.**	3061	344 (7%)	1823 (6%)	894 (6%)
***Acinetobacter* spp.**	3825	1001 (20%)	2351 (8%)	473 (3%)
***Salmonella* Typhi and Paratyphi A and B**	294	44 (1%)	148 (0.5%)	102 (1%)
Total	48,756	4,915	29,864	13,977

Details of location type were available for 48,756 patient isolates. It was observed that in the ICU patients, *Klebsiella* species was the commonly isolated pathogen (27%) followed by *Acinetobacter* species (20%), *Staph. aureus* (18%), *E. coli* (15%), *Enterococcus* species (12%) and *Pseudomonas* species (7%) (Table 3). Whereas among the in-patients *E. coli* was the commonly isolated pathogen (35%), followed by *Staph. aureus* (24%), *Klebsiella* species (16.5%), *Enterococcus* species (10%), *Acinetobacter* species (8%), and *Pseudomonas* species (6%) (Table 3).

Antibiotic resistance profile for the year 2018

The resistance profile of priority pathogens for selected antibiotics as per NCDC AMR Surveillance SOP has been tabulated in Tables 4-9 and summarized below:

Staphylococcus aureus and *Enterococcus* species

Staph. aureus isolates from blood showed 69% resistance to cefoxitin (surrogate marker for *mec*A-mediated oxacillin resistance) which was found to be higher than that reported in 2017 (57%). Overall resistance to cefoxitin, including isolates from other sterile body fluids and pus aspirates, was found to be 63% (Table 4). Emergence of linezolid resistant *Staph. aureus* and *Enterococcus* species to the extent of 1% and 6% respectively is a matter of concern (Table 4 and 5). Resistance to gentamicin was observed to be 19% in *Staph. aureus* and 57% in *Enterococcus* spp. isolates (Table 4 and 5). Notably, 64% isolates of *Enterococcus* spp. isolated from urine showed resistance to tetracycline (Table 5). 7% of

Enterococcus spp. isolates from blood were resistant to Linezolid. 3% of Vancomycin-Resistant Enterococci (VRE) from blood were also linezolid resistant.

Table 4: Resistance (%) in *Staph. aureus* observed in the year 2018

Antibiotic tested	Blood+ Pus Aspirate + OSBF (N=11066)		PA+OSBF (N=6968)		Blood (N=4098)	
	Number	%R	Number	%R	Number	%R
Cefoxitin	10607	**63%**	6645	**60%**	3962	**69%**
Gentamicin	10119	**19%**	6429	**19%**	3690	**20%**
Ciprofloxacin	9889	**60%**	6228	**67%**	3661	**49%**
Trimethoprim/Sulfamethoxazole	8186	**36%**	5614	**29%**	2572	**51%**
Clindamycin	9965	**25%**	6442	**22%**	3523	**31%**
Erythromycin	9130	**64%**	5983	**60%**	3147	**72%**
Linezolid	9040	**1%**	5737	**1%**	3303	**1%**
Vancomycin*	14	**0%**	11	**0**	3	**0**
Doxycycline	3609	**15%**	2071	**15%**	1538	**15%**
Tetracycline	3852	**16%**	2238	**15%**	1614	**18%**

Abbreviations: OSBF, Other sterile body fluids; PA, Pus aspirates;

* % resistance of *Staph. aureus* against vancomycin is of low statistical validity as the number of isolates tested using broth microdilution method are ≤30.

Table 5: Resistance (%) in *Enterococcus* species observed in the year 2018

Antibiotic tested	Blood+ Pus Aspirate + OSBF+ urine (N=5159)		Pus Aspirate + OSBF (N=715)		Blood (N=801)		Urine (N=3643)	
	Number	%R	Number	%R	Number	%R	Number	%R
Ampicillin	3447	**58%**	536	**50%**	556	**58%**	2355	**60%**
Gentamicin-High	3721	**57%**	564	**43%**	598	**55%**	2559	**60%**
Ciprofloxacin	2570	**76%**	558	**67%**	673	**70%**	1339	**84%**
Erythromycin	1821	**79%**	599	**79%**	708	**77%**	514	**81%**
Linezolid	4615	**6%**	643	**5%**	743	**7%**	3229	**6%**
Vancomycin	3656	**18%**	547	**14%**	627	**25%**	2482	**18%**
Doxycycline	1053	**46%**	118	**43%**	137	**24%**	798	**50%**
Tetracycline	1760	**62%**	170	**63%**	188	**48%**	1402	**64%**

