Annual Report

Antimicrobial Resistance Research and Surveillance Network

January 2022 to December 2022

Division of Epidemiology and Communicable Diseases

INDIAN COUNCIL OF MEDICAL RESEARCH
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CONTENTS

List of acronyms

AFLP	Amplified fragment length polymorphism
AFST	Antifungal susceptibility testing
AMRSN	Antimicrobial Resistance Research & Surveillance Network
AMS	Antimicrobial Susceptibility
AST	Antimicrobial Susceptibility Testing
BAL	Bronchoalveolar lavage
BSI	Blood stream infections
CAM	COVID-19–associated mucormycosis
CARD	Comprehensive Antibiotic Resistance Database
CAUTI	Catheter associated urinary tract infections
CDS	Coding sequence regions
CGPS	Center for Genomic Pathogen Surveillance
CLABSI	Catheter associated blood stream infections
CLSI	Clinical & Laboratory Standards Institute
CoNS	Coagulase-negative Staphylococci
CRAB	Carbapenem-resistant *Acinetobacter baumannii*
CRE	Carbapenem resistant Enterobacterales
CSF	Cerebrospinal fluid
DI	Deep infections
DEC	Diarrheagenic *E coli*
DTR	Difficult to treat
ESBLs	Extended spectrum beta lactamases
GPC	Gram-positive cocci
GNB	Gram-negative bacteria
HAI	Hospital acquired Infections
HCAI	Health Care Associated infections
HCWs	Health care workers
ICU	Intensive care unit
IPC	Infection prevention and Control
IV	Intravenous
OPD	Out-patient department
LOS	Length of stay
LRT	Lower Respiratory tract
MBL	Metallo-beta-lactamase
MFS	Major Facilitator superfamily
MIC	Minimum inhibitory concertation
MLST	Multi-locus sequence typing
MRSA	Methicillin-resistant *Staphylococcus aureus*
MSSA	Methicillin sensitive *Staphylococcus aureus*
NFGNB	Non fermenting Gram-negative bacilli
OXA	Oxacillinases
PBP2a	Penicillin binding protein 2a
PCV	Pnuemococcal Conjugate Vaccine
PMQR	Plasmid mediated quinolone resistance
QUAST	Quality assessment tool
RC	Regional centers
RGI	Resistance gene identifier
ROM	rhino-orbital mucormycosis
SCC *mec*	Staphylococcal cassette chromosome mec
SI	Superficial infections

SD	Standard deviation
SS	Sterile body fluids
ST	Sequence types
STR	Short tandem repeat
TMP-SMX	Trimethoprim sulfamethoxazole
TRF	Tandem repeat finder
UTI	Urinary Tract Infections
VAP	Ventilator Associated Pnuemonia
VRE	Vancomycin-resistant enterococci
VVE	Vanconycin Variable *Enterococcus*
WGS	Whole-genome sequencing
XDR	Extensively drug-resistant

Executive summary

ICMR- Antimicrobial Resistance Surveillance network

The Indian Council of Medical Research (ICMR) has been supporting research on antimicrobial resistance through the Antimicrobial Resistance Research & Surveillance Network (AMRSN) since 2013. The data collected from the network has enabled compilation of drug resistance data on six pathogenic groups on antimicrobial resistance from the country. Data collected from the network is used to track resistance trends and to better understand mechanisms of resistance in the key priority pathogens using genomics and whole genome sequencing (WGS). This is the sixth detailed report on AMR trends and patterns from the country, published by ICMR. Since the network collects data from tertiary care hospitals, the data presented in this report is not reflective of the community levels of AMR in the country and should not be extrapolated to community settings.

This report also includes the interpretation of antibiograms from OPD/Ward/ICU which is crucial for assessing the impact of antimicrobial resistance and its implications in clinical practice for empirical use of antibiotics. This further helps in identifying potential areas for interventions and improvements in antibiotic stewardship practices.

Highlights of surveillance data 2022:

- This report presents data from January 1st, 2022 to December 31st, 2022. Total number of culture positive isolates studied during the year 2022 was 1,07,053.
- *Escherichia coli* was the most commonly isolated pathogen followed by the *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Staphylococcus aureus*.
- Among Enterobacterales, *Escherichia coli*, *Klebsiella pneumoniae*, *Citrobacter koseri* and *Enterobacter cloacae* isolated from out-patients were more susceptible than those from in-patients for all drugs tested.
- Imipenem susceptibility of *E. coli* has dropped steadily from 81% in 2017 to 66% in 2022 and that of *Klebsiella pneumoniae* dropped steadily from 59% in 2017 to 42% in 2022.
- With regards to molecular characterisation of β-lactamases in *Escherichia coli* isolates, CTXM-15 (39%) was the most common β-lactamases identified followed by OXA-1 (34%) and CTXM-1 (21%) and for *Klebsiella pneumoniae,* SHV (55%) was the most common followed by CTXM-15 (37%) and OXA-48 (25%); but there was marked variability in distribution of β-lactamases among regional centers.

- *In P. aeruginosa,* the susceptibility percentage to anti-pseudomonal cephalosporin such as ceftazidime (56.4% vs 47.1%) and cefepime (60.3% vs 49.8%) was higher in wards isolates as compared to ICU.
- There was no change in the trend of susceptibility to piperacillin/tazobactam, ceftazidime and aminoglycosides in *P. aeruginosa*. All the tested *P. aeruginosa* isolates were highly susceptible to colistin and there was no change in the trend of susceptibility to colistin for the five years. Nearly 40% of carbapenem resistant *P. aeroginosa* isolates harbour Class B type of β-lactamases (Metallo-β-lactamase), with NDM being the most common.
- Resistance to carbapenems in *Acinetobacter baumannii* was recorded as 87.8% in the year 2022, limiting the availability of available treatment options. In *A. baumannii*, there is no significant change in the susceptibility trends to all the tested antibiotics compared to last year. Susceptibility to minocycline was close to 58% to make it the most susceptible antibiotic after colistin for *Acinetobacter baumannii.* Similar to previous years, blaOXA-23-like was the only predominant carbapenemase across all the centers contributing to 76% of carbapenem resistance.
- Among CLABSI causing pathogens, Gram-negative organisms (70.9%) were responsible for most CLABSI, followed by Gram-positive (16.9%) and fungal pathogens (12.2%), same was also true for other device associated infections like CAUTI and VAP.
- 75% of *Klebsiella pneumoniae* and 88% of *Acinetobacter baumannii* causing blood stream infections (BSIs) in ICUs were imipenem resistant. Nearly 87% of *Staphylococcus aureus* and around 42% of *Enterococcus faecium* causing BSIs in ICUs were respectively oxacillin and vancomycin resistant. Hence, the prevalence of AMR in ICU is very high, so focus on infection control practices in ICU and other critical areas should be top priority.
- *In Staphylococcus aureus*, susceptibility to erythromycin, clindamycin, ciprofloxacin and co-trimoxazole was more evident in MSSA when compared to MRSA. MRSA rates are increasing each year from 2016 to 2021 (28.4% to 42.6%). The anti MRSA antibiotics such as vancomycin and teicoplanin showed excellent in vitro activity (nearly 100% against MRSA isolates). Linezolid resistance was encountered very rarely. Levonadifloxacin was tested on 771 isolates of MRSA, and all of them were shown to be susceptible. As per available literature (limited to in-vitro and Phase 1 and Phase 2 clinical studies) , it appears to be highly efficient against acute bacterial skin and skin structure infections, as well as bacteraemia and diabetic foot infections.
- In enterococci, vancomycin resistance was 16.7% slightly higher than the rate in 2021(14.9%). However, the rate was 5 times higher in *E. faecium* compared *to E.*

faecalis (27% vs 5.3%). Vancomycin resistance among CSF isolates was much higher than the overall rate.

- The detection of *Enterococcus* species other than *faecalis* and *faecium* in high numbers is also significant as some of these species are intrinsically resistant to glycopeptides. Hence speciation of enterococci is of clinical significance.
- With regards to *S. pneumoniae,* the non-vaccine serotypes (compared to PCV-10) were more than 50% of the total isolates. Susceptibility of pencillin among meningeal isolates of *S. pneumoniae* was down to just 32% and that of cefotaxime was 82%, whereas among non-meningeal isolates, susceptibility to both these drugs was close to 100%. Hence, monotherapy with either of these antibiotics is not recommended for CNS infections, ICMR guidelines of combination therapy (cephalosporins with vancomycin) is recommended for meningitis.
- Ceftriaxone (96.1% susceptible), Cefixime (94 % susceptible), trimethoprim-sulfamethoxazole (92% susceptible) and azithromycin (97.4% susceptible) showed very good susceptibility patterns for *Salmonella typhi* isolates. Fluoroquinolones show very poor susceptibility patterns (> 95% resistance) for *Salmonella typhi* isolates
- Hence, TMP-SMX and azithromycin remain very good oral options for treatment of patients with enteric fever whereas IV Ceftriaxone may be used for patients admitted with Enteric Fever. Empirical use of fluoroquinolones is not justified to treat Enteric fever.
- There has been no significant change in the overall antimicrobial susceptibility pattern of Salmonella Typhi or S. Paratyphi A from India and the pattern remaining uniform across all the participating centers in the AMR network. S.Typhi susceptibility to cephalosporins and azithromycin has shown a declining trend as compared to the last year. Other drugs which retained good susceptility for Salmonella Typhi or S. Paratyphi A were ampicillin, chloramphenicol and trimethoprim-sulfamethoxazole.
- Diarhogenic *E. coli, Aeromonas spp. and Salmonella spp.* were most common pathogens among diarrheal pathogens reported by the network. Antibiograms of these isolates showed, high rates of resistance to fluoroquinolones; more than 90% isolates of Diarhogenic *E. coli* and *Aeromonas spp*. were resistant to fluoroquinolones. Hence, empirical use of ciprofloxacin or norfloxacin is not justified for patients with diarrhoea.
- In fungal pathogens, antifungal susceptibility profiling revealed more than 93% fluconazole susceptibility in *C. albicans and C. tropicalis* but declining susceptibility rates (77%-85%) were reported in *C. utilis, C. parapsilosis* and *C. glabrata* thus requiring close monitoring in next few years.

- *C. auris* and *C. krusei* were predominantly resistant to fluconazole with extremely low susceptibility percentages of 1.9% and 11.8%, respectively. High levels of voriconazole resistance in *C. albicans also* need to be closely examined
- There was a decline in isolation rates of *Candida* species in 2022. *C. tropicalis* isolation dropped from 1.4% in 2017 to 0.6% in 2022. Isolation rates of *C. auris* have remained same from 2017 to 2022.
- *Aspergillus flavus* was the most commonly identified Aspergillus species followed by *A. fumigatus.* Both *Aspergillus flavus and fumigates* showed excellent susceptibility (close to 100%) to voriconazole, whereas susceptibity for Amphotericin B was 87.8% for *Aspergillus flavus* and 69.2% for *A. fumigatus*.

Key takeaways: Interpretataions of common syndromic isolates and implications in clinical practice

Urine

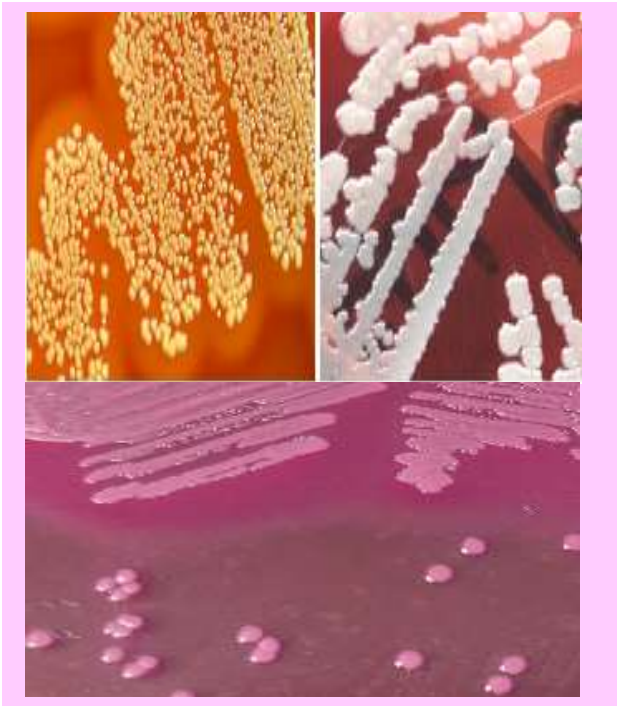
- *Escherichia coli and Klebsiella pneumoniae* are most common organisms isolated from urine from OPD, wards and ICU.
- Fosfomycin (96.9% susceptible) and Nitrofurantoin (91.3% susceptible) showed very good susceptibility patterns in *E coli* urinary isolates particularly in OPD and ward patients. Hence oral fosfomycin and oral nitrofurantoin may be used to treat cystitis.
- Amikacin (89.5% susceptible) and Ertapenem (80.8% susceptible) showed very good susceptibility patterns in *E coli* and *Klebsiella pneumoniae* urinary isolates particularly in OPD and ward patients. Hence IV Amikacin and IV Ertapenem may be used to treat upper UTI or patient presenting with fever and urinary symptoms.

Stool

- Diarhogenic *E. coli, Aeromonas spp. and Salmonella spp.* were most common pathogens isolated from stool samples of patients presenting with diarrhoea in OPD or getting admitted in wards.
- Antibiograms of these isolates showed, high rates of resistance to fluoroquinolones; more than 90% isolates of Diarhogenic *E. coli* and *Aeromonas spp*. were resistant to fluoroquinolones. Hence, empirical use of ciprofloxacin or norfloxacin is not justified for patients with diarrhoea.
- Among the tested isolates, trimethoprim-sulfamethoxazole and azithromycin showed good susceptible rates to *Salmonella spp*., Diarhogenic *E. coli* and *Shigella* respectively.

Pus

- *Staphylococcus aureus* was the most commonly isolated organism (> 30%) from pus taken from OPD patients, whereas *Escherichia coli* and *Klebsiella pneumoniae* were most commonly isolated from pus taken for ward and ICU patients.
- Clindamycin (79% susceptible) and trimethoprim-sulfamethoxazole (72% susceptible) showed good susceptibility rates among *Staphylococcus aureus* isolates from OPD and ward.
- Hence oral clindamycin and oral trimethoprim-sulfamethoxazole remain very good options for purulent skin-soft tissue infections in OPD and ward patients.



Cerebrospinal fluid (CSF)

- Gram-negative isolates were more common among the isolated organisms from the CSF, indicating high representation of hospital acquired ventriculitis in the study population.
- *Acinetobacter baumannii* was the most common organism followed by and *Klebsiella pneumoniae* and *Pseudomonas aeruginosa.*
- Most of these isolates were resistant to carbapenems, cephalosporins and fluoroquinolones. Only colistin and minocycline showed promising susceptibility rates for *Acinetobacter baumannii* and *Klebsiella pneumoniae*

Chapter 1: Summary of isolates distribution

Total number of culture positive isolates studied during the year 2022 was 1,07,053. Of these, **24,238** were from blood, **22,135** from urine, **20,508** superficial infections**, 17,244** Lower Respiratory tract (LRT), **7000** Deep infections, **3396** Sterile sites (SS), **1364** CSF, **806** Faeces and **10362** others. Majority of the isolates were from Enterobacterales except *Salmonella and Shigella* (49.2%) followed by Non fermenting Gram-negative bacilli (NFGNB) (24.6%), staphylococci (14.7%), enterococci (6.5%), fungi (3.0%), Typhoidal *Salmonella* (0.8%) and streptococci (0.4%) (**Table 1.1).**

In the distribution of major group of organisms in different specimens, member of the Enterobacterales group were the commonest isolates in urine (76.4%), sterile body fluids (SS) (56.9%), others (50.3%), deep infections (DI) (49.2%), superficial infections (SI) (43.6%), LRT (39.3%), blood (36.9%), and CSF (31.6%). Non fermenting Gram-negative bacilli (NFGNB) group were the predominant isolates in the lower respiratory tract (53.3%), CSF (41.2%), deep infection (DI) (26.6%), superficial infections (SI) (26.1%), sterile sites (SS) (21.8%), blood (17.8%), others (22.7%), and urine (8.7%). Staphylococci constituted 29.1 % of the blood infections followed the superficial infections (SI) (22.4%), deep infection (DI) (17.3%) and CSF (13.6%). Enterococci group constituted 11.3% isolates from urine followed by sterile body fluid (10.6%), CSF (8.7%), blood (6.9%), superficial infections (6.0%), and deep infections (5.1%), and Typhoidal *Salmonella* group constituted 3.3% of the isolates from blood. Yeast group were significant isolates in the blood infection (5.3%) **(Table 1.1 and Figure 1.1).**

The distribution of top 10 isolates from different specimens is presented in **Table 1.2 and Figure 1.2**. *Escherichia coli* was most commonly isolated (24.8%) followed by the *Klebsiella pneumoniae* (17.6%), *Pseudomonas aeruginosa* (12.3%), *Acinetobacter baumannii* (11.3%) and *Staphylococcus aureus* (8.7%). Among these isolates, *Escherichia coli* was the most predominant isolate from the urine (53.2%), *K. pneumoniae* from the LRT (25.1%), *Pseudomonas aeruginosa* from LRT (21.4%), *Acinetobacter baumannii* from LRT (30.3%), *S. aureus* from SI (20.7%), *Enterococcus faecalis* and *Enterococcus faecium* from urine (6.1%), and (4.2%) respectively. The relative distribution of the various species isolated from patients in the out-patient department (OPD), admitted to the wards and intensive care unit (ICUs) are presented in Table 1.3 and Figures 1.3a &1.3b. Top 5 isolates in descending order in OPD specimen were *E. coli, K. pneumoniae, P. aeruginosa, S. aureus* and *Acinetobacter baumannii*; in wards *E. coli, K. pneumoniae, P. aeruginosa, Acinetobacter baumannii* and *S. aureus*; and in ICU *Acinetobacter baumannii*, *K. pneumoniae, E. coli, P. aeruginosa* and *S. aureus. Enterococcus faecium* was common isolate from the ICU (3.7%) followed by ward and OPD; whereas, *E. faecalis* was common isolate from the OPD (3.3%) followed by the wards and the ICU. (**Table 1.3, Figure 1.3).**

Table 1.1: Specimen wise distribution of major groups of organisms

Isolate	Culture positive																			
	Total n=107053		Blood n=24238		Urine n=22135		LRT n=17244		Superficial Infection n=20508		Deep Infection n=7000		CSF n=1364		SS n=3396		Faeces n=806		Others n=10362	
	n	%	N	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Enterobacterales except *Salmonella*and *Shigella*	52692 (49.2)	100	8965 (36.9)	17	16913 (76.4)	32.1	6780 (39.3)	12.9	8945 (43.6)	17	3446 (49.2)	6.5	431 (31.6)	0.8	1935 (56.9)	3.7	65 (8.0)	0.1	5212 (50.3)	9.9
NFGNB	26352 (24.6)	100	4334 (17.8)	16.4	1933 (8.7)	7.3	9200 (53.3)	34.9	5358 (26.1)	20.3	1859 (26.6)	7.1	563 (41.2)	2.1	741 (21.8)	2.8	2 (0.2)	0	2362 (22.7)	9
Staphylococci	15748 (14.7)	100	7071 (29.1)	44.9	335 (1.5)	2.1	662 (3.8)	4.2	4599 (22.4)	29.2	1211 (17.3)	7.7	186 (13.6)	1.2	195 (5.7)	1.2	0 (0)	0	1489 (14.3)	9.5
Enterococci	6965 (6.5)	100	1685 (6.9)	24.2	2504 (11.3)	36	58 (0.3)	0.8	1231 (6.0)	17.7	356 (5.1)	5.1	119 (8.7)	1.7	362 (10.6)	5.2	9 (1.1)	0.1	641 (6.1)	9.2
Fungi	3237 (3.0)	100	1300 (5.3)	40.2	351 (1.6)	10.8	449 (2.6)	13.9	244 (1.1)	7.5	68 (0.9)	2.1	61 (4.4)	1.9	140 (4.1)	4.3	13 (1.6)	0.4	611 (5.9)	18.9
Typhoidal Salmonella	902 (0.8)	100	803 (3.3)	89	11 (0.0)	1.2	0 (0)	0	9 (0.04)	1	8 (0.1)	0.9	0 (0)	0	3 (0.1)	0.3	64 (7.9)	7.1	4 (0.0)	0.4
Diarrhoeal bacterial pathogens	670 (0.6)	100	0 (0)	0	0 (0)	0	0 (0)	0	0 (0)	0	0 (0)	0	0 (0)	0	16 (0.4)	2.4	653 (81.0)	97.5	1 (0.0)	0.1
Streptococci	487 (0.4)	100	80 (0.3)	16.4	88 (0.4)	18.1	95 (0.5)	19.5	122 (0.6)	25.1	52 (0.7)	10.7	4 (0.3)	0.8	4 (0.1)	0.8	0 (0)	0	42 (0.4)	8.6

Note:

1. **Blood** includes: Blood from venepuncture, bloodfromcentral catheter, and blood from peripheral catheter.
2. **LRT** (Lower Respiratory Tract) includes: BAL, sputum, lung aspirate, endotracheal aspirate (ETA) and lobectomy tissue (lung tissue).
3. **SSI** (Superficial infection) includes: SST (skin & soft tissue), pus/exudate, wound swab, superficial biopsy and superficial tissue.
4. **Deep Infection** includes: Abscess aspirate, pus aspirate, deep biopsy and deep tissue.
5. **SS** (Sterile Sites) includes: Fluid from sterile spaces, abdominal fluid, intercostal tube fluid, pancreatic drain fluid, pericardial fluid, peritoneal fluid and pleural fluid.