Abbreviations: OSBF, Other sterile body fluids; PA, Pus aspirates

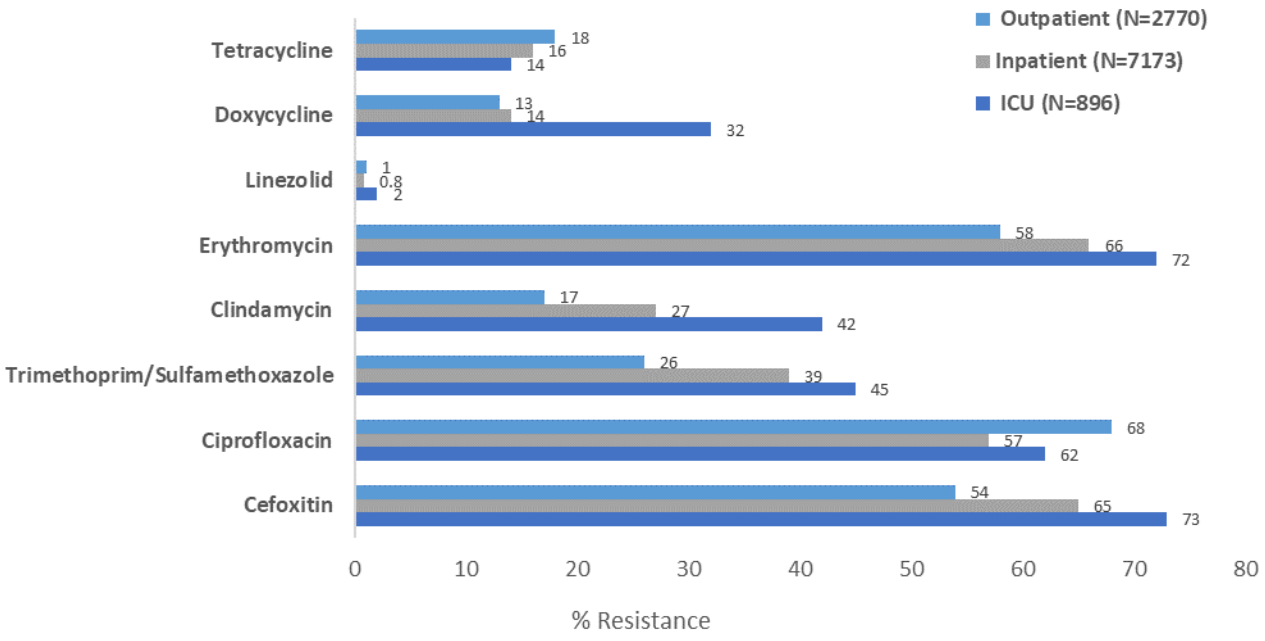


Figure 4a. Resistance profile of *Staph. aureus* from blood, pus aspirates and other sterile body fluids obtained from different location types in the health facilities

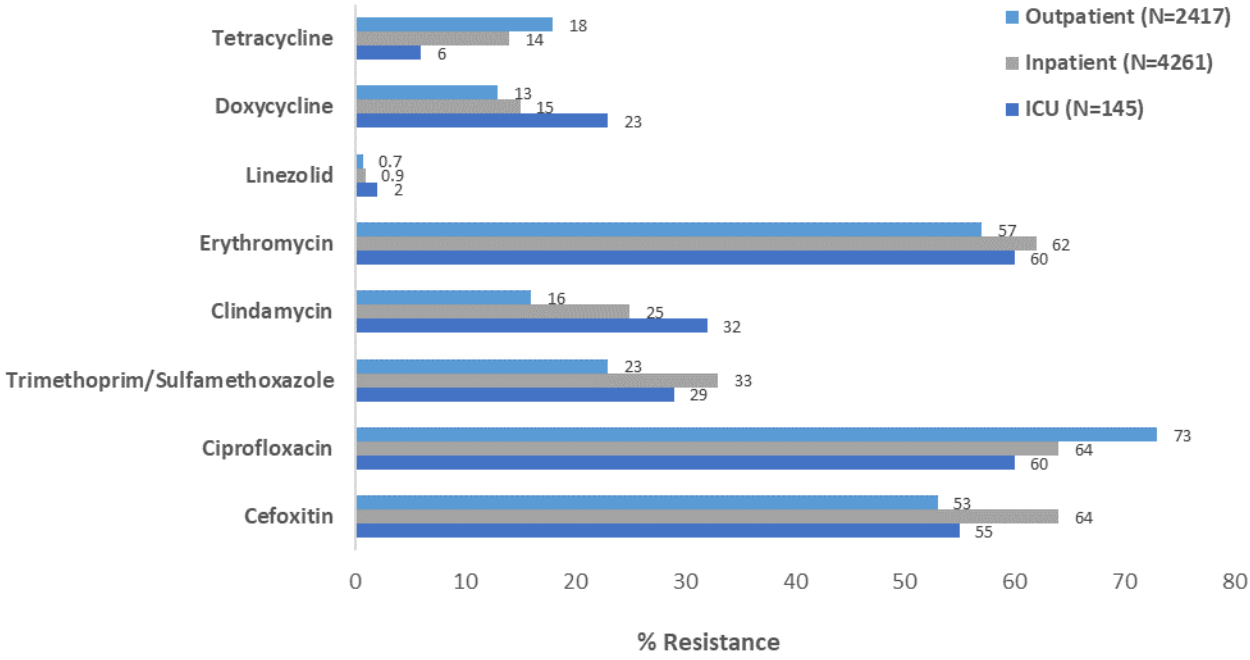


Figure 4b. Resistance profile of *Staph. aureus* from pus aspirates and other sterile body fluids obtained from different location types in the health facilities

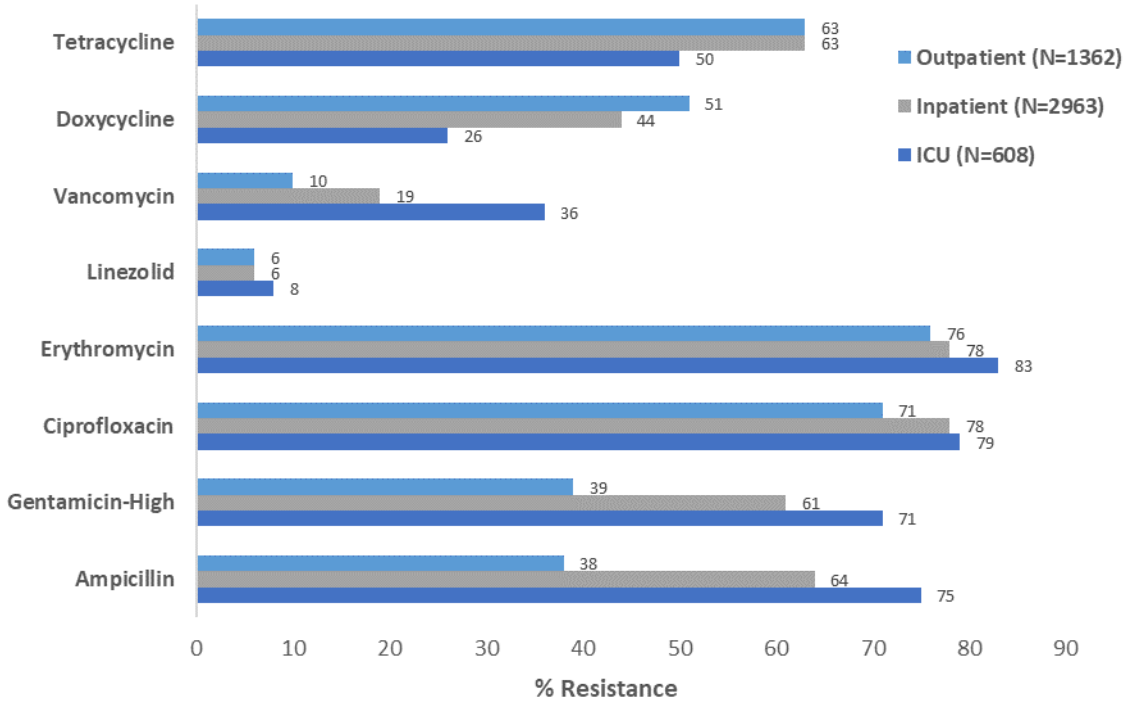


Figure 5a. Resistance profile of *Enterococcus* spp. from blood, pus aspirates, other sterile body fluids and urine obtained from different location types in the health facilities

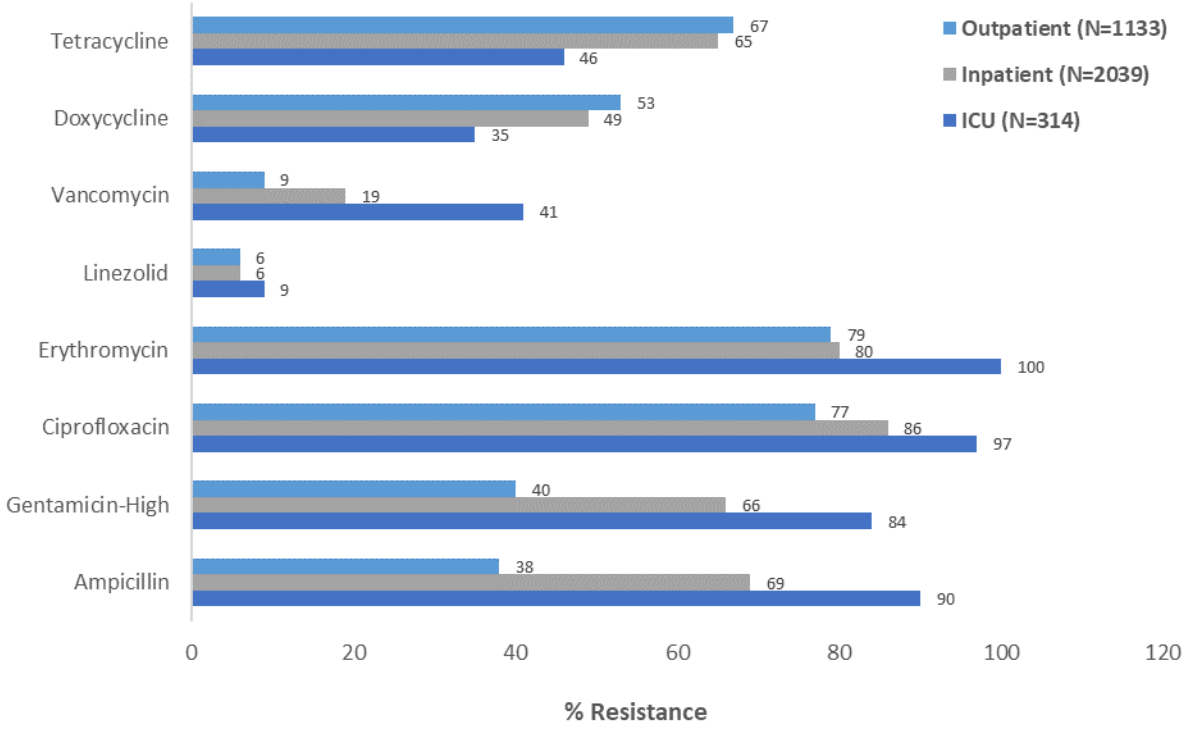


Figure 5b: Resistance profile of *Enterococcus* species from urine specimens obtained from different location types in the health facilities

E. coli and *Klebsiella* species

E. coli isolated from blood showed 84% resistance to cefotaxime and 63% to cefepime. *E. coli* from urine showed higher resistance rates to cefepime (70%) than those isolated from blood (63%). (Table 6). Resistance to carbapenems that is ertapenem and imipenem was observed to be 40% and 33% in *E.coli* blood isolates which is higher than that observed in 2017 (37% to ertapenem and 25% to imipenem in year 2017) (Table 6). Compared to *E. coli*, *Klebsiella* species showed comparatively higher resistance to carbapenems i.e. 53% to imipenem and 60% to ertapenem in blood isolates (Table 7). Similarly as compared to *E. coli* higher resistance was observed in *Klebsiella* species to cefotaxime and cefepime isolated from blood (89% to cefotaxime and 75% to cefepime) (Table 7). The most common pathogen in ICU setting is *Klebsiella* species whereas *E.coli* is most commonly isolated in inpatients (Table 3).

Table 6: Resistance (%) in *E. coli* observed in year 2018

Antibiotic tested	Blood+ Pus Aspirate + OSBF+urine (N=18109)		Blood (N=831)		Urine (N=14130)		PA+OSBF (N=3148)	
	Number	%R	Number	%R	Number	%R	Number	%R
Ampicillin	6585	**92%**	509	**86%**	4791	**93%**	1285	**89%**
Cefotaxime	10096	**83%**	500	**84%**	7721	**82%**	1875	**87%**
Cefepime	6480	**71%**	496	**63%**	4289	**70%**	1695	**76%**
Ertapenem	6208	**38%**	402	**40%**	4278	**37%**	1528	**39%**
Imipenem	5885	**35%**	589	**33%**	3479	**37%**	1817	**32%**
Ciprofloxacin	11110	**74%**	731	**59%**	7536	**75%**	2843	**75%**
Trimethoprim/Sulfamethoxazole	12821	**66%**	392	**56%**	11301	**66%**	1128	**69%**
Nitrofurantoin	13358	**12%**			13194	**12%**		

Abbreviations: OSBF, Other sterile body fluids; PA, Pus aspirates; Sensitivity of *E.coli* against colistin is not tested using broth microdilution test method therefore results are not considered.