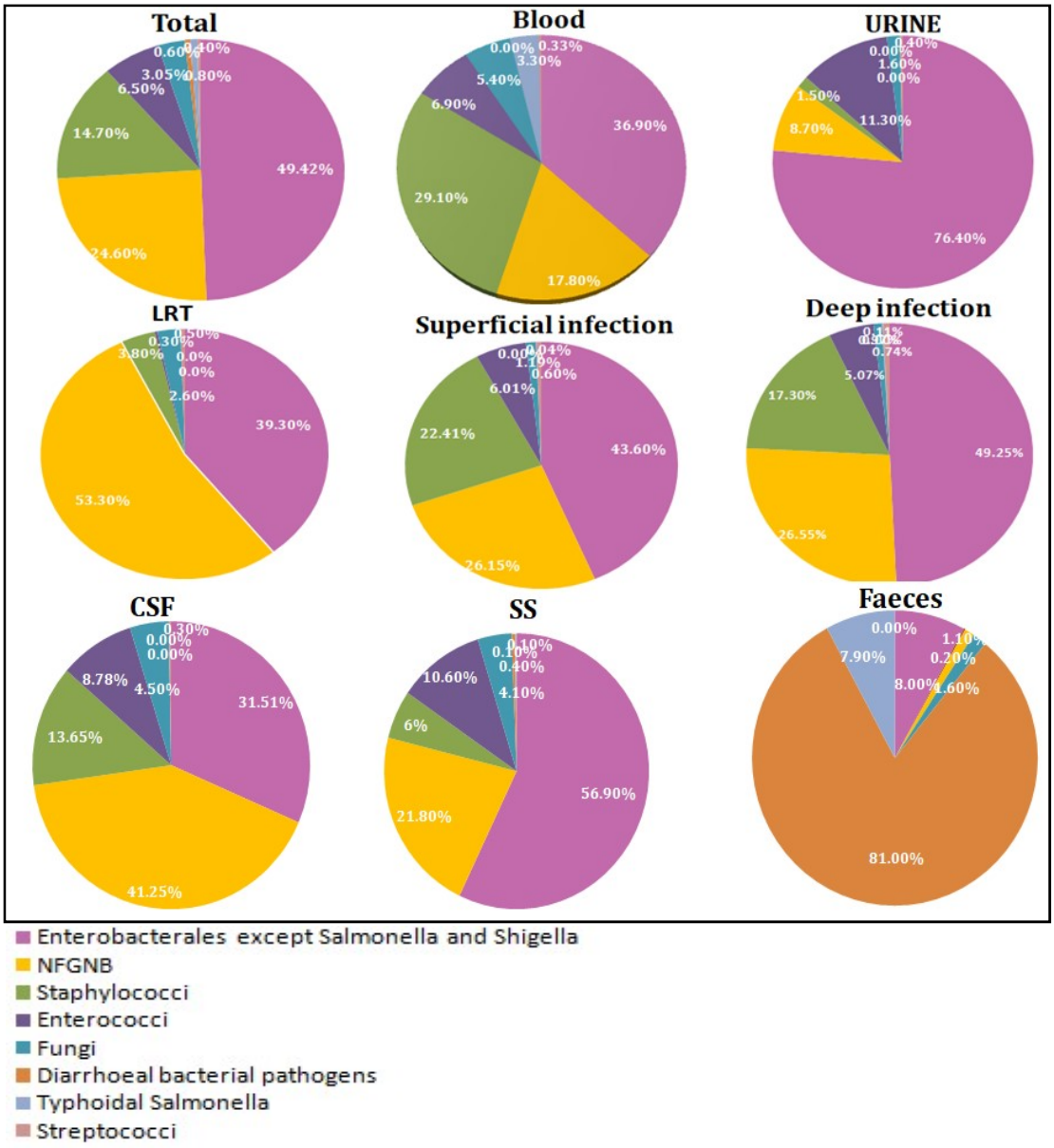


Figure 1.1: Specimen wise distribution of major groups of organisms

Table 1.2: Top 10 isolates overall and their isolation rates from different specimens

Organism	Total	Blood	LRT	Superficial Infection	Deep Infection	SS	Faeces	Urine
Escherichia coli	26550 / 107053 (24.8%)	3902 / 24238 (16.1%)	1540 / 17244 (8.93%)	4080 / 20508 (19.9%)	1468 / 7000 (20.9%)	1075 / 3396 (31.6%)	41 / 806 (5.1%)	11781 / 22135 (53.2%)
Klebsiella pneumoniae	18847 / 107053 (17.6%)	3959 / 24238 (16.3%)	4325 / 17244 (25.1%)	2923 / 20508 (14.2%)	1107 / 7000 (15.8%)	3396 (17.1%)	14 / 806 (1.7%)	3825 / 22135 (17.2%)
Pseudomonas aeruginosa	13228 / 107053 (12.3%)	1479 / 24238 (6.1%)	3693 / 17244 (21.4%)	3299 / 20508 (16.1%)	1224 / 7000 (17.5%)	348 / 3396 (10.2%)	1 / 806 (0.1%)	1594 / 22135 (7.2%)
Acinetobacter baumannii	12158 / 107053 (11.3%)	2413 / 24238 (9.9%)	5230 / 17244 (30.3%)	1978 / 20508 (9.6%)	611 / 7000 (8.7%)	354 / 3396 (10.4%)	1 / 806 (0.1%)	312 / 22135 (1.4%)
Staphylococcus aureus	9415 / 107053 (8.7%)	1784 / 24238 (7.3%)	594 / 17244 (3.4%)	4245 / 20508 (20.7%)	1112 / 7000 (15.9%)	156 / 3396 (4.6%)	0 / 806 (0%)	241 / 22135 (1.1%)
Enterococcus faecalis	3241 / 107053 (3.0%)	556 / 24238 (2.3%)	20 / 17244 (0.1%)	689 / 20508 (3.3%)	152 / 7000 (2.1%)	91 / 3396 (2.6%)	1 / 806 (0.1%)	1362 / 22135 (6.1%)
Enterococcus faecium	3006 / 107053 (2.8%)	950 / 24238 (3.9%)	33 / 17244 (0.2%)	405 / 20508 (1.9%)	167 / 7000 (2.4%)	206 / 3396 (6.0%)	8 / 806 (0.9%)	938 / 22135 (4.2%)
Staphylococcus haemolyticus	2373 / 107053 (2.2%)	2038 / 24238 (8.4%)	39 / 17244 (0.2%)	110 / 20508 (0.5%)	31 / 7000 (0.4%)	16 / 3396 (0.4%)	0 / 806 (0%)	22 / 22135 (0.1%)
Proteus mirabilis	1781 / 107053 (1.6%)	97 / 24238 (0.4%)	155 / 17244 (0.9%)	637 / 20508 (3.1%)	288 / 7000 (4.1%)	41 / 3396 (1.2%)	0 / 806 (0%)	278 / 22135 (1.2%)
Staphylococcus epidermidis	1775 / 107053 (1.6%)	1457 / 24238 (6.0%)	10 / 17244 (0.0%)	122 / 20508 (0.6%)	41 / 7000 (0.6%)	9 / 3396 (0.2%)	0 / 806 (0%)	13 / 22135 (0.0%)

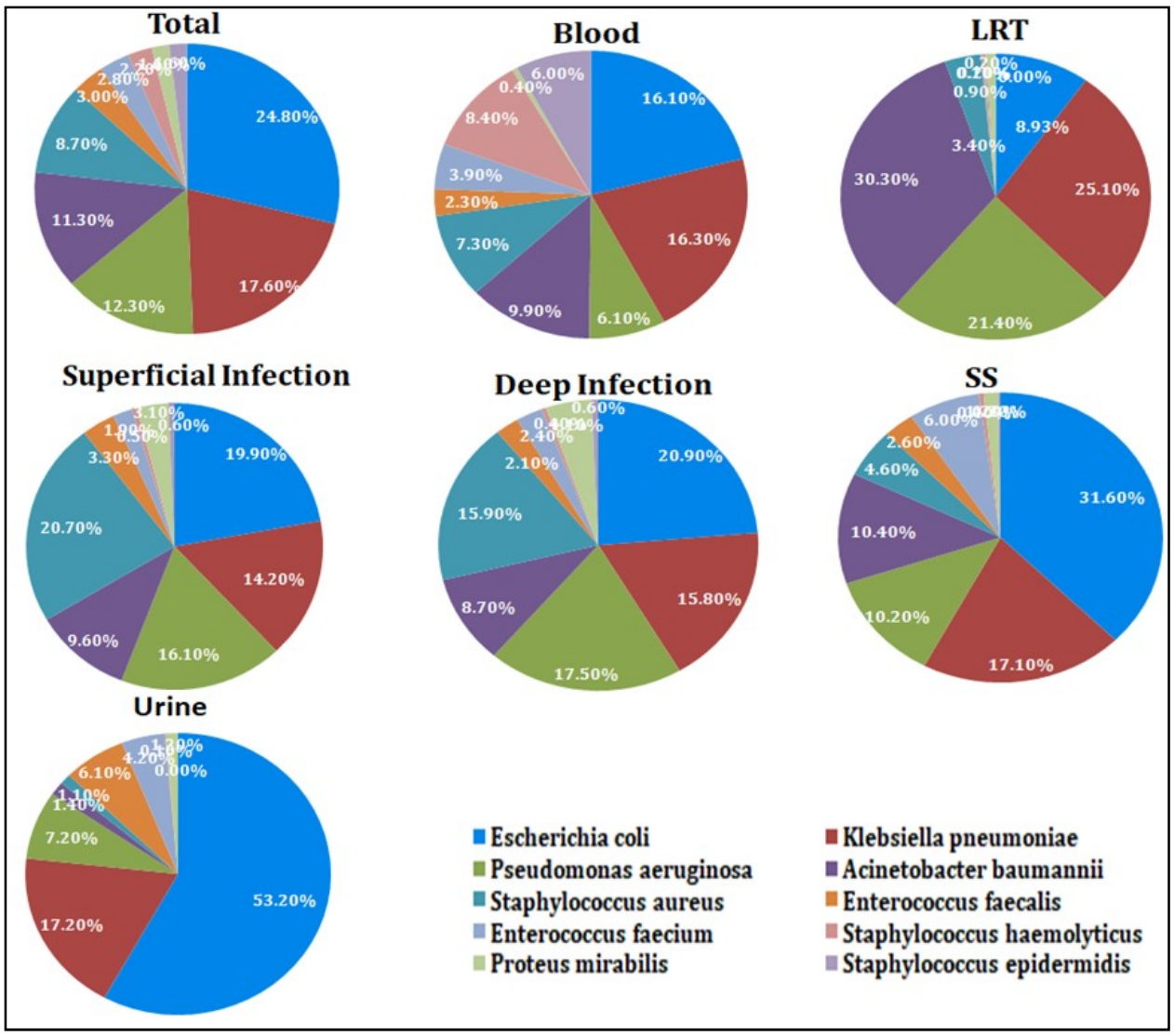


Figure 1.2: Isolation distribution of top 10 isolates from different specimens

Table 1.3: Distribution of top 10 isolates from all specimens across OPD, ward and ICU

Organism	Total n(%)	OPD n(%)	Ward n(%)	ICU n(%)
Escherichia coli	26550 / 107053 (24.8%)	9951 / 31726 (31.3%)	14051 / 55709 (25.2%)	2548 / 19618 (12.9%)
Klebsiella pneumoniae	18847 / 107053 (17.6%)	4665 / 31726 (14.7%)	9965 / 55709 (17.8%)	4217 / 19618 (21.5%)
Pseudomonas aeruginosa	13228 / 107053 (12.3%)	4155 / 31726 (13.1%)	6646 / 55709 (11.9%)	2427 / 19618 (12.3%)
Acinetobacter baumannii	12158 / 107053 (11.3%)	1523 / 31726 (4.8%)	5998 / 55709 (10.7%)	4637 / 19618 (23.6%)
Staphylococcus aureus	9415 / 107053 (8.7%)	3940 / 31726 (12.4%)	4571 / 55709 (8.2%)	904 / 19618 (4.6%)
Enterococcus faecalis	3241 / 107053 (3.0%)	1061 / 31726 (3.3%)	1737 / 55709 (3.1%)	443 / 19618 (2.2%)
Enterococcus faecium	3006 / 107053 (2.8%)	454 / 31726 (1.4%)	1826 / 55709 (3.2%)	726 / 19618 (3.7%)
Staphylococcus haemolyticus	2373 / 107053 (2.2%)	572 / 31726 (1.8%)	1314 / 55709 (2.3%)	487 / 19618 (2.4%)
Proteus mirabilis	1781 / 107053 (1.6%)	700 / 31726 (2.2%)	855 / 55709 (1.5%)	226 / 19618 (1.1%)
Staphylococcus epidermidis	1775 / 107053 (1.66%)	409 / 31726 (1.29%)	955 / 55709 (1.71%)	411 / 19618 (2.1%)

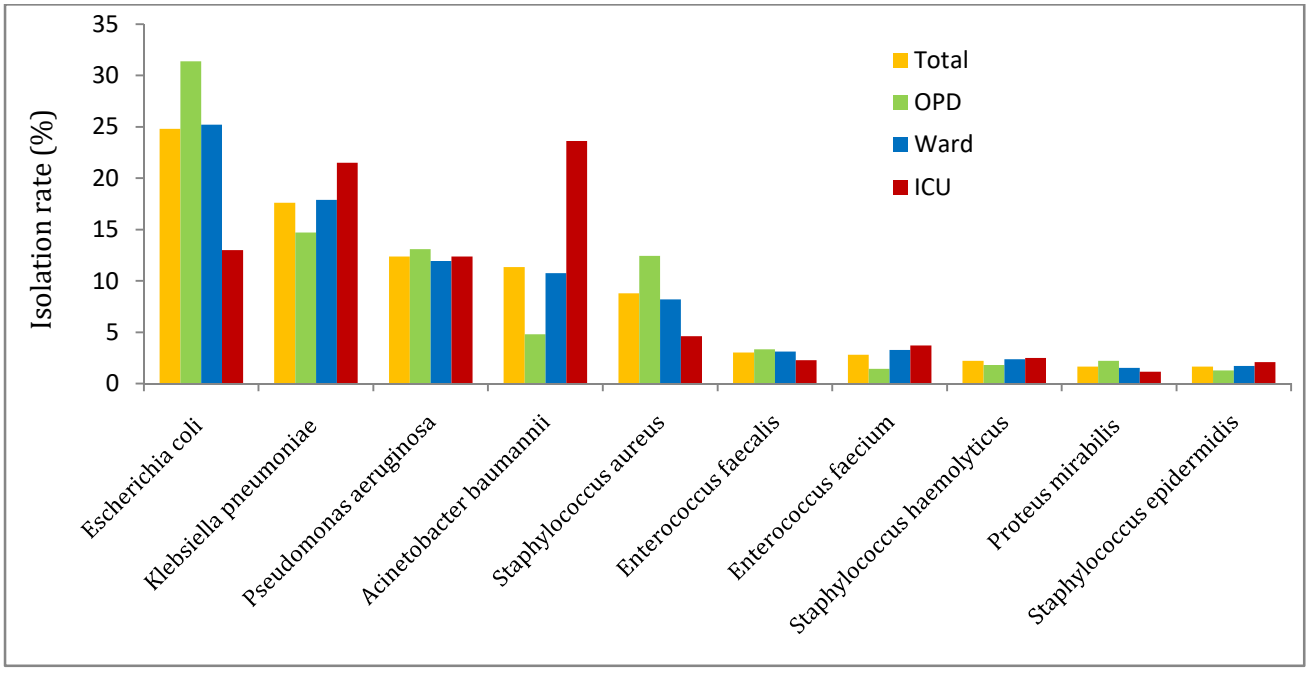


Figure 1.3: Distribution of top 10 isolates from all specimens across OPD, ward and ICU

Yearly isolation rates of top ten isolates from all samples showed a steady increase of *Klebsiella pneumoniae* from 14.7% in 2017 to 17.6% in 2022 (Table 1.4, Figure 1.4) and *A. baumannii* from 7.7% in 2017 to 11.3% in 2022 without much change in the isolation rates of the other species. There was also a decline in isolation rates of *Staphylococcus aureus* from 12.5% in 2017 to 8.7% in 2022.