Table 7: Resistance (%) in *Klebsiella* species observed in year 2018

Antibiotic tested	Blood+ Pus Aspirate + OSBF+Urine (N=8850)		Blood (N=1942)		Urine (N=4171)		PA+OSBF (N=2737)	
	Number	**%R**	**Number**	**%R**	**Number**	**%R**	**Number**	**%R**
Cefotaxime	5476	**85%**	1346	**89%**	2442	**81%**	1688	**87%**
Cefepime	3431	**75%**	923	**75%**	1221	**72%**	1287	**78%**
Ertapenem	3465	**56%**	891	**60%**	1388	**52%**	1186	**58%**
Imipenem	4283	**54%**	1256	**53%**	1458	**54%**	1569	**56%**
Ciprofloxacin	6290	**62%**	1649	**51%**	2147	**65%**	2494	**66%**
Trimethoprim/ Sulfamethoxazole	5595	**65%**	1065	**64%**	3458	**64%**	1072	**69%**
Nitrofurantoin	4019	**48%**			3799	**46%**		

Abbreviations: OSBF, Other sterile body fluids; PA, Pus aspirates; Sensitivity of *Klebsiella* spp. against colistin is not tested using broth microdilution test method therefore results were not considered.

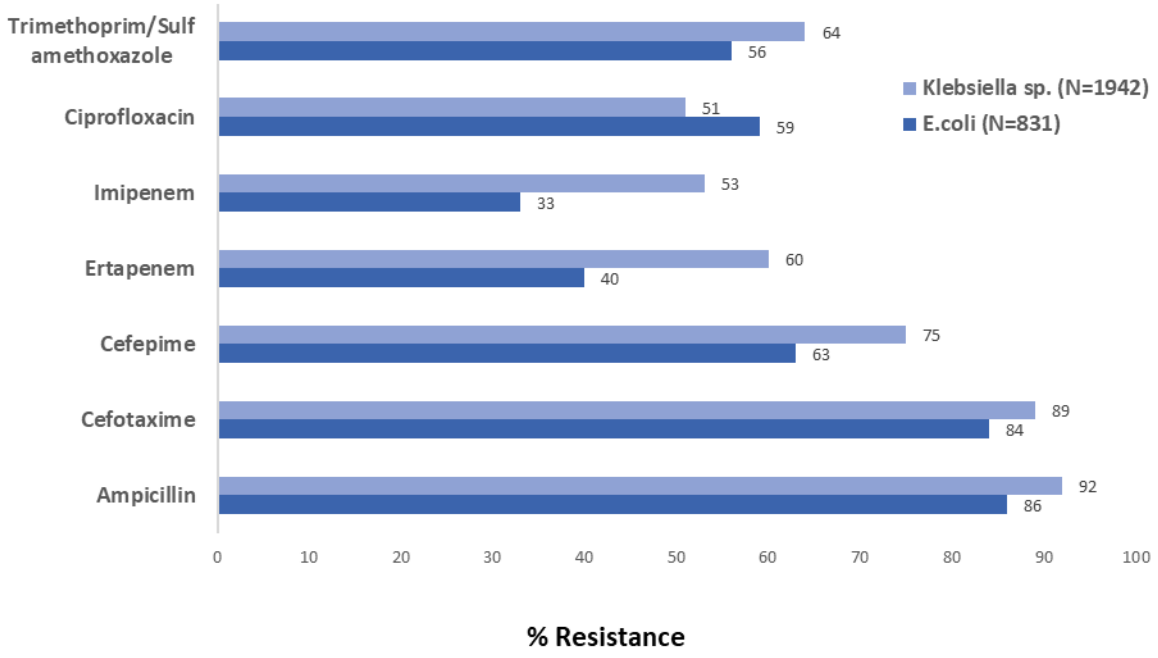


Figure 6. Resistance profile of *Escherichia coli* and *Klebsiella* species obtained from blood specimens