Table 1.4: Yearly isolation trends of top 10 isolates from all samples

Bacteria	Year-2017 (%)	Year-2018 (%)	Year-2019 (%)	Year-2020 (%)	Year-2021 (%)	Year-2022 (%)
Escherichia coli	10441 / 45714 22.8(%)	19459 / 75182 25.8(%)	30953 / 110268 28.0(%)	16921 / 68081 24.8(%)	23748 / 96650 24.5(%)	26550 / 107053 (24.8%)
Klebsiella pneumoniae	6743 / 45714 14.7(%)	11136 / 75182 14.8(%)	18729 / 110268 16.9(%)	12173 / 68081 17.8(%)	17313 / 96650 17.9(%)	18847 / 107053 (17.6%)
Pseudomonas aeruginosa	5695 / 45714 12.4(%)	8921 / 75182 11.8(%)	12650 / 110268 11.4(%)	8013 / 68081 11.7(%)	11704 / 96650 12.1(%)	13228 / 107053 (12.3%)
Acinetobacter baumannii	3524 / 45714 7.7(%)	5446 / 75182 7.2(%)	8839 / 110268 8.0(%)	7301 / 68081 10.7(%)	12484 / 96650 12.9(%)	12158 / 107053 (11.3%)
Staphylococcus aureus	5723 / 45714 12.5(%)	8874 / 75182 11.8(%)	12625 / 110268 11.4(%)	6562 / 68081 9.6(%)	8888 / 96650 9.2(%)	9415 / 107053 (8.7%)
Enterococcus faecalis	1040 / 45714 2.2(%)	2022 / 75182 2.6(%)	2916 / 110268 2.6(%)	2177 / 68081 3.2(%)	2397 / 96650 2.4(%)	3241 / 107053 (3.0%)
Enterococcus faecium	181 / 7283 2.4(%)	937 / 45714 2.0(%)	1479 / 75182 1.9(%)	2742 / 110268 2.4(%)	2038 / 68081 2.9(%)	3006 / 107053 (2.8%)
Staphylococcus haemolyticus	634 / 45714 1.4(%)	871 / 75182 1.1(%)	827 / 110267 0.7(%)	626 / 68081 0.9(%)	839 / 96658 0.8(%)	2373 / 107053 2.2(%)
Proteus mirabilis	887 / 45714 1.9(%)	1289 / 75182 1.7(%)	1969 / 110267 1.7(%)	1272 / 68081 1.8(%)	1644 / 96658 1.7(%)	1781 / 107053 1.6(%)
Staphylococcus epidermidis	579 / 45714 1.2(%)	912 / 75182 1.2(%)	730 / 110267 0.6(%)	397 / 68081 0.5(%)	596 / 96658 0.6(%)	1775 / 107053 1.6(%)

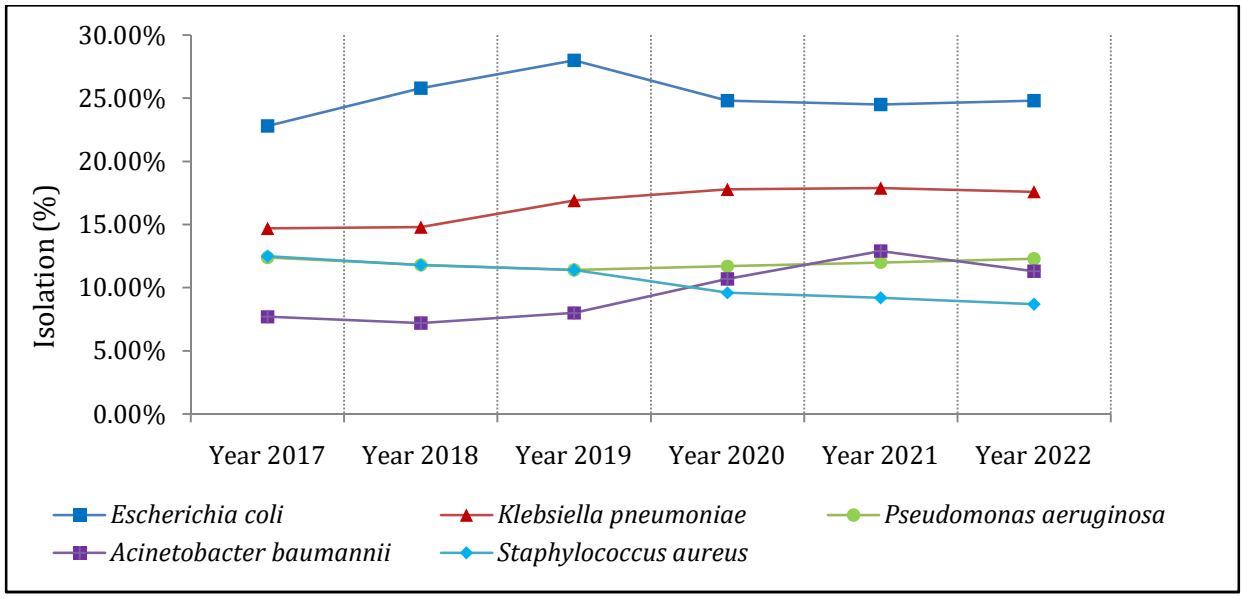


Figure 1.4: Yearly isolation trends of top 5 isolates from all samples

Enterobacterales

Of the overall isolates Enterobacterales (except *Salmonella and Shigella*) constituted a major group (49.2%) (Table 1.1). Out of a total of 1,07,053 culture positive isolates, specimen percentage wise distribution of major species within family Enterobacterales is shown in the **Table 1.5 and Figures 1.5.** Overall, *Escherichia coli* was the commonest species (24.8%) followed by *Klebsiella pneumoniae* (17.6%), *Enterobacter cloacae* and *Proteus mirabilis* (1.6%) (Table 1.5). *Escherichia coli* was the most predominant isolate from the urine (53.2%), sterile site (31.6%), others (24.3%), Deep infections (20.9%), superficial infection (19.8%), blood (16.1%) and CSF (10.5%). *Klebsiella pneumoniae* was the most predominant isolate in the lower respiratory tract (25.1%), others (18.3%), urine (17.2%), sterile sites (SS) (17.1%), blood (16.3%), and deep infection (DI) (15.8%), CSF (15.7%) and superficial infection (14.2%). *Proteus mirabilis* was common in 4.1 % of deep and 3.1% of superficial infections and other specimens (2.6%). *Enterobacter cloacae* constituted 3.3 % of deep infections and 2.3% of superficial infections and CSF (1.5%). *Klebsiella species* constituted 1.2% of sterile site infections (SS).

Isolates from the regional centers (RC 14) had higher percentage isolate rate of *E. coli*, RC 18 had higher percentage isolate rate of *K. pneumonaie*. Rc 4 had higher percentage isolate rate of *Proteus mirabilis and Enterobacter cloacae* than the rest of RCs **(Table 1.6).**

Table 1.5: Specimen wise distributions of major species of Family Enterobacterales except *Salmonella and Shigella*

Isolate	Culture positive																			
	Total n=107053		Blood n=24238		Urine n=22135		LRT n=17244		Superficial Infection n=20508		Deep Infection n=7000		CSF n=1364		SS n=3396		Faeces n=806		Others n=10362	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Escherichia coli	26550 (24.8)	100	3902 (16.1)	14.7	11781 (53.2)	44.4	1540 (8.9)	5.8	4080 (19.8)	15.4	1468 (20.9)	5.5	144 (10.5)	0.5	1075 (31.6)	4	41 (5.1	0.2	2519 (24.3)	9.5
Klebsiella pneumoniae	18847 (17.6)	100	3959 (16.3)	21	3825 (17.2)	20.3	4325 (25.1)	22.9	2923 (14.2)	15.5	1107 (15.8)	5.9	215 (15.7)	1.1	582 (17.1)	3.1	14 (1.7)	0.1	1897 (18.3)	10.1
Proteus mirabilis	1781 (1.6)	100	97 (0.4)	5.4	278 (1.2)	15.6	155 (0.9)	8.7	637 (3.1)	35.8	288 (4.1)	16.2	13 (0.9)	0.7	41 (1.2)	2.3	0 (0)	0	272 (2.6)	15.3
Enterobacter cloacae	1769 (1.6)	100	389 (1.6)	22	243 (1.1)	13.7	170 (0.9)	9.6	486 (2.3)	27.5	231 (3.3)	13.1	21 (1.5)	1.2	76 (2.2)	4.3	2 (0.2)	0.1	151 (1.4)	8.5
Citrobacter koseri	631 (0.5)	100	80 (0.3)	12.7	241 (1.1)	38.2	70 (0.4)	11.1	156 (0.7)	24.7	29 (0.4)	4.6	2 (0.1)	0.3	18 (0.5)	2.9	0 (0)	0	35 (0.3)	5.5
Morganella morganii	578 (0.5)	100	47 (0.1)	8.1	134 (0.6)	23.2	18 (0.1)	3.1	206 (1)	35.6	83 (1.1)	14.4	3 (0.2)	0.5	17 (0.5)	2.9	0 (0)	0	70 (0.6)	12.1
Serratia marcescens	500 (0.4)	100	135 (0.5)	27	37 (0.1)	7.4	196 (1.1)	39.2	46 (0.2)	9.2	36 (0.5)	7.2	6 (0.4)	1.2	5 (0.1)	1	0 (0)	0	39 (0.3)	7.8
Klebsiella spp.	254 (0.2)	100	72 (0.3)	28.3	25 (0.1)	9.8	87 (0.5)	34.3	10 (0.0)	3.9	8 (0.1)	3.1	2 (0.1)	0.8	43 (1.2)	16.9	6 (0.7)	2.4	1 (0.0)	0.4
Providencia stuartii	194 (0.1)	100	31 (0.1)	16	16 (0.1)	8.2	40 (0.2)	20.6	60 (0.2)	30.9	26 (0.3)	13.4	0 (0)	0	2 (0.0)	1	0 (0)	0	19 (0.1)	9.8

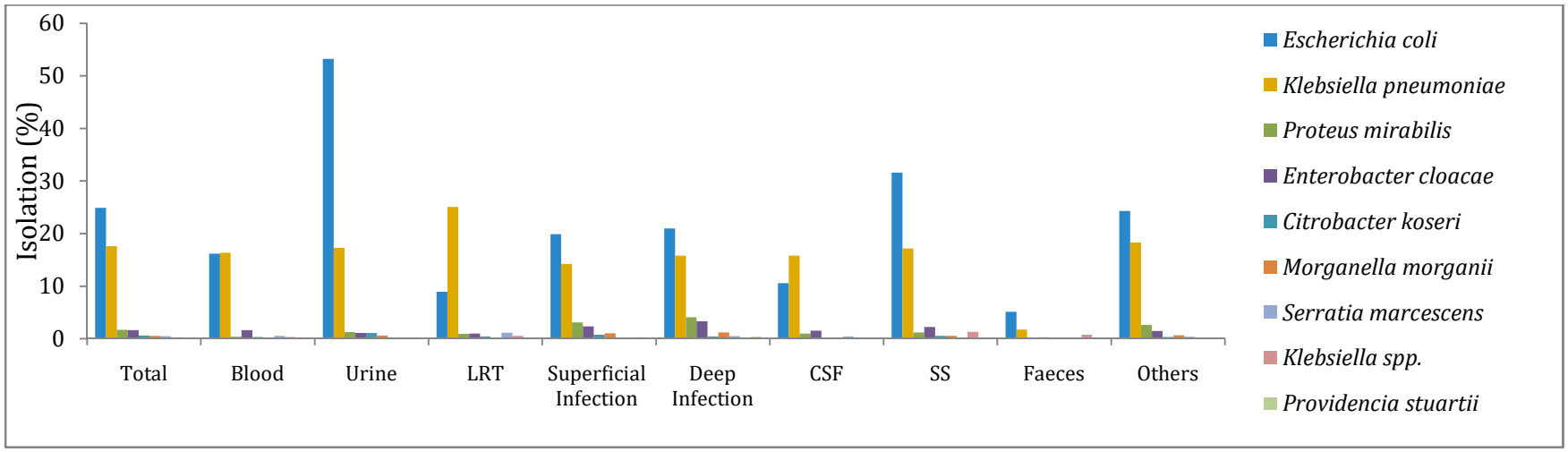


Figure 1.5: Specimen wise distribution of major species of Family Enterobacterales except Salmonella and Shigella

Table 1.6: Regional centre wise distribution of major species of family Enterobacterales (except *Salmonella*) in all specimens (except faeces)

Regional Centre	Total (except faeces) Isolates	*Escherichia coli*	*Klebsiella pneumoniae*	*Proteus mirabilis*	*Enterobacter cloacae*	*Citrobacter koseri*	*Enterobacter spp.*	*Citrobacter spp.*	*Citrobacter freundii*	*Proteus vulgaris*
	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
RC4	13318 (12.5)	2798 (21)	1892 (14.2)	407 (3.1)	331 (2.5)	93/ (0.7)	*0 (-)	*0 (-)	*0 (-)	*0 (-)
RC2	11915 (11.2)	1802 (15.1)	2097 (17.6)	185 (1.6)	209 (1.8)	8 (0.1)	79 (0.7)	51 (0.4)	*0 (-)	12 (0.1)
RC19	10202 (9.6)	1793 (17.6)	1655 (16.2)	142 (1.4)	60 (0.6)	7 (0.1)	*0 (-)	6 (0.1)	*0 (-)	11 (0.1)
RC1	7470 (7.03)	1560 (20.9)	1457 (19.5)	56 (0.7)	103 (1.4)	25 (0.3)	9 (0.1)	7 (0.1)	7 (0.1)	*0 (-)
RC6	6208 (5.8)	1546 (24.9)	1237 (19.9)	161 (2.6)	110 (1.8)	17 (0.3)	4 (0.1)	33 (0.5)	21 (0.3)	12 (0.2)
RC13	6103 (5.7)	1822 (29.9)	1003 (16.4)	42 (0.7)	49 (0.8)	10 (0.2)	47 (0.8)	8 (0.1)	*0 (-)	*0 (-)

RC15	6075 (5.7)	1433 (23.6)	1250 (20.6)	160 (2.6)	45 (0.7)	*0 (-)	60 (1)	4 (0.1)	4 (0.1)	*0 (-)
RC14	5886 (5.5)	2357 (40)	1151 (19.6)	39 (0.7)	219 (3.7)	59 (1)	*0 (-)	6 (0.1)	4 (0.1)	*0 (-)
RC10	4353 (4.0)	1305 (30)	836 (19.2)	97 (2.2)	111 (2.5)	54 (1.2)	*0 (-)	4 (0.1)	8 (0.2)	*0 (-)
RC3	4305 (4.0)	1011 (23.5)	513 (11.9)	35 (0.8)	23 (0.5)	13 (0.3)	100 (2.3)	22 (0.5)	4 (0.1)	4 (0.1)
RC16	3774 (3.5)	1255 (33.3)	603 (16)	72 (1.9)	10 (0.3)	48 (1.3)	7 (0.2)	6 (0.2)	41 (1.1)	27 (0.7)
RC18	3296 (3.1)	870 (26.4)	821 (24.9)	30 (0.9)	27 (0.8)	12 (0.4)	*0 (-)	*0 (-)	7 (0.2)	7 (0.2)
RC20	3212 (3.0)	1078 (33.6)	566 (17.6)	49 (1.5)	*0 (-)	5 (0.2)	*0 (-)	*0 (-)	6 (0.2)	18 (0.6)
RC5	3015 (2.8)	951 (31.5)	525 (17.4)	59 (2)	54 (1.8)	42 (1.4)	3 (0.1)	8 (0.3)	5 (0.2)	3 (0.1)
RC17	2972 (2.8)	1312 (44.1)	507 (17.1)	27 (0.9)	70 (2.4)	6 (0.2)	*0 (-)	*0 (-)	*0 (-)	*0 (-)
RC9	2864 (2.7)	926 (32.3)	328 (11.5)	7 (0.2)	16 (0.6)	197 (6.9)	*0 (-)	*0 (-)	3 (0.1)	8 (0.3)
RC11	2802 (2.6)	361 (12.9)	484 (17.3)	31 (1.1)	150 (5.4)	*0 (-)	*0 (-)	*0 (-)	12 (0.4)	3 (0.1)
RC8	2661 (2.5)	587 (22.1)	609 (22.9)	67 (2.5)	63 (2.4)	15 (0.6)	10 (0.4)	3 (0.1)	6 (0.2)	*0 (-)
RC7	2459 (2.3)	704 (28.6)	515 (20.9)	89 (3.6)	58 (2.4)	16 (0.7)	13 (0.5)	*0 (-)	8 (0.3)	8 (0.3)
RC12	2098 (1.9)	692 (33)	435 (20.7)	4 (0.2)	42 (2)	3 (0.1)	2 (0.1)	*0 (-)	*0 (-)	2 (0.1)
RC21	1259 (1.2)	346 (27.5)	349 (27.7)	22 (1.7)	16 (1.3)	*0 (-)	*0 (-)	*0 (-)	*0 (-)	2 (0.2)
Total National	106247	26509 (25.0)	18833 (17.7)	1781 (1.7)	1767 (1.7)	631 (0.6)	340 (0.3)	162 (0.2)	150 (0.1)	126 (0.1)

Typhoidal Salmonella

This distribution showed that isolates from the RC 6 had higher percentage isolate rate (12.7%) of *Salmonella* Typhi from blood than the rest of RCs (Table 1.7). *Salmonella* Paratyphi A isolate percentage was more in RC 10 (4.1) and in RC 6 (3.0%) as compared to other RCs. The relative distribution of Typhoidal *Salmonella* isolated from blood in the OPD, admitted to the wards and ICUs are presented in Table 1.8 and Figures 1.6. Typhoidal *Salmonella* was common isolate from the OPD (8.7%) followed by the wards and was least isolated from the ICU. (Table 1.8). Among Typhoidal Salmonella, *Salmonella* Typhi had higher percentage isolation rate than *Salmonella* Paratyphi A. Yearly isolation trends showed that there is a decline in isolation rates of *Salmonella* Typhii n 2022 from the last five years from all over India (Table 1.9 & Figure 1.7).

Table 1.7: Isolates percentages across Regional Centres of Typhoidal *Salmonella* isolated from blood

Regional Centre	Total Blood Isolates n (%)	*Salmonella* Typhi n(%)	*Salmonella* Paratyphi A n(%)
RC2	5231 (21.5)	32/5231 (0.6)	8/5231 (0.2)
RC3	2143 (8.8)	79/2143 (3.7)	16/2143 (0.7)
RC1	2013 (8.3)	70/2013 (3.5)	*0/0 (-)
RC4	1815 (7.4)	12/1815 (0.7)	2/1815 (0.1)
RC6	1514 (6.2)	192/1514 (12.7)	45/1514 (3.0)
RC13	988 (4.0)	6/988 (0.6)	1/988 (0.1)
RC14	859 (3.5)	29/859 (3.4)	*0/0 (-)
RC17	761 (3.1)	9/761 (1.2)	4/761 (0.5)
RC15	750 (3.0)	18/750 (2.4)	3/750 (0.4)
RC10	702 (2.9)	42/702 (6)	29/702 (4.1)
RC8	682 (2.8)	*0/0 (-)	*0/0 (-)
RC5	674 (2.7)	23/674 (3.4)	2/674 (0.3)
RC9	609 (2.5)	5/609 (0.8)	1/609 (0.2)
RC12	444 (1.8)	48/444 (10.8)	4/444 (0.9)
RC11	438 (1.8))	3/438 (0.7)	1/438 (0.2)
RC21	323 (1.3)	2/323 (0.6)	*0/0 (-)

RC7	281 (1.1)	9/281 (3.2)	*0/0 (-)
RC16	165 (0.6)	1/165 (0.6)	1/165 (0.6)
RC20	150 (0.6)	4/150 (2.7)	1/150 (0.7)
Total National	24238	584 (2.4)	118 (0.5)

Table 1.8: Isolation Distribution of Typhoidal *Salmonella* from blood location wise

Organism	Total	OPD	Ward	ICU
Total Typhoidal Salmonella	803 / 24238 (3.3%)	418 / 4779 (8.7%)	348 / 12713 (2.7%)	37 / 6746 (0.5%)
Salmonella Typhi	584 / 24238 (2.4%)	317 / 4779 (6.6%)	245 / 12713 (1.9%)	22 / 6746 (0.3%)
Salmonella Paratyphi A	118 / 24238 (0.5%)	73 / 4779 (1.5%)	38 / 12713 (0.3%)	7 / 6746 (0.1%)

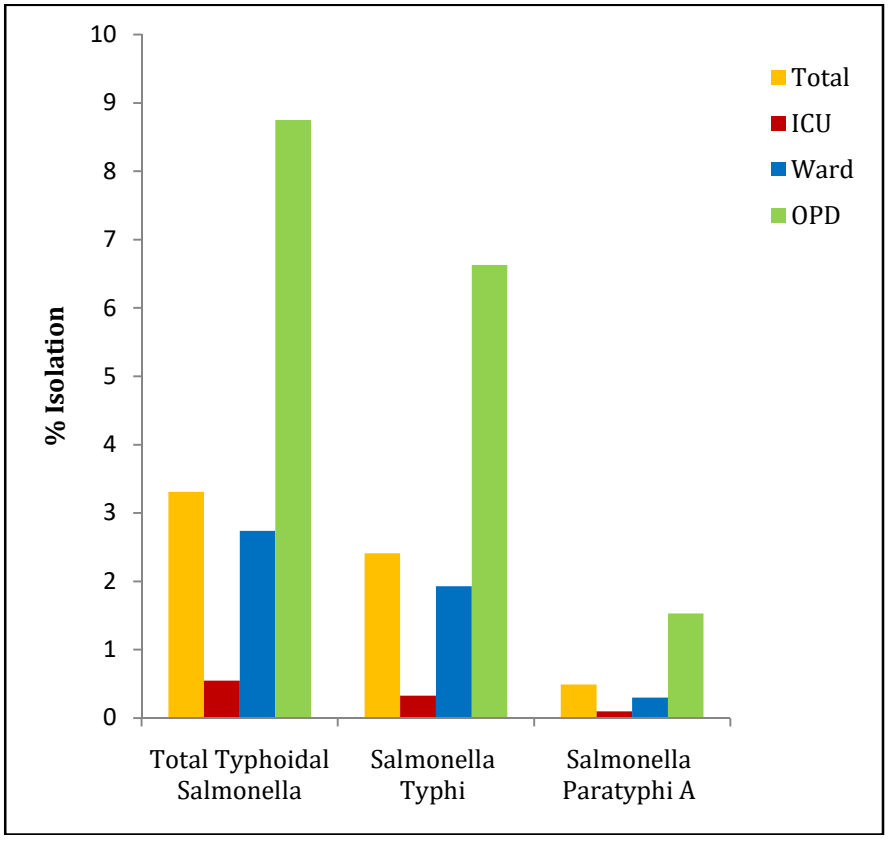


Figure 1.6: Location-wise Isolation pattern of Typhoidal *Salmonella* isolated from blood across OPD, Ward and ICU

Table 1.9: Yearly-isolation trend of *Salmonella* Typhi from blood across different regions

Years	2017	2018	2019	2020	2021	2022
North	138/4272 (3.2%)	246/5248 (4.7%)	174/4533 (3.8%)	47/3479 (1.4%)	126/6498 (1.9%)	298/12206 (2.4%)
Central	0/0* (-)	12/110 (10.9%)	36/570 (6.3%)	14/448 (3.1%)	12/584 (2.1%)	51/882 (5.7%)
East	0/171* (0%)	2/712 (0.3%)	4/1443 (0.3%)	1/935 (0.1%)	1/1746 (0.1%)	3/1568 (0.2%)
West	31/648 (4.8%)	116/2011 (5.8%)	164/2761 (5.9%)	41/2041 (2%)	41/2973 (1.4%)	61/3302 (1.8%)
South	176/4400 (4%)	204/6018 (3.4%)	350/8033 (4.4%)	103/6206 (1.7%)	113/7187 (1.6%)	171/6280 (2.7%)
National	345/9491 (3.6%)	580/14099 (4.1%)	728/17340 (4.2%)	206/13109 (1.6%)	293/18988 (1.5%)	584 / 24238 (2.41%)

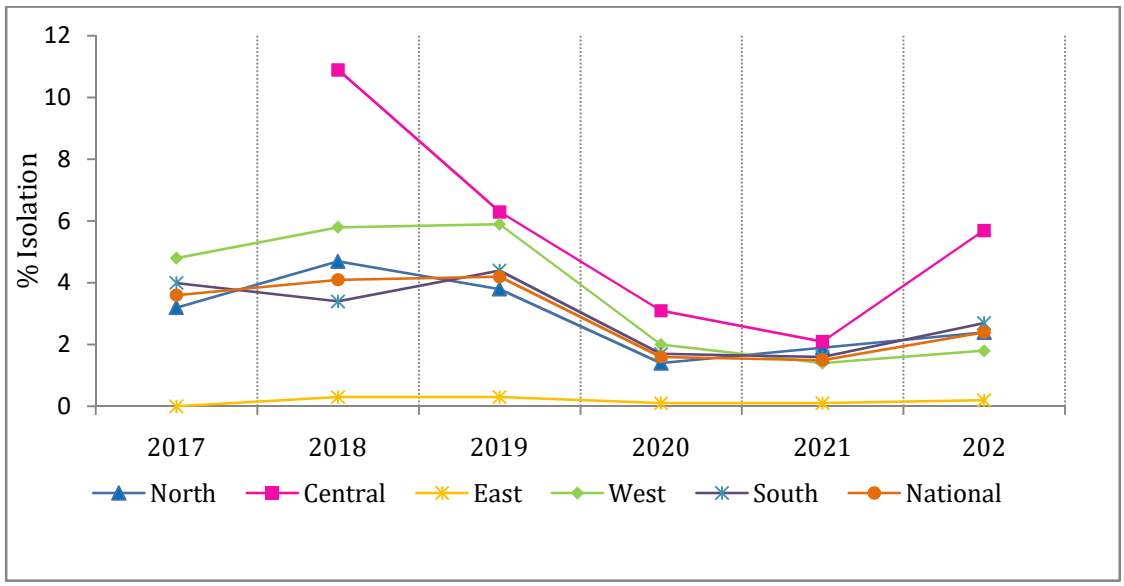


Figure 1.7: Yearly-isolation trends of *Salmonella* Typhi from blood across different regions

Non-fermenting Gram negative bacteria

Non-fermenting Gram-negative bacteria (NFGNB) constituted 24.6% of the total isolates (26,352 out of 107053) (Table 1.10). Among the NFGNB, *Pseudomonas aeruginosa* was the commonest isolate (12.4%) followed by *Acinetobacter baumannii* (11.3%), *Stenotrophomonas maltophilia* and *Burkholderia cepacia* accounted for 0.8% and 0.1% of all isolates respectively. *Pseudomonas aeruginosa* was grossly predominant in LRT (21.4%) followed by deep infections (17.5%), superficial infection (16.1%), and others (14.2%). *Acinetobacter baumannii* was the predominant isolate from CSF (31.2%) and LRT (30.3%) followed by SS (10.4%) and blood (10.0%) (Table 1.10).

Regional center (RC) wise distribution showed that RC 11 had higher percentage isolate rate of *Acinetobacter baumannii* and RC 3 had higher percentage isolate rate of *Pseudomonas aeruginosa* than the rest of RCs (Table 1.11). Among clinical settings, *P. aeruginosa* was predominantly isolated in all ward, ICU and OPD (11.9-13.1%), while *A. baumannii* was predominant in ICU (23.5%), followed by ward (10.7%) and OPD (4.7%) respectively (Table 1.12a and Figure 1.8).

However, trend analysis over the years 2017 – 2022 has shown a stable pattern in the isolation rates of *P. aeruginosa* from 12.4% to 12.4% in 2017 to 2022, respectively (Table 1.12b). In contrast, isolation rates of *A. baumannii* increased from 7.7% to 11.4% between 2017 and 2022 respectively. No significant changes in the isolation rates of other pathogens such as *B. cepacia* and *S. maltophilia* have been noted (Figure 1.9).

Table 1.10: Specimen wise distribution of NFGNB

Isolate	Culture positive																			
	Total n=107053		Blood n=24238		Urine n=22135		LRT n=17244		Superficial Infection n=20508		Deep Infection n=7000		CSF n=1364		SS n=3396		Faeces n=806		Others n=10354	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
NFGNB	26352 (24.6)	100	4334 (17.9)	16.4	1933 (8.7)	7.3	9200 (53.4)	34.9	5358 (26.1)	20.3	1859 (26.6)	7.1	563 (41.3)	2.1	741 (21.8)	2.8	2 (0.2)	0	2362 (22.8)	9
Pseudomonas aeruginosa	13228 (12.4)	100	1479 (6.1)	11.2	1594 (7.2)	12.1	3693 (21.4)	27.9	3299 (16.1)	24.9	1224 (17.5)	9.3	117 (8.6)	0.9	348 (10.2)	2.6	1 (0.1)	0	1473 (14.2)	11.1
Acinetobacter baumannii	12158 (11.3)	100	2413 (10)	19.9	312 (1.4)	2.6	5230 (30.3)	43	1978 (9.6)	16.3	611 (8.7)	5	425 (31.2)	3.5	354 (10.4)	2.9	1 (0.1)	0	834 (8.1)	6.9
Stenotrophomonas maltophilia	827 (0.8)	100	366 (1.5)	44.3	19 (0.1)	2.3	238 (1.4)	28.8	76 (0.4)	9.2	22 (0.3)	2.7	18 (1.3)	2.2	38 (1.1)	4.6	0 (0)	0	50 (0.5)	6
Burkholderia cepacia complex	114 (0.1)	100	58 (0.2)	51.3	8 (0)	7.1	34 (0.2)	30.1	5 (0)	4.3	2 (0)	1.8	2 (0.1)	1.8	1 (0)	0.9	0 (0)	0	4 (0)	3.5

Table 1.11: Isolates percentages across Regional Centres of *Pseudomonas aeruginosa, Acinetobacter baumannii, Stenotrophomonas maltophilia* and *Burkholderia cepacia* from all specimens (except Faeces)

Regional Centre	Total Isolates	*Pseudomonas aeruginosa*	*Acinetobacter baumannii*	*Stenotrophomonas maltophilia*	*Burkholderia cepacia*
	n(%)	n(%)	n(%)	n(%)	n(%)
RC4	13318 (12.5)	1637/13318 (12.3)	1441/13318 (10.8)	248/13318 (1.9)	51/13318 (0.4)
RC2	11915 (11.2)	1502/11915 (12.6)	1523/11915 (12.8)	66/11915 (0.6)	*0/0 (-)
RC19	10202 (9.6)	1114/10202 (10.9)	1777/10202 (17.4)	40/10202 (0.4)	*0/0 (-)
RC1	7470 (7.0)	982/7470 (13.1)	1176/7470 (15.7)	225/7470 (3)	*0/0 (-)
RC6	6209 (5.8)	1015/6208 (16.3)	402/6208 (6.5)	68/6208 (1.1)	28/6208 (0.5)
RC13	6103 (5.7)	718/6103 (11.8)	718/6103 (11.8)	20/6103 (0.3)	15/6103 (0.2)
RC15	6075 (5.7)	937/6075 (15.4)	945/6075 (15.6)	14/6075 (0.2)	*0/0 (-)
RC14	5886 (5.5)	563/5886 (9.6)	186/5886 (3.2)	3/5886 (0.1)	*0/0 (-)
RC10	4353 (4.0)	489/4353 (11.2)	205/4353 (4.7)	25/4353 (0.6)	15/4353 (0.3)
RC3	4305 (4.0)	758/4305 (17.6)	654/4305 (15.1)	*0/0 (-)	*0/0 (-)
RC16	3774 (3.5)	288/3774 (7.6)	214/3774 (5.7)	6/3774 (0.2)	*0/0 (-)
RC18	3296 (3.1)	311/3296 (9.4)	533/3296 (16.2)	16/3296 (0.5)	*0/0 (-)
RC20	3212 (3.0)	311/3212 (9.7)	579/3212 (18)	*0/0 (-)	*0/0 (-)
RC5	3015 (2.8)	423/3015 (14)	64/3015 (2.1)	29/3015 (1)	*0/0 (-)
RC17	2972 (2.7)	207/2972 (7)	258/2972 (8.7)	*0/0 (-)	*0/0 (-)
RC9	2864 (2.6)	303/2864 (10.6)	376/2864 (13.1)	*0/0 (-)	*0/0 (-)

RC11	2802 (2.6)	546/2802 (19.5)	681/2802 (24.3)	11/2802 (0.4)	*0/0 (-)
RC8	2661 (2.5)	446/2661 (16.8)	161/2661 (6.1)	24/2661 (0.9)	*0/0 (-)
RC7	2459 (2.3)	264/2459 (10.7)	92/2459 (3.7)	14/2459 (0.6)	*0/0 (-)
RC12	2098 (1.9)	286/2098 (13.6)	43/2098 (2)	6/2098 (0.3)	*0/0 (-)
RC21	1259 (1.1)	127/1259 (10.1)	129/1259 (10.2)	11/1259 (0.9)	*0/0 (-)
Total National	106247	13227 (12.4)	12142 (11.4)	827 (0.8)	113 (0.1)

Table 1.12a: Location-wise isolates percentage of *Pseudomonas aeruginosa, Acinetobacter baumannii, Stenotrophomonas maltophilia* and *Burkholderia cepacia* from all samples across OPD, Ward and ICU

Organism	Total	OPD	Ward	ICU
Pseudomonas aeruginosa	13228 / 107053 (12.3%)	4155 / 31726 (13.1%)	6646 / 55709 (11.9%)	2427 / 19618 (12.3%)
Acinetobacter baumannii	12158 / 107053 (11.3%)	1523 / 31726 (4.7%)	5998 / 55709 (10.7%)	4637 / 19618 (23.5%)
Stenotrophomonas maltophilia	827 / 107053 (0.7%)	136 / 31726 (0.4%)	462 / 55709 (0.8%)	229 / 19618 (1.17%)
Burkholderia cepacia complex	114 / 107053 (0.1%)	16 / 31726 (0.1%)	38 / 55709 (0.1%)	60 / 19618 (0.3%)

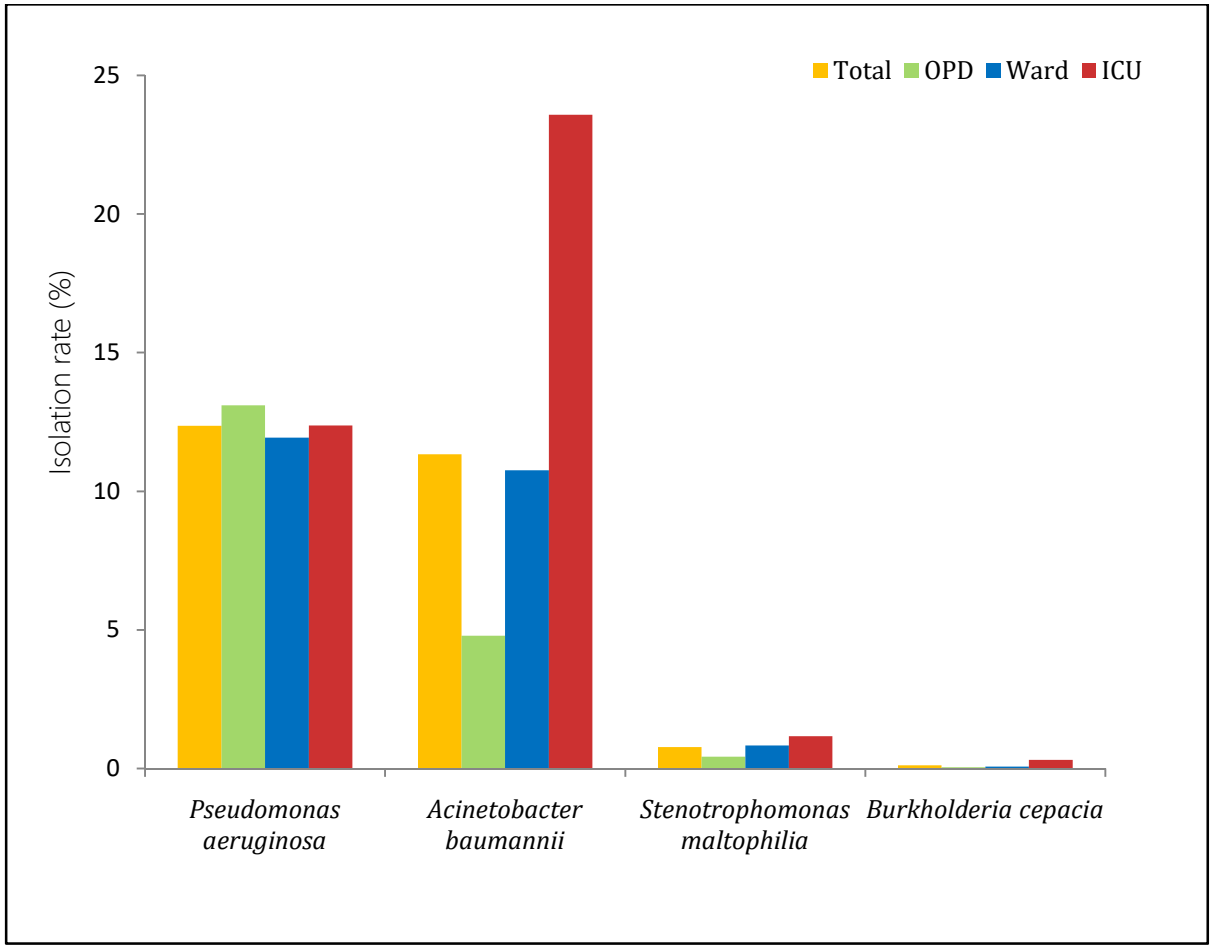


Figure 1.8: Location-wise isolation pattern of *A. baumannii, B. cepacia, P. aeruginosa,* and *S. maltophilia* isolated from all samples

Table 1.12b: Yearly Isolation trend of *P. aeruginosa, A. baumannii, S. maltophilia* and *B. cepacia* isolated from all samples

Bacteria	Year-2017 (%)	Year-2018 (%)	Year-2019 (%)	Year-2020 (%)	Year-2021 (%)	Year-2022 (%)
Pseudomonas aeruginosa	5695 / 45714 12.4(%)	8921 / 75182 11.8(%)	12650 / 110268 11.4(%)	8013 / 68081 11.7(%)	11704 / 96650 12.1(%)	13151 / 106143 12.4(%)
Acinetobacter baumannii	3524 / 45714 7.7(%)	5446 / 75182 7.2(%)	8839 / 110268 8.0(%)	7301 / 68081 10.7(%)	12484 / 96650 12.9(%)	12110 / 106143 11.4(%)
Stenotrophomonas maltophilia	157 / 45714 0.3(%)	313 / 75182 0.4(%)	382 / 110268 0.3(%)	372 / 68081 0.5(%)	772 / 96650 0.8(%)	826 / 106143 0.7(%)
Burkholderia cepacia	120 / 45714 0.2(%)	213 / 75182 0.2(%)	233/ 110267 0.2(%)	239 / 68081 0.3(%)	389 / 96658 0.4 (%)	114/ 107053 0.1(%)

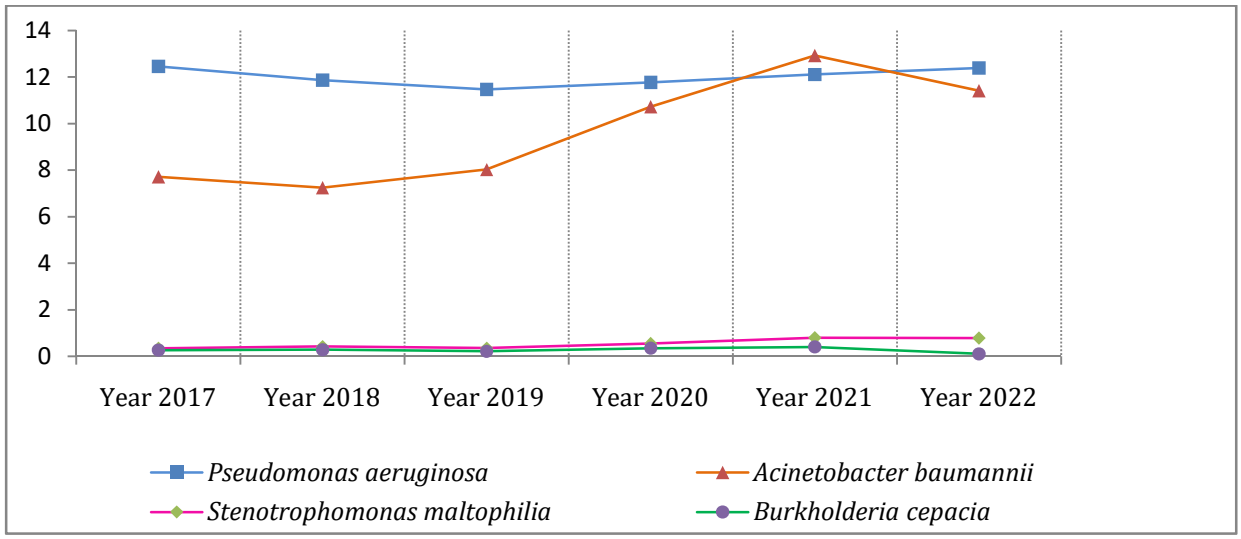


Figure 1.9: Yearly Isolation trend of *P. aeruginosa, A. baumannii, S. maltophilia* and *B. cepacia* isolated from all samples

Staphylococci

Staphylococci constituted 14.7% of the total isolates (Table 1.13). *Staphylococcus aureus* was the predominant species in the blood (29.2%) followed by superficial infections (22.4%), deep infections (17.3%), others (14.4%), sterile body fluids (5.7%), LRT (3.8) and urine (1.5%) (Table 1.13). Coagulase-negative staphylococci (CoNS) were the predominant isolates in blood (21.8%) and CSF (8.6%) reflecting the high incidence of shunt infections and intra vascular device associated infections respectively. In blood and CSF, *Staphylococcus epidermidis* isolation rate was 6.0% and 2.4% respectively, reflecting the ability of the species to form biofilms and high incidence of shunt associated and dialysis associated infections. Predominant percentage isolation of methicillin resistant *Staphylococcus aureus* (MRSA) was from the superficial infections (SI) 8.9%, followed by isolation from deep infection (DI) 8.2% and 3.4% from blood. Methicillin sensitive *Staphylococcus aureus* (MSSA) were the predominant isolates from the superficial infection (SI) 11.6% followed by isolation from Deep infections (DI) (7.3%) 6.4% and 3.9% from others and blood respectively (Figure 1.10). Amongst the coagulase-negative staphylococci (CoNS), *S. haemolyticus* (37.4%) were the commonest species followed by *S. epidermidis* (28.0%) and *S. hominis* (23.2%) (Table1.13).

Regional centre wise distribution showed the predominance of isolation of *Staphylococcus aureus* in RC15 (14.6%) with MRSA percentage isolation (7.1%). The least percentage isolation of *Staphylococcus aureus* and MRSA was found among RC 19 i.e., 4.1% and 2.6% respectively (Table 1.14).