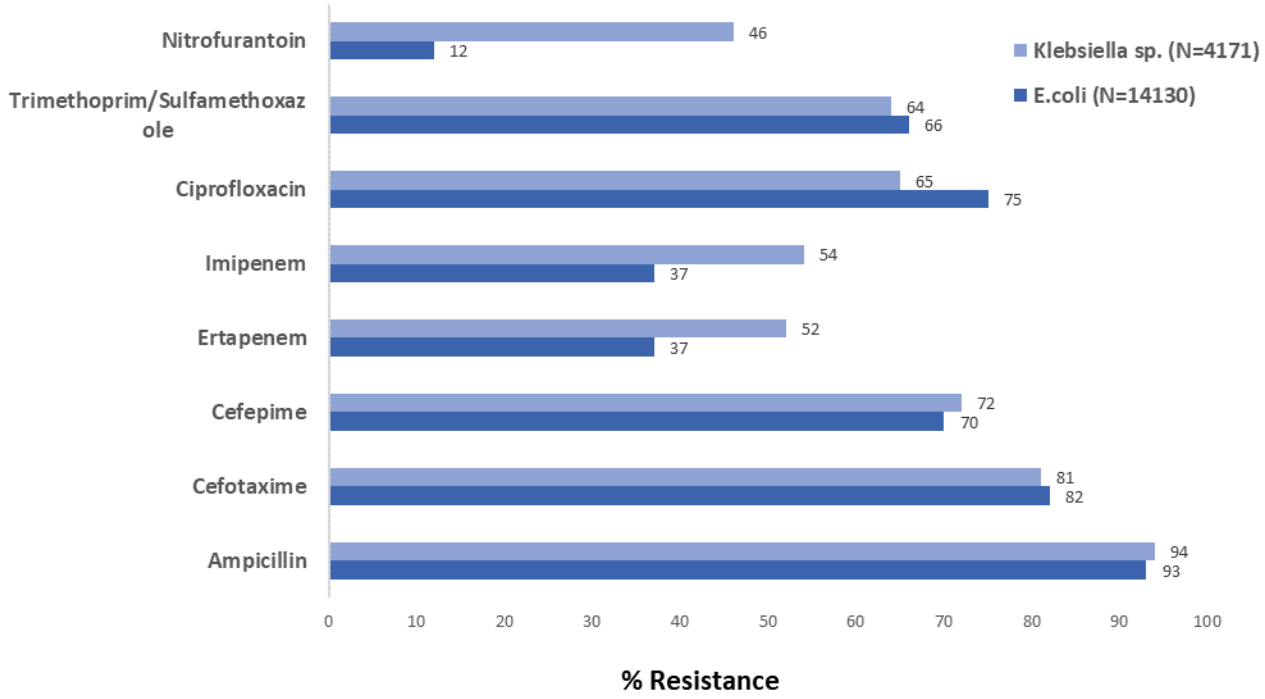


Figure 7. Resistance profile of *E. coli* and *Klebsiella* species obtained from urine specimens