Among clinical settings, *Staphylococcus aureus* was predominantly isolated in OPD (12.4%), followed by ward (8.2%) and ICU (4.6%), while the coagulase-negative staphylococci (CoNS) was predominant both in ward and ICU (6.3%), then OPD (4.8%) (Table 1.15 and Figure 1.11). Trend analysis over the years 2017 – 2022 have shown a steady decline in the isolation rates of *Staphylococcus aureus* from 12.5% to 8.7% in 2017 to 2022 respectively (Table 1.16 and Figure 1.12).

Table 1.13: Specimen wise relative distribution of *S. aureus* and CoNS species

Isolate	Culture positive																			
	Total n=107053		Blood n=24238		Urine n=22135		LRT n=17244		Superficial Infection n=20508		Deep Infection n=7000		CSF n=1364		SS n=3396		Faeces n=806		Others n=10354	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Staphylococcus spp.	15748 (14.7)	100	7071 (29.2)	44.9	335 (1.5)	2.1	662 (3.8)	4.2	4599 (22.4)	29.2	1211 (17.3)	7.7	186 (13.6)	1.2	195 (5.7)	1.2	0 (0)	0	1487 (14.4)	9.4
Staphylococcus aureus	9415 (8.8)	100	1784 (7.4)	18.9	241 (1.1)	2.6	594 (3.4)	6.3	4245 (20.7)	45.1	1112 (15.9)	11.8	69 (5.1)	0.7	156 (4.6)	1.7	0 (0)	0	1213 (11.7)	12.9
MSSA	5050 (4.7)	100	946 (3.9)	18.7	93 (0.4)	1.8	332 (1.9)	6.6	2388 (11.6)	47.3	511 (7.3)	10.1	35 (2.6)	0.7	86 (2.5)	1.7	0 (0)	0	659 (6.4)	13
MRSA	4266 (4)	100	821 (3.4)	19.2	143 (0.6)	3.4	257 (1.5)	6	1824 (8.9)	42.8	577 (8.2)	13.5	33 (2.4)	0.8	65 (1.9)	1.5	0 (0)	0	545 (5.3)	12.8
CoNS	6333 (5.9)	100	5287 (21.8)	83.5	94 (0.4)	1.5	68 (0.4)	1.1	354 (1.7)	5.6	99 (1.4)	1.6	117 (8.6)	1.8	39 (1.1)	0.6	0 (0)	0	274 (2.6)	4.3
Staphylococcus haemolyticus	2373 (2.2)	100	2038 (8.4)	85.9	22 (0.1)	0.9	39 (0.2)	1.6	110 (0.5)	4.6	31 (0.4)	1.3	39 (2.9)	1.6	16 (0.5)	0.7	0 (0)	0	78 (0.8)	3.3
Staphylococcus epidermidis	1775 (1.7)	100	1457 (6)	82.1	13 (0.1)	0.7	10 (0.1)	0.6	122 (0.6)	6.9	41 (0.6)	2.3	33 (2.4)	1.9	9 (0.3)	0.5	0 (0)	0	89 (0.9)	5
Staphylococcus hominis	1473 (1.4)	100	1356 (5.6)	92.1	5 (0)	0.3	6 (0)	0.4	42 (0.2)	2.9	7 (0.1)	0.5	21 (1.5)	1.4	7 (0.2)	0.5	0 (0)	0	29 (0.3)	2
Coagulase- negative Staphylococcus spp.	561 (0.5)	100	374 (1.5)	66.7	12 (0.1)	2.1	13 (0.1)	2.3	58 (0.3)	10.3	9 (0.1)	1.6	21 (1.5)	3.7	6 (0.2)	1.1	0 (0)	0	68 (0.7)	12.1

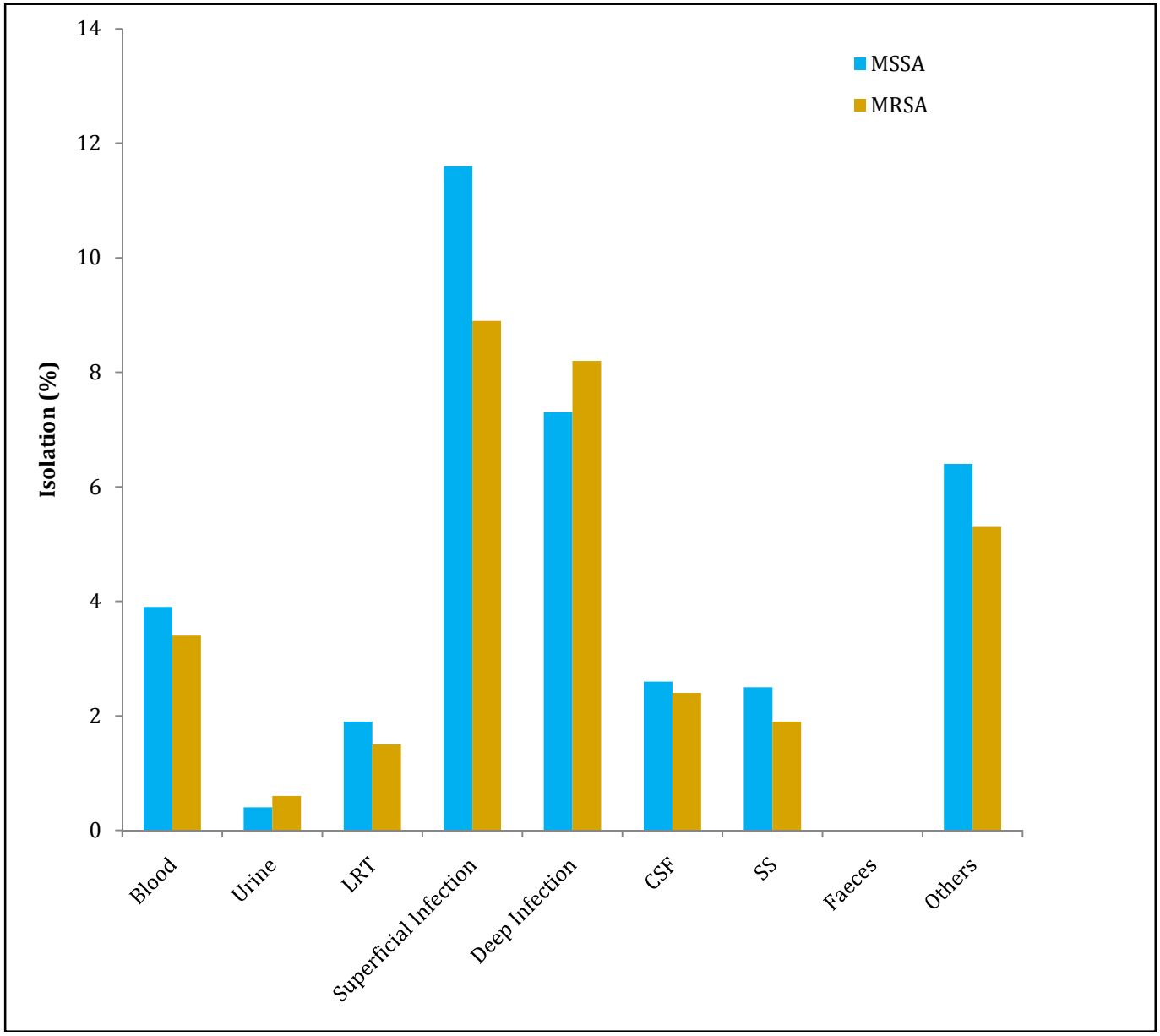


Figure1.10: Specimen wise relative distribution of MSSA and MRSA

Table 1.14 Isolates percentages across Regional Centres of *S. aureus*, MRSA, MSSA and CoNS species isolated from all samples (Except Faeces)

Regional Centre	Total Isolates	*S. aureus*	MRSA	MSSA	*S. haemolyticus*	*S. epidermidis*	*S. hominis*	*S. lugdunensis*	*S. saprophyticus*	*Staphylococcus spp.*
	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
RC4	13318 (12.5)	1872/13318 (14.1)	445/13318 (3.3)	1426/13318 (10.7)	37/13318 (0.3)	42/13318 (0.3)	*0/0 (-)	8/13318 (0.1)	*0/0 (-)	*0/0 (-)
RC2	11915 (11.2)	596/11915 (5)	195/11915 (1.6)	397/11915 (3.3)	495/11915 (4.2)	786/11915 (6.6)	421/11915 (3.5)	*0/0 (-)	*0/0 (-)	221/11915 (1.9)
RC19	10202 (9.6)	420/10202 (4.1)	264/10202 (2.6)	156/10202 (1.5)	1114/10202 (10.9)	257/10202 (2.5)	607/10202 (5.9)	*0/0 (-)	*0/0 (-)	7/10202 (0.1)
RC1	7470 (7.0)	594/7470 (8)	250/7470 (3.3)	344/7470 (4.6)	242/7470 (3.2)	194/7470 (2.6)	178/7470 (2.4)	*0/0 (-)	*0/0 (-)	89/7470 (1.2)
RC6	6208 (5.8)	409/6208 (6.6)	218/6208 (3.5)	191/6208 (3.1)	88/6208 (1.4)	100/6208 (1.6)	24/6208 (0.4)	5/6208 (0.1)	7/6208 (0.1)	*0/0 (-)
RC13	6103 (5.7)	555/6103 (9.1)	313/6103 (5.1)	207/6103 (3.4)	86/6103 (1.4)	93/6103 (1.5)	85/6103 (1.4)	*0/0 (-)	*0/0 (-)	78/6103 (1.3)
RC15	6075 (5.7)	889/6075 (14.6)	432/6075 (7.1)	456/6075 (7.5)	*0/0 (-)	*0/0 (-)	10/6075 (0.2)	*0/0 (-)	*0/0 (-)	35/6075 (0.6)
RC14	5886 (5.5)	674/5886 (11.5)	262/5886 (4.5)	412/5886 (7)	*0/0 (-)	8/5886 (0.1)	*0/0 (-)	*0/0 (-)	15/5886 (0.3)	*0/0 (-)
RC10	4353 (4.1)	285/4353 (6.5)	110/4353 (2.5)	175/4353 (4)	8/4353 (0.2)	13/4353 (0.3)	*0/0 (-)	3/4353 (0.1)	*0/0 (-)	*0/0 (-)
RC3	4305 (4.0)	282/4305 (6.6)	117/4305 (2.7)	165/4305 (3.8)	77/4305 (1.8)	74/4305 (1.7)	55/4305 (1.3)	*0/0 (-)	*0/0 (-)	41/4305 (1)
RC16	3774 (3.5)	474/3774 (12.6)	316/3774 (8.4)	158/3774 (4.2)	21/3774 (0.6)	21/3774 (0.6)	13/3774 (0.3)	2/3774 (0.1)	4/3774 (0.1)	26/3774 (0.7)
RC18	3296 (3.1)	290/3296 (8.8)	250/3296 (7.6)	40/3296 (1.2)	*0/0 (-)	*0/0 (-)	*0/0 (-)	*0/0 (-)	*0/0 (-)	*0/0 (-)
RC20	3212 (3.0)	272/3212 (8.5)	227/3212 (7.1)	39/3212 (1.2)	3/3212 (0.1)	10/3212 (0.3)	4/3212 (0.1)	*0/0 (-)	*0/0 (-)	*0/0 (-)
RC5	3015 (2.8)	264/3015 (8.8)	91/3015 (3)	171/3015 (5.7)	22/3015 (0.7)	85/3015 (2.8)	24/3015 (0.8)	6/3015 (0.2)	4/3015 (0.1)	34/3015 (1.1)
RC17	2972 (2.8)	225/2972 (7.6)	127/2972 (4.3)	98/2972 (3.3)	33/2972 (1.1)	*0/0 (-)	*0/0 (-)	*0/0 (-)	*0/0 (-)	*0/0 (-)
RC9	2864 (2.7)	346/2864 (12.1)	161/2864 (5.6)	185/2864 (6.5)	3/2864 (0.1)	2/2864 (0.1)	2/2864 (0.1)	70/2864 (2.4)	*0/0 (-)	4/2864 (0.1)
RC11	2802 (2.6)	239/2802 (8.5)	129/2802 (4.6)	80/2802 (2.8)	4/2802 (0.1)	*0/0 (-)	4/2802 (0.1)	*0/0 (-)	*0/0 (-)	*0/0 (-)
RC8	2661 (2.5)	243/2661 (9.1)	66/2661 (2.5)	177/2661 (6.7)	11/2661 (0.4)	12/2661 (0.5)	4/2661 (0.2)	*0/0 (-)	2/2661 (0.1)	*0/0 (-)

RC7	2459 (2.3)	166/2459 (6.8)	103/2459 (4.2)	45/2459 (1.8)	81/2459 (3.3)	63/2459 (2.6)	27/2459 (1.1)	*0/0 (-)	4/2459 (0.2)	8/2459 (0.3)
RC12	2098 (1.9)	232/2098 (11.1)	147/2098 (7)	83/2098 (4)	20/2098 (1)	3/2098 (0.1)	6/2098 (0.3)	*0/0 (-)	*0/0 (-)	*0/0 (-)
RC21	1259 (1.18)	88/1259 (7)	43/1259 (3.4)	45/1259 (3.6)	23/1259 (1.8)	11/1259 (0.9)	2/1259 (0.2)	*0/0 (-)	1/1259 (0.1)	8/1259 (0.6)
Total National	106247	9415 (8.9)	4266 (4.0)	5050 (4.8)	2373 (2.2)	1775 (1.7)	1473 (1.4)	98 (0.1)	0	561 (0.5)

Table 1.15: Location-wise isolates percentage of *S. aureus*, MSSA, MRSA and CoNS from all samples across OPD, Ward and ICU

Organism	Total	OPD	Ward	ICU
Total staphylococci	15748 / 107053 (14.7%)	5484 / 31726 (17.2%)	8112 / 55709 (14.5%)	2152 / 19618 (10.9%)
Staphylococcus aureus	9415 / 107053 (8.7%)	3940 / 31726 (12.4%)	4571 / 55709 (8.2%)	904 / 19618 (4.6%)
MSSA	5050/107053 (4.7)	2297 / 31726 (7.2)	2348/ 55709 (4.2)	405 / 19618 (2.0)
MRSA	4266 /107053 (4)	1610/ 31726 (5.0)	2170/ 55709 (3.9)	486/ 19618 (2.4)
CoNS	6333/107053 (6.0)	1544/ 31726 (4.8)	3541/ 55709 (6.3)	1248/ 19618 (6.3)

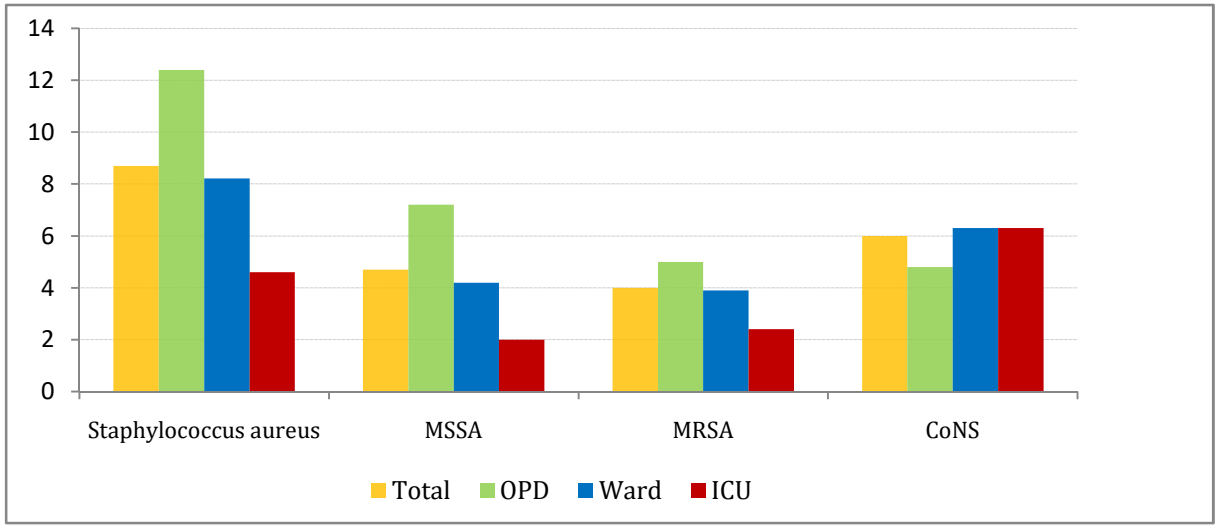


Figure 1.11: Location-wise Isolation pattern of *Staphylococcus aureus*, CoNS, MRSA, MSSA isolated from all samples

Table 1.16: Yearly isolation trend of *Staphylococcus* species

Bacteria	Year-2017 (%)	Year-2018 (%)	Year-2019 (%)	Year-2020 (%)	Year-2021 (%)	Year-2022 (%)
Total staphylococci	8564/45714 (18.7)	12950 (17.2)	16277/110264 (14.8)	5163/65561 (12.7)	11482/95728 (12)	15748/107053 (14.7)
S. aureus	5722/45714 (12.5)	8782/75182 (11.8)	12623/110264 (11.4)	6293/65561 (9.6)	8827/95728 (9.2)	9415 / 107053 (8.7%)
MRSA	1874/45714 (4.1)	3549 (4.7)	5353/110264 (4.9)	2622/65561 (4)	3423/95728 (3.6)	4266 /107053 (4)
MSSA	3820/45714 (8.4)	5233 (7)	7149/110264 (6.5)	3671/65561 (5.6)	5273/95728 (5.5)	5050/107053 (4.7)
CoNS	2842/45714 (6.2)	4076 (5.4)	3654/110264 (3.3)	1966/65561 (3)	2655/95728 (2.8)	6333/107053 (6.0)
S. haemolyticus	634/45714 (1.4)	871/75182 (1.2)	827/110264 (0.8)	626/65561 (0.9)	836/95728 (0.9)	2373 / 107053 2.22(%)
S. epidermidis	579/45714 (1.3)	912/75182 (1.2)	730/110264 (0.7)	397/65561 (0.6)	595/95728 (0.6)	1775/107053 (1.6)
S. hominis	383/45714 (0.8)	490/75182 (0.7)	451/110264 (0.4)	313/65561 (0.5)	400/95728 (0.4)	1473/107053 (1.4)
***Staphylococcus* spp.**	1216 / 45714 (2.6)	1717 / 75182 (2.3)	1540 / 110267 (1.4)	657 / 68081 (0.9)	676 / 96658 (0.7)	561 / 107053 (0.5)

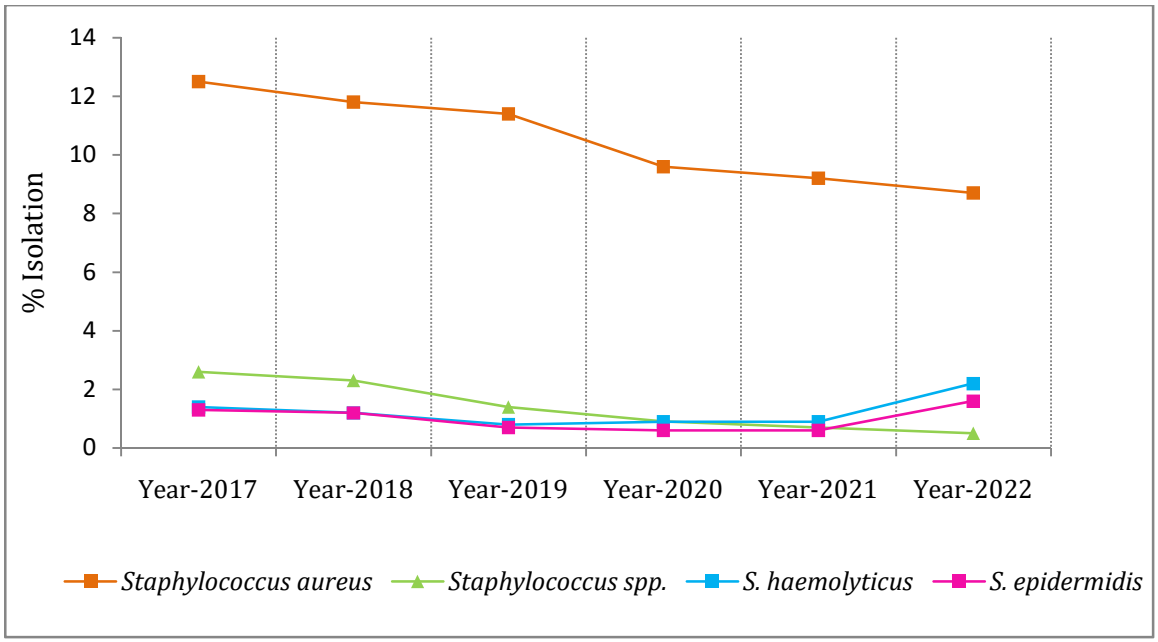


Figure 1.12 Yearly isolation trends of *Staphylococcus* species

Enterococci

Enterococci constituted overall 6.5% of all the isolates (Table 1.17). Among the *Enterococcus* species, *E. faecalis* and *E. faecium* accounted for 85% of all the total isolates, both *E. faecalis* (46.5%) and *E. faecium* (43.1%) were the predominant species. *E. faecalis* was more frequent in the urine (6.2%) and SI (3.4%) while *E. faecium* was relatively more frequent in the SS (6.1%) and CSF (4.8 %) (Table 1.17 and Figure 1.13). Among clinical settings, *E. faecalis* were common isolates from the OPD (3.3%) and *E. faecium* from the ICU (3.7%) (Table 1.18a). Regional centre wise distribution showed the predominance of isolation of *E. faecalis* in RC10 (7.3%) and *E. faecium* in RC18 (5.3%) (Table 1.18b).
The trend analysis over the years have shown a stable trend in the isolation rates of *E. faecium* from 2.0% to 2.8% in 2017 to 2022 and in *E. faecalis* from 2.2% to 3.0% in 2017 to 2022 respectively (Table 1.19 and Figure 1.14).