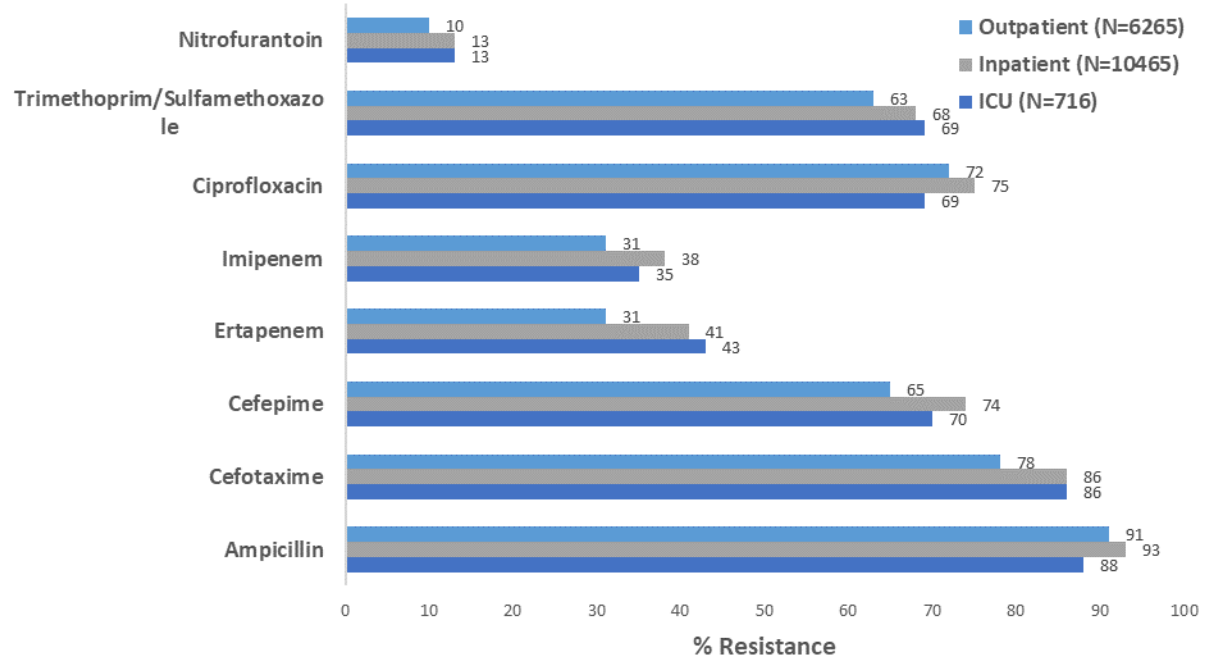


Figure 8a. Resistance (%) in *E. coli* in different location types

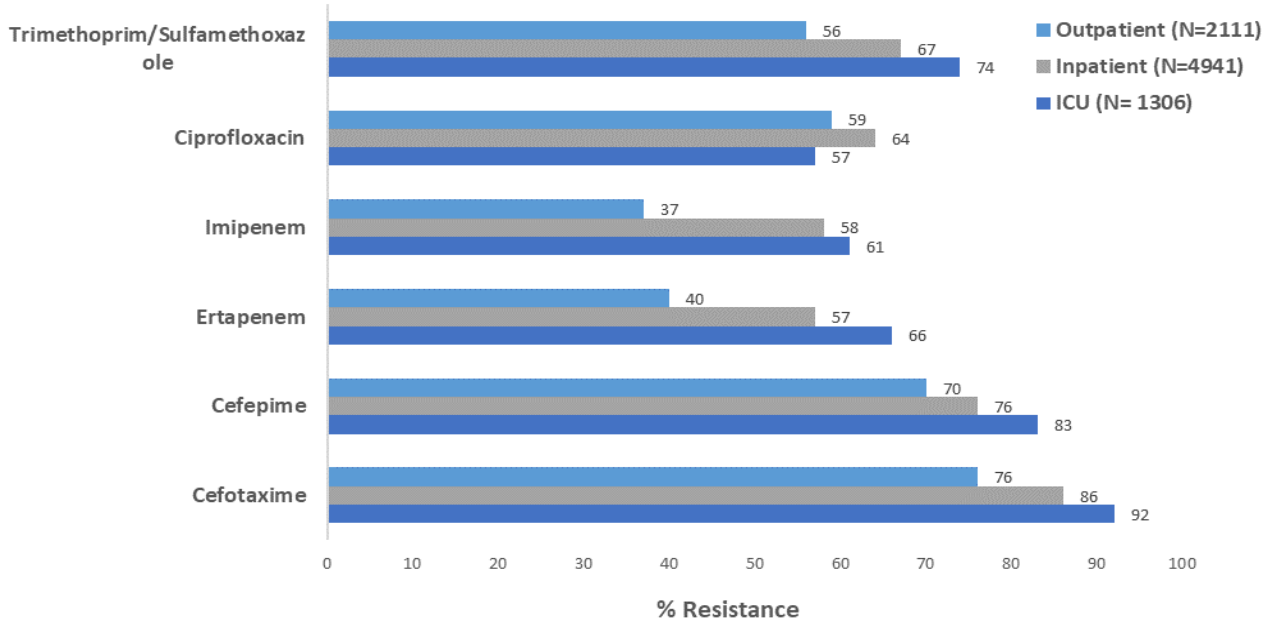


Figure 8b. Resistance (%) in *Klebsiella* species in different location types

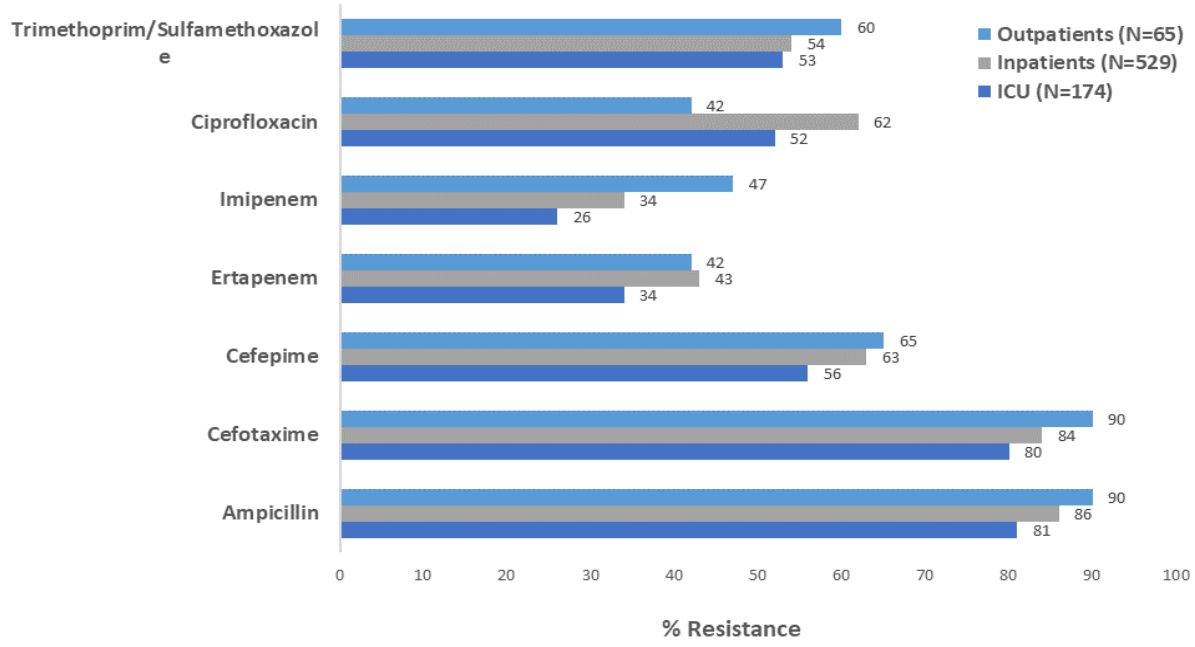


Figure 9. Resistance profile of *Escherichia coli* in blood specimens obtained from different location types in the health facilities

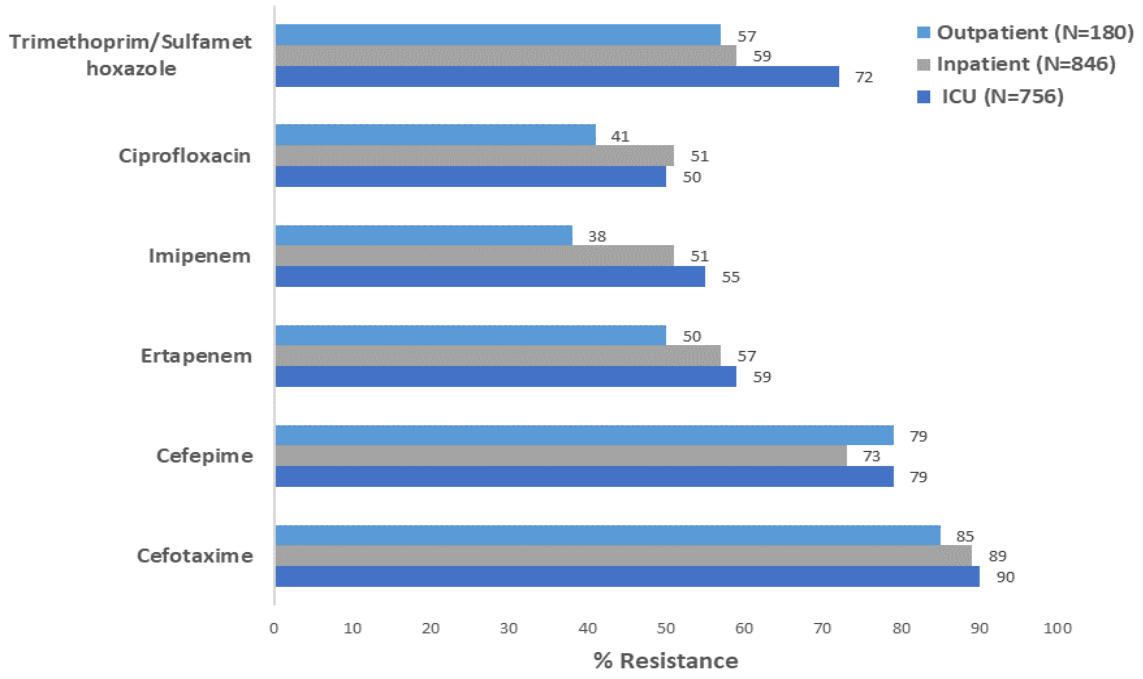


Figure 10. Resistance profile of *Klebsiella* spp. from blood specimens obtained from different location types in the health facilities

Pseudomonas and *Acinetobacter* species

Pseudomonas species showed lowest resistance to piperacillin-tazobactam (27%) followed by imipenem (36%), aminoglycosides (amikacin: 43%; tobramycin: 45%), ciprofloxacin (43%) and ceftazidime (51%) (Tables 8). However, *Acinetobacter* species showed high resistance to imipenem (66%) and aminoglycosides (amikacin: 66%; gentamicin: 54%) (Table 9). Among the anti-pseudomonal agents, piperacillin/tazobactam was found to be more active than imipenem. Not surprisingly, the isolates of both the species from ICU showed higher resistance as compared to isolates from non-ICU settings (Figure 11 and 12). Isolates of *Acinetobacter* species showed >50% resistance to almost all the antibiotics tested except for minocycline (29%) (Table 9).

Table 8: Resistance (%) in *Pseudomonas* species

Antimicrobials tested	Blood+ Pus Aspirate + OSBF (N=3197)		Pus Aspirate + OSBF (N=2420)		Blood (N=777)	
	Number	**%R**	**Number**	**%R**	**Number**	**%R**
Piperacillin/Tazobactam	2660	**27%**	2068	**28%**	592	**24%**
Ceftazidime	2806	**51%**	2140	**52%**	666	**49%**
Imipenem	2371	**36%**	1842	**39%**	529	**28%**
Amikacin	2729	**43%**	2089	**44%**	640	**41%**
Gentamicin	1403	**39%**	1017	**39%**	386	**38%**
Tobramycin	804	**45%**	608	**48%**	196	**35%**
Ciprofloxacin	2756	**43%**	2105	**47%**	651	**30%**
Colistin	45	4%	28	7%	17	0

Abbreviations: OSBF, Other sterile body fluids; PA, Pus aspirates; Sensitivity of *Pseudomonas* spp. against colistin is tested for only 45 isolates using broth microdilution test method.

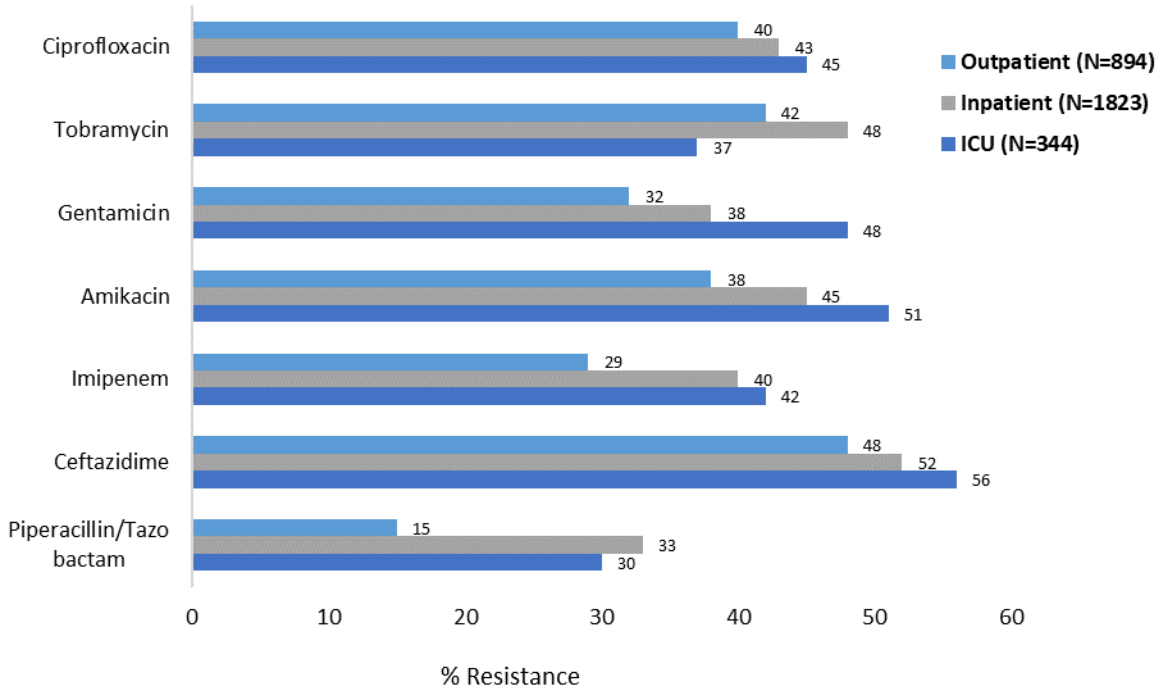


Figure 11. Resistance profile of *Pseudomonas* species obtained from different location types in health facilities

Table 9: Resistance (%) in *Acinetobacter* species observed in year 2018

Antimicrobials tested	Blood + Pus Aspirate + OSBF (N=4039)		Pus Aspirate + OSBF (N=2003)		Blood (N=2036)	
	Number	%R	Number	%R	Number	%R
Piperacillin/Tazobactam	3227	**66%**	1674	**74%**	1553	**57%**
Ceftazidime	2527	**83%**	1322	**87%**	1205	**79%**
Imipenem	2822	**66%**	1384	**76%**	1438	**57%**
Amikacin	3272	**68%**	1636	**74%**	1636	**61%**
Gentamicin	2335	**56%**	1183	**66%**	1152	**46%**
Ciprofloxacin	3425	**67%**	1745	**77%**	1680	**57%**
Minocycline	489	**29%**	225	**43%**	264	**16%**
Tetracycline	524	**50%**	224	**49%**	300	**51%**

Abbreviations: OSBF, Other sterile body fluids; PA, Pus aspirates; Sensitivity of *Acinetobacter* spp. against colistin is not tested using broth microdilution test method therefore results are not considered.