Table 1.17: Specimen wise distribution of *Enterococcus* species

	Total n=107053		Blood n=24238		Urine n=22135		LRT n=17244		Superficial Infection n=20508		Deep Infection n=7000		CSF n=1364		SS n=3396		Faeces n=806	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Enterococci	6965 (6.5)	100	1685 (7)	24.2	2504 (11.3)	36	58 (0.3)	0.8	1231 (6)	17.7	356 (5.1)	5.1	119 (8.7)	1.7	362 (10.7)	5.2	9 (1.1)	0.1
Enterococcus faecalis	3241 (3)	100	556 (2.3)	17.2	1362 (6.2)	42	20 (0.1)	0.6	689 (3.4)	21.3	152 (2.2)	4.7	38 (2.8)	1.2	91 (2.7)	2.8	1 (0.1)	0
Enterococcus faecium	3006 (2.8)	100	950 (3.9)	31.6	938 (4.2)	31.2	33 (0.2)	1.1	405 (2)	13.5	167 (2.4)	5.6	65 (4.8)	2.2	206 (6.1)	6.9	8 (1)	0.3
Enterococcus spp.	718 (0.7)	100	179 (0.7)	24.9	204 (0.9)	28.4	5 (0)	0.7	137 (0.7)	19.1	37 (0.5)	5.2	16 (1.2)	2.2	65 (1.9)	9.1	0 (0)	0

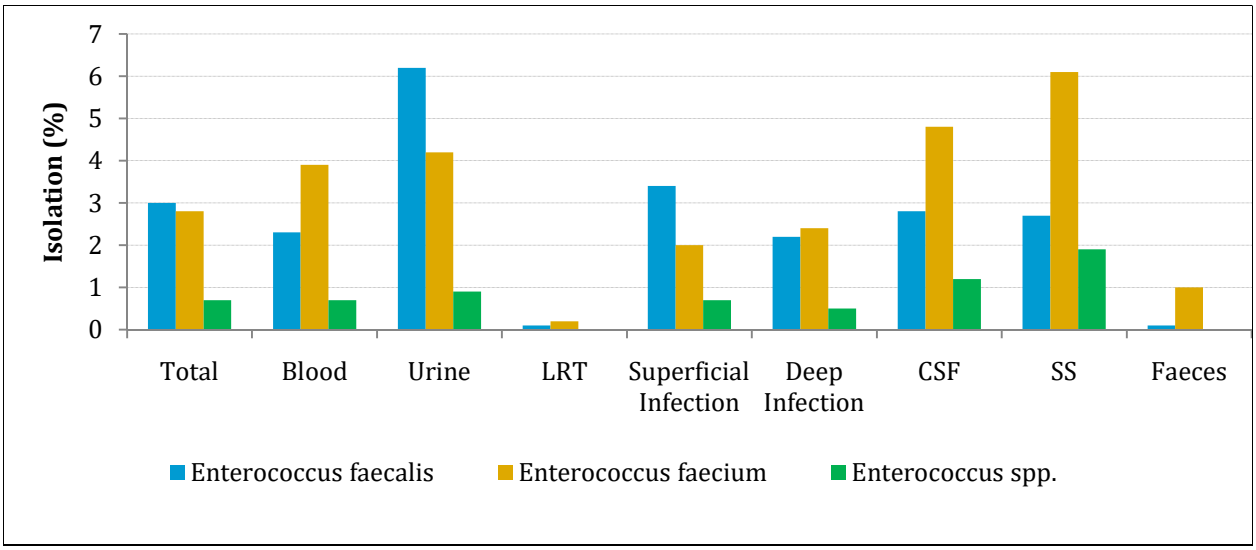


Figure 1.13: Specimen wise distribution of *Enterococcus* species

Table 1.18a. Location-wise isolation of *Enterococcus faecalis, Enterococcus faecium, Enterococcus* spp. from all specimens (Except Faeces)

Organism	Total	OPD	Ward	ICU
Enterococcus faecalis	3240 / 106247 (3.0%)	1061 / 31348 (3.3%)	1736 / 55297 (3.1%)	443 / 19602 (2.2%)
Enterococcus faecium	2998 / 106247 (2.8%)	453 / 31348 (1.4%)	1820 / 55297 (3.2%)	725 / 19602 (3.7%)
Enterococcus spp.	718 / 106247 (0.6%)	172 / 31348 (0.5%)	428 / 55297 (0.7%)	118 / 19602 (0.6%)

Table 1.18b. Isolates percentages across Regional Centres of *Enterococcus faecalis, Enterococcus faecium, Enterococcus* spp. from all specimen (Except Faeces)

Regional Centre	Total Isolates	*Enterococcus faecalis*	*Enterococcus faecium*	Enterococcus spp.
	n(%)	n(%)	n(%)	n(%)
RC4	13318 (12.5)	755/13318 (5.7)	426/13318 (3.2)	152/13318 (1.1)
RC2	11915 (11.2)	60/11915 (0.5)	140/11915 (1.2)	110/11915 (0.9)
RC19	10202 (9.6)	533/10202 (5.2)	312/10202 (3.1)	6/10202 (0.1)
RC1	7470 (7.0)	101/7470 (1.4)	212/7470 (2.8)	42/7470 (0.6)
RC15	6075 (6.7)	60/6075 (1)	69/6075 (1.1)	16/6075 (0.3)
RC6	6208 (5.8)	62/6208 (1)	212/6208 (3.4)	5/6208 (0.1)
RC13	6103 (5.7)	140/6103 (2.3)	200/6103 (3.3)	168/6103 (2.8)
RC14	5886 (5.5)	172/5886 (2.9)	86/5886 (1.5)	6/5886 (0.1)
RC10	4353 (4.1)	318/4353 (7.3)	156/4353 (3.6)	20/4353 (0.5)
RC3	4305 (4.0)	61/4305 (1.4)	134/4305 (3.1)	59/4305 (1.4)
RC16	3774 (3.5)	206/3774 (5.5)	124/3774 (3.3)	57/3774 (1.5)
RC18	3296 (3.1)	122/3296 (3.7)	176/3296 (5.3)	*0/0 (-)
RC20	3212 (3.0)	122/3212 (3.8)	71/3212 (2.2)	19/3212 (0.6)
RC5	3015 (2.8)	60/3015 (2)	63/3015 (2.1)	20/3015 (0.7)
RC17	2972 (2.8)	69/2972 (2.3)	105/2972 (3.5)	*0/0 (-)
RC9	2864 (2.6)	160/2864 (5.6)	82/2864 (2.9)	*0/0 (-)
RC11	2802 (2.6)	9/2802 (0.3)	107/2802 (3.8)	2/2802 (0.1)
RC8	2661 (2.5)	54/2661 (2)	90/2661 (3.4)	15/2661 (0.6)
RC7	2459 (2.3)	107/2459 (4.4)	52/2459 (2.1)	9/2459 (0.4)
RC12	2098 (1.9)	48/2098 (2.3)	123/2098 (5.9)	*0/0 (-)
RC21	1259 (1.2)	21/1259 (1.7)	58/1259 (4.6)	11/1259 (0.9)
Total	106247	3240 (3.0)	2998 (2.8)	718 (0.7)

Table 1.19: Yearly isolation trend of *Enterococcus* species

Bacteria	Year-2017 (%)	Year-2018 (%)	Year-2019 (%)	Year-2020 (%)	Year-2021 (%)	Year-2022 (%)
Total Enterococcus	2403/45521 (5.3)	4256/74295 (5.7)	6767/108465 (6.1)	4942/65561 (7.5)	5706/95728 (5.9)	6965/107053 (6.5)
Enterococcus faecium	937 / 45714 2.0(%)	1479 / 75182 1.9(%)	2742 / 110268 2.4(%)	2038 / 68081 2.9(%)	2455 / 96650 2.5(%)	3006 / 107053 2.8(%)
Enterococcus faecalis	1040 / 45714 2.2(%)	2022 / 75182 2.6(%)	2916 / 110268 2.6(%)	2177 / 68081 3.2(%)	2397 / 96650 2.4(%)	3241 / 107053 3.0(%)
Enterococcus spp.	426 / 45714 0.9(%)	755 / 75182 1(%)	1109 / 110268 1.0(%)	727 / 68081 1.0(%)	854 / 96650 0.8(%)	718 / 107053 0.6(%)

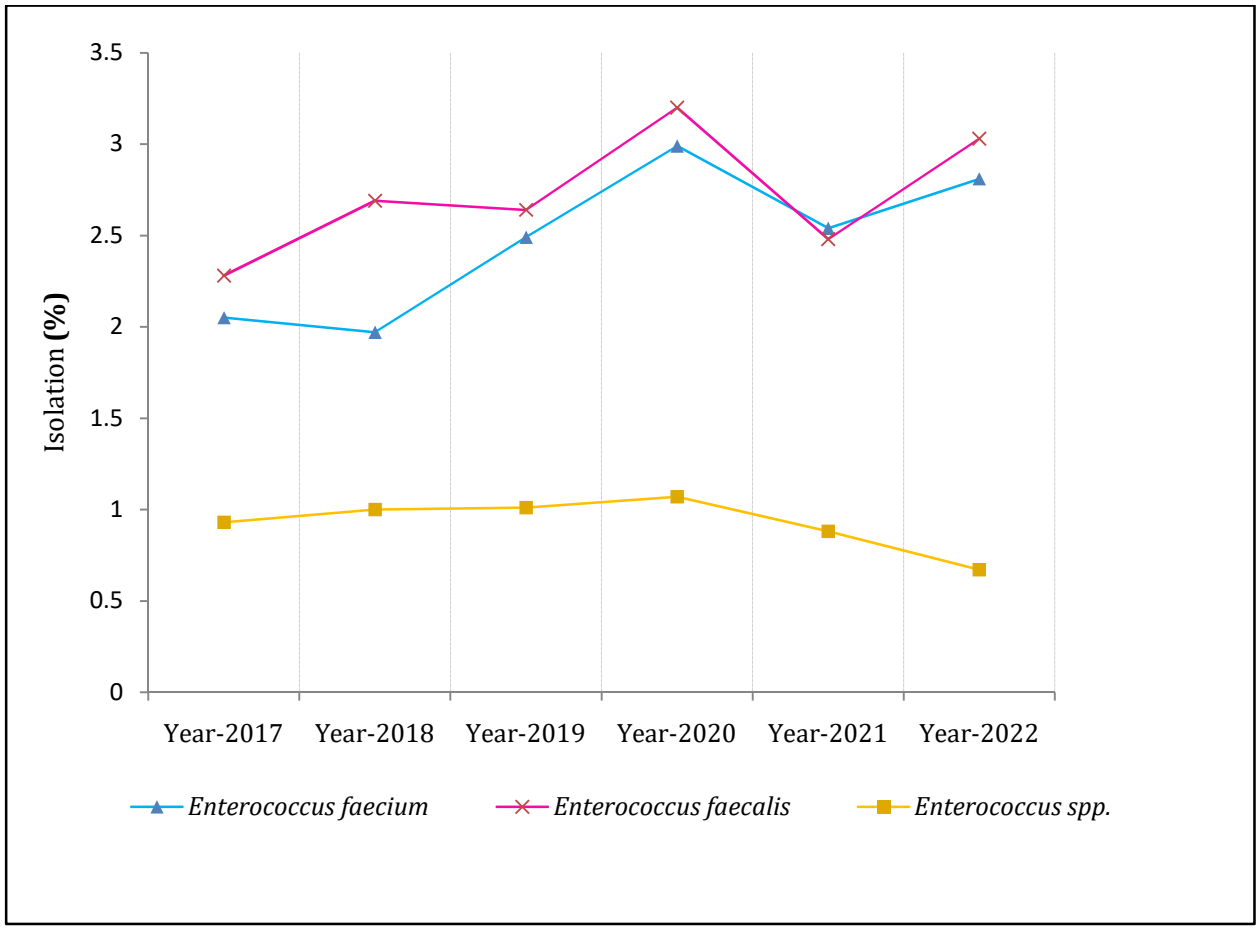


Figure 1.14 Yearly isolation trends of *Enterococcus* species

Fungal species

Total number of yeast isolates studied during the year 2022 was 2574, of those 49.1% (1265) were isolated from blood. Majority of the isolates were from *Candida tropicalis* (n=733) followed by *Candida albican*s (n=719) (Table 1.20). In the distribution of fungi species in different specimens, *C. tropicalis* was the predominant isolates in the blood (1.5%), *Candida albican*s was also the predominant isolates in the others (2.1%) followed by blood (0.9%) (Table 1.20). Among clinical settings, in ICUs, *C. tropicalis and* were common isolates from the ICU (1.0%) and *C. albican*s from the ward (0.75%) (Table 1.21 and Figure 1.15).

Yearly isolation trend showed that there is a steady decline in isolation of *C. tropicalis* from 1.4% in 2017 to 0.6% in 2022. Yearly isolation trend *of Candida albican*s showed a steady decline from 1.0% in 2017 to 0.6 in 2022. Both *C. auris and C. parapsilosis* isolates showed an increased trend from 2017 to 2022 (Table 1.22 and Figure 1.16).

Among *Aspergillus* species, *A. flavus* was the predomiant isolates followed by *A. fumigates* (Table 1.23).

Table 1.20: *Candida* species isolated from different sample types except faeces

Isolate	Total n=107053		Blood n=24238		Urine n=22135		LRT n=17244		Superficial Infection n=20508		Deep Infection n=7000		CSF n=1364		Genital n=*8		Others n=10354	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Fungal isolates	3237 (3)	100	1300 (5.4)	40.2	351 (1.6)	10.8	449 (2.6)	13.9	244 (1.2)	7.5	68 (1)	2.1	61 (4.5)	1.9	*1 (-)	0	610 (5.9)	18.8
Candida tropicalis	733 (0.68)	100	349 (1.5)	47.6	120 (0.5)	16.4	28 (0.2)	3.8	80 (0.4)	10.9	12 (0.2)	1.6	8 (0.6)	1.1	*0 (-)	0	85 (0.8)	11.6
Candida albicans	719 (0.67)	100	212 (0.9)	29.5	111 (0.5)	15.4	43 (0.3)	6	66 (0.3)	9.2	19 (0.3)	2.6	8 (0.6)	1.1	*0 (-)	0	219 (2.1)	30.6
Candida glabrata	322 (0.3)	100	123 (0.5)	38.2	53 (0.2)	16.5	2 (0)	0.6	34 (0.2)	10.6	11 (0.2)	3.4	1 (0.1)	0.3	*0 (-)	0	75 (0.7)	23.3
Candida parapsilosis	322 (0.3)	100	234 (1)	727	15 (0.1)	4.7	6 (0)	1.9	18 (0.1)	5.6	5 (0.1)	1.6	5 (0.4)	1.6	*0 (-)	0	28 (0.3)	8.7
Candida auris	164 (0.2)	100	108 (0.4)	65.9	22 (0.1)	13.4	5 (0)	3	7 (0)	4.3	7 (0.1)	4.3	5 (0.4)	3	*0 (-)	0	7 (0.1)	4.3
Candida utilis	63 (0.1)	100	58 (0.2)	92.1	0 (0)	0	0 (0)	0	0 (0)	0	0 (0)	0	3 (0.2)	4.8	*0 (-)	0	2 (0)	3.2
Candida krusei	86 (0.1)	100	47 (0.2)	54.7	3 (0)	3.5	1 (0)	1.2	9 (0)	10.5	3 (0)	3.5	0 (0)	0	*0 (-)	0	17 (0.2)	19.8
Candida pelliculosa	95 (0.1)	100	94 (0.4)	98.9	0 (0)	0	0 (0)	0	0 (0)	0	1 (0)	1.1	0 (0)	0	*0 (-)	0	0 (0)	0
Candida kefyr	21 (0)	100	5 (0)	23.8	5 (0)	23.8	1 (0)	4.8	2 (0)	9.5	2 (0)	9.5	0 (0)	0	*0 (-)	0	4 (0)	19
Candida lusitaniae	5 (0)	-	2 (0)	-	1 (0)	-	0 (0)	-	1 (0)	-	0 (0)	-	0 (0)	-	*0 (-)	-	1 (0)	-
Candida	2574 (2.4)	100	1265 (5.2)	49.1	335 (1.5)	13	86 (0.5)	3.3	222 (1.1)	8.6	60 (0.9)	2.3	30 (2.2)	1.2	*0 (-)	0	439 (4.2)	17.1

Notes:

1. Percentages are out of particular specimen (column).
2. Percentages in rows below Culture positive are out of Culture positive in respective columns.
3. **Blood** includes: Blood-central catheter, Blood-peripheral and Peripheral catheter-blood.
4. **LRT** (Lower Respiratory Tract) includes: BAL, Sputum, Lung aspirate, Endotracheal aspirate (ETA) and Lobectomy tissue (Lung tissue).
5. **Superficial Infection** includes: SST (Skin & Soft Tissue), Pus/exudate, Wound swab, Superficial Biopsy and Superficial Tissue.
6. **Deep Infection** includes: Abscess aspirate, Pus aspirate, Deep Biopsy and Deep Tissue.
7. **SS** (Sterile sites) includes: Fluid from sterile spaces, abdominal fluid, Intracostal tube fluid, Pancreatic drain fluid, Pericardial fluid, Peritoneal fluid and Pleural fluid.