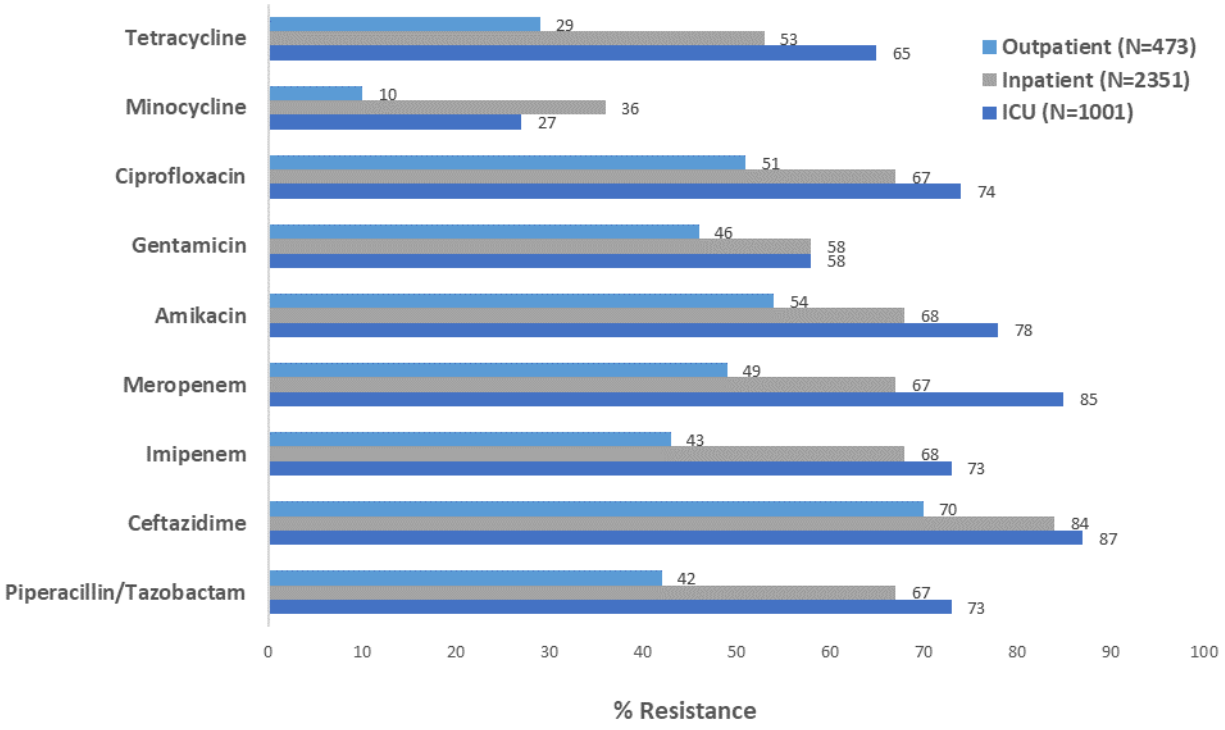


Figure 12. Resistance profile of *Acinetobacter* species obtained from different location types in health facilities

Salmonella enterica serotypes Typhi and Paratyphi

Noticeably, isolates of *Salmonella enterica* serotype Typhi and Paratyphi obtained from blood showed 35% resistance to ciprofloxacin which has increased from previous year resistance rate (27%). Surprisingly, resistance to azithromycin in *Salmonella* Typhi isolates has almost doubled (8%) than from previous year (4.5%) (Table 10). However the number of *Salmonella* Typhi isolates tested for Azithromycin were much lower last year.

Table 10: Resistance (%) in *Salmonella enterica* serotypes Typhi and Paratyphi isolated from blood specimen

Antibiotic tested	S. Typhi (N=279)		S. Paratyphi (N=23)*	
	No. tested	%R	No. tested	%R
Ampicillin	238	10	18	0
Ceftriaxone	202	8	15	0
Imipenem	53	13	1	0
Nalidixic acid	254	97	18	100
Ciprofloxacin	263	35	21	29
Trimethoprim/Sulfamethoxazole	230	3	18	0
Azithromycin #	245	8		
Chloramphenicol	237	4	16	0

*Statistical validity of % resistance of *Salmonella* Paratyphi is low as the number of isolates are <30.

AST for Azithromycin was performed only on isolates of S. Typhi

Annexure I

National AMR Surveillance Network laboratories under National Programme on AMR Containment, National Centre for Disease Control, New Delhi

1. Lady Harding Medical College and associated hospitals, New Delhi
2. VMMC and associated Safdarjung Hospital, New Delhi
3. Government Medical College & Hospital, Chandigarh (UT)
4. GSVM Medical College, Kanpur, Uttar Pradesh
5. SMS Medical College, Jaipur, Rajasthan
6. BJ Medical College, Ahmedabad, Gujarat
7. BJ Medical College, Pune, Maharashtra
8. Mysore Medical College and Research Institute, Mysore, Karnataka
9. KAPV Govt Medical College Hospital, Thiruchirapally, Tamil Nadu
10. Government Medical College, Thiruvananthapuram, Kerala
11. MGM Medical College & MY Hospital, Indore, Madhya Pradesh
12. NEIGRIHMS, Shillong, Meghalaya
13. Indira Gandhi Medical College, Shimla, Himachal Pradesh
14. Government Medical College, Aurangabad, Maharashtra
15. Gauhati, Medical College Hospital, Guwahati, Assam
16. Agartala Govt. Medical College, Agartala, Tripura
17. Osmania Medical College, Hyderabad, Telangana
18. Guntur Medical College, Guntur, Andhra Pradesh
19. SCB Medical College, Cuttack, Odisha
20. Government Medical College & Hospital, Jammu, Jammu & Kashmir