Table 1.21: *Candida* species isolated from all samples across OPD, Ward and ICUs

Organism	Total	OPD	Ward	ICU
Candida tropicalis	733 / 107053 (0.6%)	114 / 31726 (0.3%)	415 / 55709 (0.74%)	204 / 19618 (1.0%)
Candida albicans	719 / 107053 (0.6%)	149 / 31726 (0.4%)	420 / 55709 (0.75%)	150 / 19618 (0.7%)
Candida glabrata	322 / 107053 (0.3%)	74 / 31726 (0.2%)	179 / 55709 (0.3%)	69 / 19618 (0.3%)
Candida parapsilosis	322 / 107053 (0.3%)	51 / 31726 (0.1%)	191 / 55709 (0.3%)	80 / 19618 (0.4%)
Candida auris	164 / 107053 (0.1%)	16 / 31726 (0.1%)	90 / 55709 (0.1%)	58 / 19618 (0.3%)
Candida pelliculosa	95 / 107053 (0.1%)	0 / 31726 (0%)	78 / 55709 (0.1%)	17 / 19618 (0.1%)
Candida krusei	86 / 107053 (0.08%)	11 / 31726 (0.0%)	57 / 55709 (0.1%)	18 / 19618 (0.1%)
Candida utilis	63 / 107053 (0.1%)	11 / 31726 (0.0%)	32 / 55709 (0.1%)	20 / 19618 (0.1%)
Candida kefyr	21 / 107053 (0.0%)	3 / 31726 (0.0%)	15 / 55709 (0.0%)	3 / 19618 (0.0%)
Candida lusitaniae	5 / 107053 (0%)	1 / 31726 (0%)	2 / 55709 (0%)	2 / 19618 (0.01%)

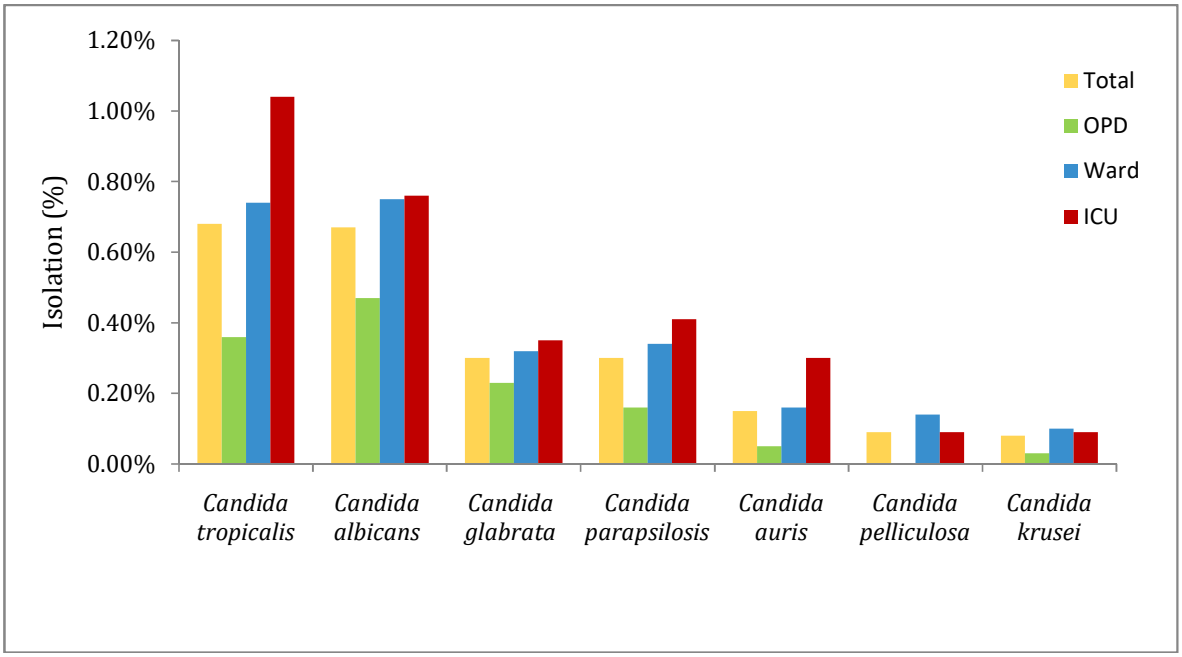


Figure 1.15: Location-wise pattern of *Candida* species isolated from all samples across OPD, Wards and ICUs.

Table 1.22: Yearly trends for isolation of *Candida* species isolated from all samples

Bacteria	Year-2017 (%)	Year-2018 (%)	Year-2019 (%)	Year-2020 (%)	Year-2021 (%)	Year-2022 (%)
Total Candida	1498/45521 (3.3)	1704/74295 (2.3)	2403/108465 (2.2)	1869/65561 (2.8)	2605/95728 (2.7)	2574/107053 (2.4)
Candida tropicalis	654 / 45714 1.4(%)	500 / 75182 0.6(%)	673 / 110268 0.6(%)	579 / 68081 0.8(%)	889 / 96650 0.9(%)	733 / 107053 (0.6%)
Candida albicans	461 / 45714 1.0(%)	560 / 75182 0.7(%)	687 / 110268 0.6(%)	438 / 68081 0.6(%)	712 / 96650 0.7(%)	719 / 107053 (0.6%)
Candida glabrata	138 / 45714 0.3(%)	179 / 75182 0.2(%)	205 / 110268 0.2(%)	157 / 68081 0.2(%)	326 / 96650 0.3(%)	322 / 107053 (0.3%)
Candida parapsilosis	107 / 45714 0.2(%)	134 / 75182 0.1(%)	278 / 110268 0.2(%)	220 / 68081 0.3(%)	306 / 96650 0.3(%)	322 / 107053 (0.3%)
Candida auris	17 / 45714 0.0(%)	56 / 75182 0.1(%)	125 / 110268 0.1(%)	156 / 68081 0.2(%)	220 / 96650 0.2(%)	164 / 107053 (0.1%)

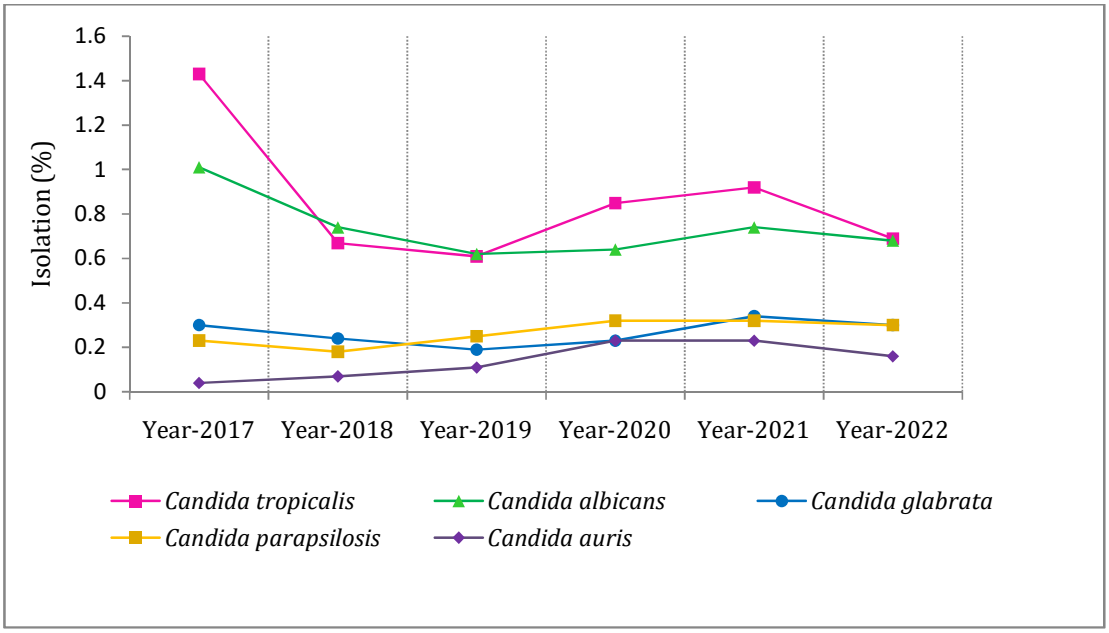


Figure 1.16: Yearly trends for isolation of *Candida* species isolated from all samples

Table 1.23: Isolation patterns of *Aspergillus* species from all specimens

Organism	Total n=107053
Aspergillus flavus	292 (0.3)
Aspergillus fumigatus	214 (0.2)
Aspergillus niger	43 (0)
Aspergillus terreus	17 (0)
Aspergillus versicolor	1 (0)

Diarrheal pathogens

A total of 670 diarrheal pathogen isolates were studied during the year 2022 which constituted 0.6% of total isolates (Table 1.1). The predominant species among diarrheal pathogens isolated from faeces sample identified was *Escherichia coli Diarrheagenic* (23.4%), followed by *Aeromonas spp* (20.3%), Salmonella spp Faecal (13.1%), *Shigella* (11.6%) and *Vibrio spp.* (4.8%) (Table 1.24). From non-faecal specimens, *Aeromonas spp* was isolated (n=16) and constituted 0.01% of total cultures (Table 1.25).

Diarrheagenic pathogens were predominantly isolated from patients in OPD and wards (Table 1.26). Non Typhoidal Salmonella was mainly isolated in ward (26.7%) followed by ICU and OPD (12.4%). *Escherichia coli* Diarrheagenic was mainly isolated in OPD (38.6%) followed by ward (6%), while the *Aeromonas spp* was predominant in ward (28.2%), followed by OPD (10.4%) and ICU (Table 1.26 and Figure 1.17). *Shigella flexneri* was predominant in OPD and *Vibrio cholerae* in ward. The isolation trend over the period of five years (2017– 2022) showed a decreasing trend in the isolation of *Aeromonas spp*. whereas, the isolation trend of Non Typhoidal Salmonella showed an increasing trend from last year (Table 1.27 and Figure 1.18). The isolation trend of *Vibrio spp showed* an increasing trend from 2017 (4.8%) to 2021(8.9%) and decreasing trend from 2021 (8.9%) to 2022 (3.9%)

Table 1.24: Isolation rates of faecal isolates from faeces samples

Isolates	n	% Isolation from faecal isolates (n= 806)	% Isolation from total positive cultures (n=107053)
Non Typhoidal Salmonella	160	34.1	0.1
Salmonella Typhimurium Faecal	54	6.7	0.1
Escherichia coli diarrhoeagenic	189	23.4	0.2
Aeromonas spp.	164	20.3	0.17
Salmonella spp. faecal	106	13.1	0.1
Shigella spp	94	11.6	0.1
Shigella flexneri	51	6.3	0
Shigella sonnei	39	4.8	0
Vibrio spp	39	4.8	0
Vibrio cholerae	32	3.9	0
Shigella boydii	2	0.2	0

Table 1.25: Isolation rates of Diarrhoeagenic pathogens from non-faecal specimens

Isolates	n	% Isolation from total positive cultures except faeces (n=106247)
Aeromonas spp. *	16	0.01
Escherichia coli diarrhoeagenic	0	0
Shigella	1	0
Vibrio	0	0
Non typhoidal*Salmonella*	0	0

Specimen: sterile sites (SS)

Table 1.26: Location-wise isolation pattern of top 5 faecal isolates isolated from faeces across OPD, Ward and ICU

Organism	Total	OPD	Ward	ICU
Non Typhoidal Salmonella	160/806 (34.1%)	47/378 (12.4%)	110/412 (26.7%)	3/16* (-)
Aeromonas spp.	164 / 806 (20.3%)	86 / 378 (22.7%)	74 / 412 (17.9%)	4 / 16* (-)
Escherichia coli Diarrhoeagenic	189 / 806 (23.4%)	146 / 378 (38.6%)	43 / 412 (10.4%)	0 / 16* (-)
Vibrio cholerae	32 / 806 (3.9%)	9 / 378 (2.3%)	22 / 412 (5.3%)	1 / 16* (-)
Shigella flexneri	51 / 806 (6.3%)	29 / 378 (7.6%)	21 / 412 (5.1%)	1 / 16* (-)

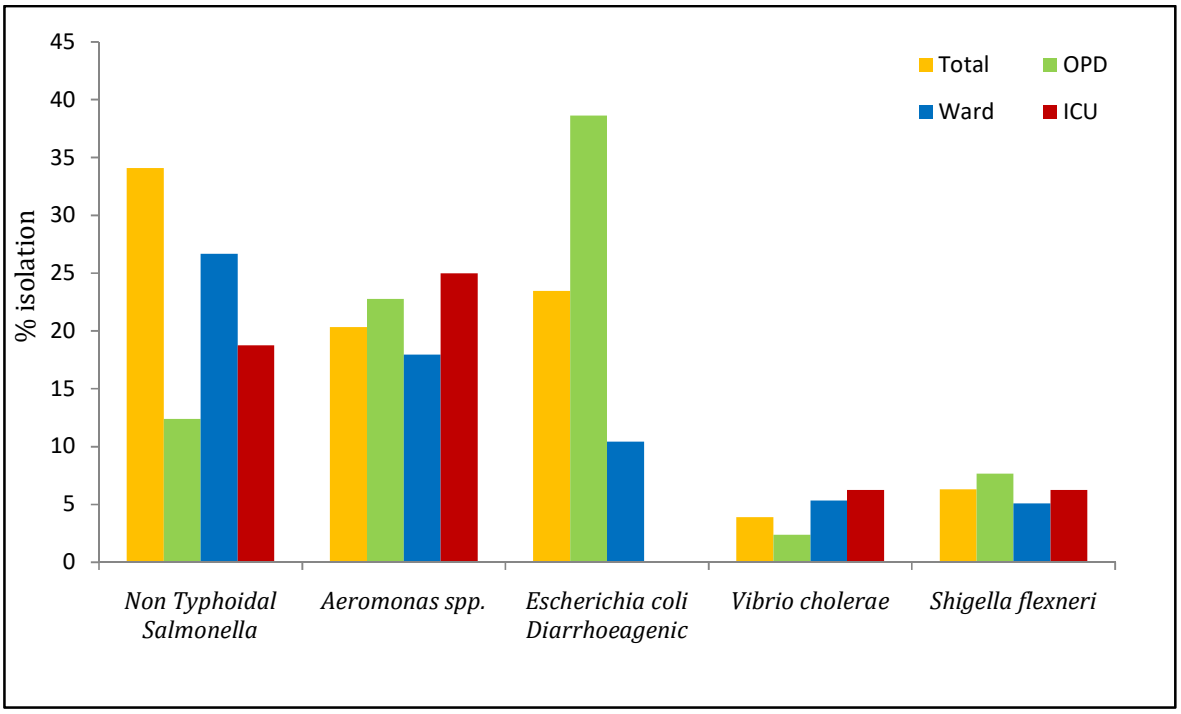


Figure 1.17: Location-wise isolation pattern of top 5 faecal isolates isolated from Faeces across OPD, Ward and ICU

Table 1.27. Yearly Isolation trends of top 5 faecal isolates isolated from Faeces

Bacteria	Year-2017 (%)	Year-2018 (%)	Year-2019 (%)	Year-2020 (%)	Year-2021 (%)	Year-2022 (%)
Escherichia coli Diarrhoeagenic	0/501 (0)	0/621 (0)	134/1063 (12.6)	102/572 (17.8)	88/651 (13.5)	189 / 806 23.4(%)
Aeromonas spp.	131/501 (26.1)	114/621 (18.4)	170/1063 (16.0)	77/572 (13.5)	179/651 (27.5)	164 / 806 20.3(%)
Shigella flexneri	89/501 (17.8)	47/621 (7.6)	95/1063 (8.9)	55/572 (9.6)	37/651 (5.7)	51 / 806 (6.3%)
Vibrio cholerae	24/501 (4.8)	25/621 (4)	39/1063 (3.7)	31/572 (5.4)	58/651 (8.9)	32 / 806 (3.9%)
Non Typhoidal Salmonella	20/501 (4)	39/621 (6.3)	60/1063 (5.6)	24/572 (4.2)	222/651 (34.1)	160/806 (34.1)

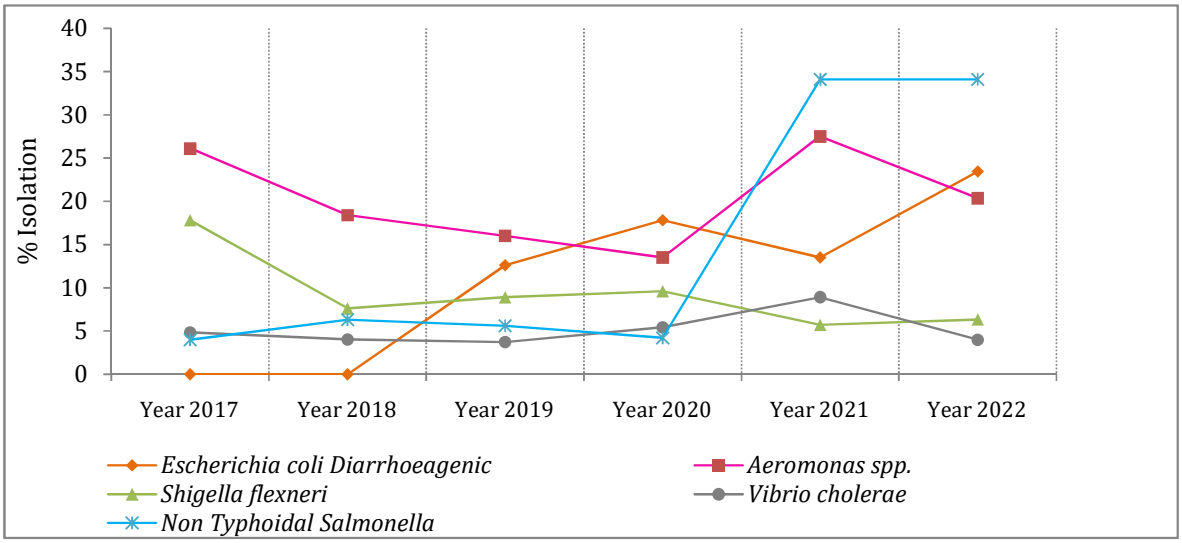


Figure 1.18: Yearly Isolation trends of top 5 faecal isolates isolated from Faeces

Streptococcus species

Total number of *Streptococcus* isolates studied during the year 2022 was 487, of those 1.8% were isolated from the upper respiratory tract. Majority of the isolates were from *Streptococcus agalactiae* (n=183) followed by *Streptococcus pyogenes* (n=156) and *Streptococcus pneumoniae* (n=144) (Table 1.28). Among clinical settings, *Streptococcus* isolates were common isolates from the OPD (0.7%) followed by ward and ICU (Table 1.29 and Figure 1.19).

Table 1.28: Sample-wise Isolation pattern of *Streptococcus* species

Organism	All Specimens	Blood	LRT	Superficial Infection	Deep Infection	SS	Faeces	Urine	Upper respiratory tract	Others
Streptococcus	487 / 107053 (0.4%)	80 / 24238 (0.3%)	95 / 17244 (0.5%)	122 / 20508 (0.6%)	52 / 7000 (0.7%)	4 / 3396 (0.1%)	0 (0)	88 / 22135 (0.4%)	9/495 (1.8%)	5 / 1984 (0.2%)
Streptococcus agalactiae	183 / 107053 (0.1%)	8 / 24238 (0.0%)	0 / 17244 (0%)	53 / 20508 (0.2%)	12 / 7000 (0.1%)	1 / 3396 (0.0%)	0 (0)	85 / 22135 (0.4%)	1/495 (0.2%)	2 / 1984 (0.1%)
Streptococcus pyogenes	156 / 107053 (0.1%)	28 / 24238 (0.1%)	12 / 17244 (0.1%)	65 / 20508 (0.3%)	38 / 7000 (0.5%)	1 / 3396 (0.0%)	0 (0)	1 / 22135 (0%)	5/495 (1.0%)	0 / 1984 (0%)
Streptococcus pneumoniae	144 / 107053 (0.1%)	42/ 24238 (0.1%)	83 / 17244 (0.4%)	2 / 20508 (0.0%)	2 / 7000 (0.0%)	2 / 3396 (0.0%)	0 (0)	2/ 22135 (0%)	3/495 (0.6%)	3 / 1984 (0.1%)
Viridans streptococci	4 / 107053 (0.0%)	2/ 24238 (0.0%)	0 / 17244 (0%)	2 / 20508 (0.0%)	0 / 7000 (0.0%)	0 / 3396 (0.0%)	0 (0)	0 / 22135 (0%)	0/495 (0%)	0 / 1984 (0%)

Table 1.29: Location-wise Isolation pattern of *Streptococcus* isolated from all specimens across OPD, Ward and ICU

Organism	Total	OPD	Ward	ICU
Streptococcus	487 / 107053 (0.4%)	242 / 31726 (0.7%)	187 / 55709 (0.3%)	58 / 19618 (0.3%)
Streptococcus agalactiae	183 / 107053 (0.1%)	123 / 31726 (0.4%)	49 / 55709 (0.1%)	11 / 19618 (0.0%)
Streptococcus pyogenes	156 / 107053 (0.1%)	59 / 31726 (0.19%)	79 / 55709 (0.1%)	18 / 19618 (0.1%)
Streptococcus pneumoniae	144 / 107053 (0.1%)	58 / 31726 (0.1%)	59 / 55709 (0.1%)	27 / 19618 (0.1%)
Viridans streptococci	4 / 107053 (0%)	2 / 31726 (0.0%)	0 / 55709 (0%)	2 / 19618 (0.0%)

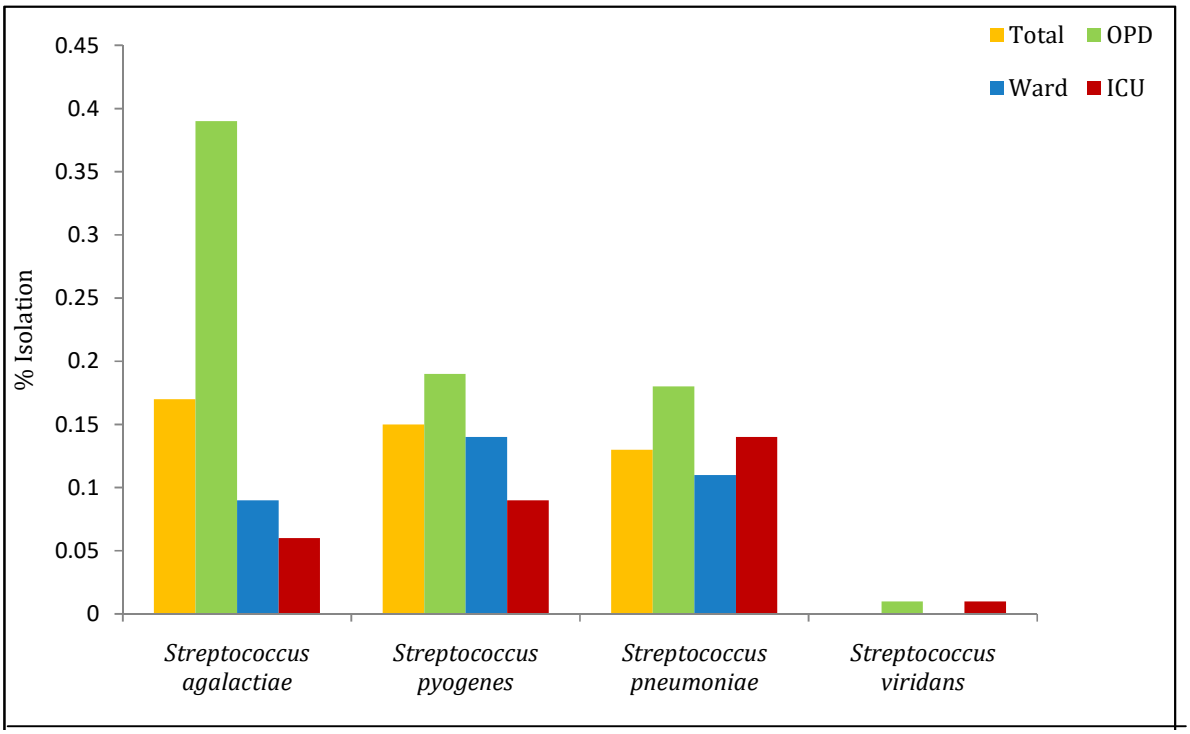


Figure 1.19: Location wise Isolation of *streptococcus* species

Chapter 2. Analysis of common syndromic isolates, their susceptibilities and implications in clnical practice

This chapter includes the interpretation of antibiograms from OPD/Ward/ICU which is crucial for assessing the impact of antimicrobial resistance and its implications in clinical practice for empirical use of antibiotics. This further helps in identifying potential areas for interventions and improvements in antibiotic stewardship practices.

Section A: Location wise distribution of isolates

Distribution of isolates from total samples

The distribution of top 5 isolates from OPD, ICU and ward from all specimens is presented in **Table 2.1 and Figure 2.1**. Among OPD, *Escherichia coli* was most commonly isolated (31.3%) followed by the *Klebsiella pneumoniae* (14.7%), *Pseudomonas aeruginosa* (13.1%), *Staphylococcus aureus* 12.4%) and *Acinetobacter baumannii* (4.7%). Among ward, again *Escherichia coli* was most commonly isolated (25.2%) followed by *Klebsiella pneumoniae* (17.8%), and *Pseudomonas aeruginosa* (11.9%). In ICU, *A. baumannii* was most commonly isolated (23.5%) %) followed by *Klebsiella pneumoniae* (21.5%) *and E.coli* (12.9%).

Table 2.1: Top 5 isolates from all specimens

OPD		Ward		ICU	
Organisms	Isolation rate	Organisms	Isolation rate	Organisms	Isolation rate
Escherichia coli	9951/31726 (31.37)	*Escherichia coli*	14051 / 55709 (25.22)	*Acinetobacter baumannii*	4625 / 19618 (23.58)
Klebsiella pneumoniae	4665/31726 (14.7)	*Klebsiella pneumoniae*	9965 / 55709 (17.89)	*Klebsiella pneumoniae*	4217 / 19618 (21.5)
Pseudomonas aeruginosa	4155/31726 (13.1)	*Pseudomonas aeruginosa*	6646 / 55709 (11.93)	*Escherichia coli*	2548 / 19618 (12.99)
Staphylococcus aureus	3940/31726 (12.42)	*Acinetobacter baumannii*	5997 / 55709 (10.76)	*Pseudomonas aeruginosa*	2427 / 19618 (12.37)
Acinetobacter baumannii	1521/31726 (4.79)	*Staphylococcus aureus*	4571 / 55709 (8.21)	*Staphylococcus aureus*	904 / 19618 (4.61)

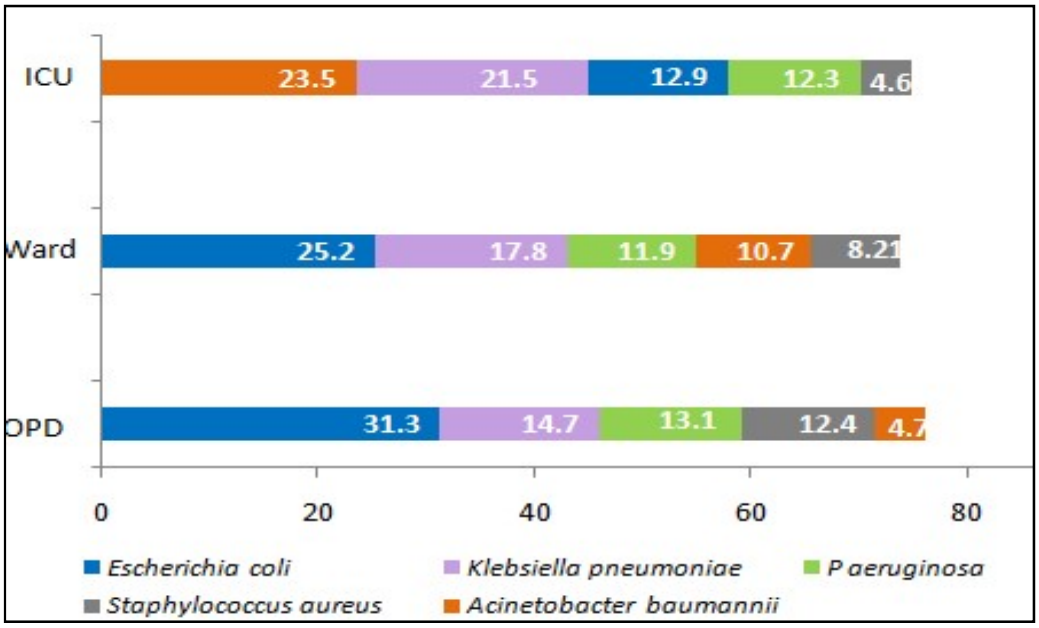


Figure 2.1: Distribution of top 5 organisms form OPD, ward and ICU from total specimens

Distribution of isolates from blood

Among blood specimen, *Escherichia coli* was the most predominant isolate from both OPD(19.82%) and ward (17.5%), followed by *K. pneumoniae and Staphylococcus haemolyticus* , whereas *K. pneumoniae* (20.43%) was most common from ICU, followed by *Acinetobacter baumannii* and *Escherichia coli* (Table 2.2).

Table 2.2: Top 5 isolates from blood

OPD		Ward		ICU	
Organisms	**Isolation rate**	**Organisms**	**Isolation rate**	**Organisms**	**Isolation rate**
Escherichia coli	947 / 4779 (19.82)	*Escherichia coli*	2225 / 12713 (17.5)	*Klebsiella pneumoniae*	1378 / 6746 (20.43)
Klebsiella pneumoniae	713 / 4779 (14.92)	*Klebsiella pneumoniae*	1868 / 12713 (14.69)	*Acinetobacter baumannii*	1077 / 6746 (15.97)
Staphylococcus haemolyticus	480 / 4779 (10.04)	*Staphylococcus haemolyticus*	1118 / 12713 (8.79)	*Escherichia coli*	730 / 6746 (10.82)
Staphylococcus aureus	363 / 4779 (7.6)	*Acinetobacter baumannii*	1098 / 12713 (8.64)	*Staphylococcus haemolyticus*	440 / 6746 (6.52)
Staphylococcus hominis	331 / 4779 (6.93)	*Staphylococcus aureus*	997 / 12713 (7.84)	*Pseudomonas aeruginosa*	435 / 6746 (6.45)

Distribution of isolates from urine

Among urinary specimens, *Escherichia coli* was the most common organism isolated from OPD, Wards and ICU, followed by *K. pneumoniae and Pseudomonas aeruginosa* in all three places (Table 2.3).

Table 2.3: Top 5 isolates from urine

OPD		Ward		ICU	
Organisms	**Isolation rate**	**Organisms**	**Isolation rate**	**Organisms**	**Isolation rate**
Escherichia coli	6691 / 10829 (61.79)	*Escherichia coli*	4537 / 9692 (46.81)	*Escherichia coli*	553 / 1614 (34.26)
Klebsiella pneumoniae	1650 / 10829 (15.24)	*Klebsiella pneumoniae*	1846 / 9692 (19.05)	*Klebsiella pneumoniae*	329 / 1614 (20.38)
Pseudomonas aeruginosa	595 / 10829 (5.49)	*Pseudomonas aeruginosa*	808 / 9692 (8.34)	*Pseudomonas aeruginosa*	191 / 1614 (11.83)
Enterococcus faecalis	574 / 10829 (5.3)	*Enterococcus faecalis*	693 / 9692 (7.15)	*Enterococcus faecium*	145 / 1614 (8.98)
Enterococcus faecium	197 / 10829 (1.82)	*Enterococcus faecium*	596 / 9692 (6.15)	*Enterococcus faecalis*	95 / 1614 (5.89)

Distribution of isolates from pus/exudates

Staphylococcus aureus was the most common organism isolated from pus/exudate samples sent from OPD followed by *Pseudomonas aeruginosa* and *Escherichia coli.* From wards, *Escherichia coli,* was most common followed by *Staphylococcus aureus*. From ICUs, *E. coli* was most common followed by *K. pneumoniae* and *Pseudomonas aeruginosa* (Table 2.4).

Table 2.4: Top 5 isolates from pus/exudates

OPD		Ward		ICU	
Organisms	**Isolation rate**	**Organisms**	**Isolation rate**	**Organisms**	**Isolation rate**
Staphylococcus aureus	1196 / 3688 (32.43)	*Escherichia coli*	1248 / 4778 (26.12)	*Escherichia coli*	164 / 736 (22.28)
Pseudomonas aeruginosa	639 / 3688 (17.33)	*Staphylococcus aureus*	866 / 4778 (18.12)	*Klebsiella pneumoniae*	157 / 736 (21.33)
Escherichia coli	622 / 3688 (16.87)	*Klebsiella pneumoniae*	779 / 4778 (16.3)	*Pseudomonas aeruginosa*	87 / 736 (11.82)
Klebsiella pneumoniae	390 / 3688 (10.57)	*Pseudomonas aeruginosa*	539 / 4778 (11.28)	*Acinetobacter baumannii*	87 / 736 (11.82)
Acinetobacter baumannii	157 / 3688 (4.26)	*Acinetobacter baumannii*	376 / 4778 (7.87)	*Staphylococcus aureus*	79 / 736 (10.73)

Distribution of isolates from CSF

Gram-negative isolates were more common among the isolated organisms from the CSF, indicating high representation of hospital acquired ventriculitis in the study population. *Acinetobacter baumannii* was the most common organism followed by and *Klebsiella pneumoniae* and *E. coli* (Table 2.5).

Table 2.5: Top 5 isolates from CSF from all locations

Organisms	Isolation rate
Acinetobacter baumannii	425 / 1364 (31.16)
Klebsiella pneumoniae	215/1364 (15.76)
Escherichia coli	144 / 1364 (10.56)
Pseudomonas aeruginosa	117/1364 (5.06)
Staphylococcus aureus	69 / 1364 (5.06)

Distribution of isolates from faeces

Diarrhoeagenic *Escherichia coli* were the most common organism isolated from stool specimen from OPDs followed by *Aeromonas* and *Salmonella* spp. Salmonella and *Aeromonas* were also the most common from wards (Table 2.6).

Table 2.6: Top 5 isolates from faeces

OPD		Ward	
Organisms	**Isolation rate**	**Organisms**	**Isolation rate**
Escherichia coli Diarrhoeagenic	146 / 378 (38.62)	*Salmonella* spp. Faecal	75 / 412 (18.2)
Aeromonas spp.	86 / 378 (22.75)	*Aeromonas* spp.	74 / 412 (17.96)
Salmonella spp. Faecal	30 / 378 (7.94)	*Salmonella* spp.	43 / 412 (10.44)
Shigella flexneri	29 / 378 (7.67)	*Escherichia coli* Diarrhoeagenic	43 / 412 (10.44)
Shigella sonnei	24 / 378 (6.35)	*Escherichia coli*	39 / 412 (9.47)

Section B: Specimen wise Antibiograms

AMR Patterns from various specimens

- Resistance to 3rd Gen cephalosporins was very high among Gram-negative isolates (*Escherichia coli, Klebsiella pneumoniae and Acinetobacter baumannii)* from all the three loactions with exception of *P. aeruginosa,* in which susceptibility to ceftazidime was close to 80% in OPD isolates and close to 50% in ICU isolates.

- Amikacin showed good susceptibility rates among *E. coli* and *P. aeruginosa* isolates (close to 80%), but its susceptibility rates remained poor in *Klebsiella pneumoniae and Acinetobacter baumannii.*

- In *Acinetobacter baumannii* isolates, only Minocycline (> 60%) and colistin (>95%) showed good susceptibility rates.

- For carbapenems, *E coli and P. aeruginosa* isolates were fairly susceptible but carbapenem resistance rates were very high for *Klebsiella pneumoniae and Acinetobacter baumannii* even among OPD isolates.

- MRSA rates were close to 50% among ICU isolates whereas the same was close to 35% among OPD isolates. Antibiotics like TMP-SMX and clindamycin were fairly susceptible also vancomycin and linezolid showed good susceptibility rates of close to 100%.

- Ceftriaxone (96.1% susceptible), Cefixime (94 % susceptible), trimethoprim-sulfamethoxazole (92% susceptible) and azithromycin (97.4% susceptible) showed very good susceptibility patterns for Salmonella Typhi isolates. Fluoroquinolones show very poor susceptibility patterns (> 95% resistance) for Salmonella Typhi isolates.

- Antibiograms of stool samples, showed, high rates of resistance to fluoroquinolones; more than 90% isolates of Diarhogenic *E. coli* and *Aeromonas spp*. were resistant to fluoroquinolones. Among the tested isolates, trimethoprim-sulfamethoxazole and azithromycin showed good susceptible rates to *Salmonella spp*., Diarhogenic *E. coli* and *Shigella* respectively.

- Most of these isolates were resistant to carbapenems, cephalosporins and fluoroquinolones. Only colistin and minocycline showed promising susceptibility rates for *Acinetobacter baumannii* and *Klebsiella pneumoniae.*

The AMR patterns of top five pathogens identified in various specimens are depicted in tables.

Blood

Table 2.7: Susceptibility percentages of *E. coli* isolates from blood

AMA	*Escherichia coli*		
	OPD n=947	Ward n=2225	ICU n=730
Amikacin	744 / 947 (78.6%)	1695 / 2222 (76.3%)	546 / 726 (75.2%)
Ceftriaxone	36 / 127 (28.3%)	125 / 572 (21.9%)	46 / 243 (18.9%)
Ciprofloxacin	135 / 951 (14.2%)	297 / 2219 (13.4%)	90 / 721 (12.5%)
Colistin	402 / 403 (99.8)	826 / 834 (99.0)	264 / 267 (98.9)
Ertapenem	533 / 690 (77.2%)	1263 / 1777 (71.1%)	387 / 593 (65.3%)
Fosfomycin	79 / 81 (97.5%)	134 / 136 (98.5%)	36 / 37 (97.3%)
Imipenem	650 / 893 (72.8%)	1402 / 2044 (68.6%)	467 / 693 (67.4%)
Levofloxacin	44 / 320 (13.8%)	135 / 804 (16.8%)	33 / 211 (15.6%)
Meropenem	676 / 900 (75.1%)	1583 / 2188 (72.3%)	497 / 720 (69%)
Minocycline	113 / 135 (83.7%)	256 / 350 (73.1%)	86 / 125 (68.8%)
Piperacillin-tazobactam	390 / 957 (40.8%)	898 / 2253 (39.9%)	324 / 729 (44.4%)
Trimethoprim-sulfamethoxazole	47 / 144 (32.6%)	128 / 357 (35.9%)	72 / 167 (43.1%)

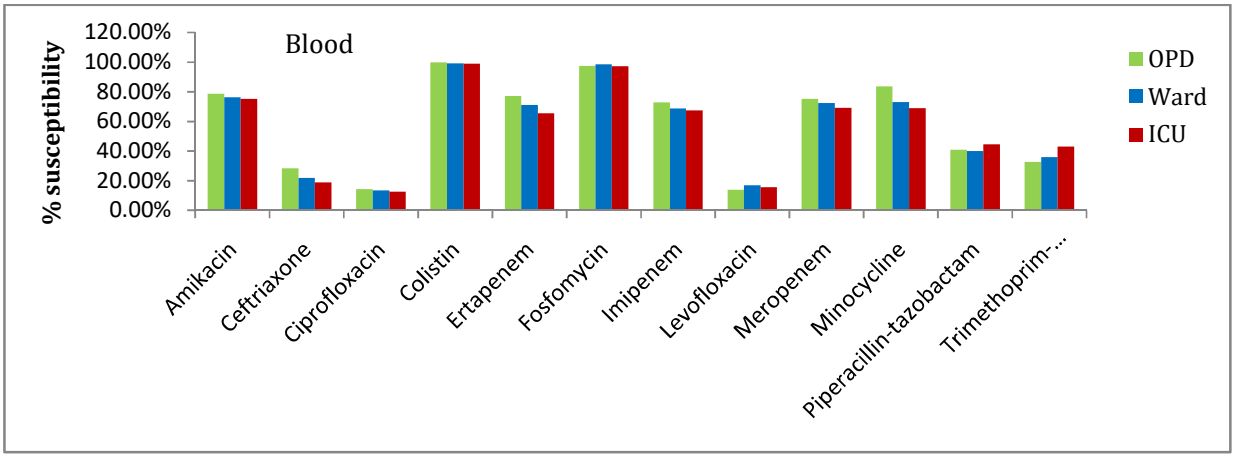


Figure 2.2: Susceptibility pattern of *E. coli* from blood samples

Table 2.8: % Susceptibility of *Klebsiella pneumoniae* isolates from blood

AMA	*Klebsiella pneumoniae*		
	OPD n=713	Ward n=1868	ICU n=1378
Amikacin	272 / 709 (38.4%)	673 / 1862 (36.1%)	510 / 1365 (37.4%)
Ceftriaxone	21 / 56 (37.5%)	97 / 391 (24.8%)	68 / 461 (14.8%)
Ciprofloxacin	143 / 705 (20.3%)	343 / 1864 (18.4%)	202 / 1364 (14.8%)
Colistin	367 / 371 (98.9)	960 / 1017 (94.4)	677 / 713 (95.0)
Ertapenem	184 / 397 (46.3%)	453 / 1278 (35.4%)	322 / 1030 (31.3%)
Fosfomycin	20 / 30 (66.7%)	83 / 135 (61.5%)	71 / 142 (50%)
Imipenem	258 / 701 (36.8%)	620 / 1793 (34.6%)	438 / 1333 (32.9%)
Levofloxacin	75 / 286 (26.2%)	155 / 792 (19.6%)	102 / 499 (20.4%)
Meropenem	252 / 684 (36.8%)	639 / 1820 (35.1%)	451 / 1360 (33.2%)
Minocycline	50 / 69 (72.5%)	226 / 412 (54.9%)	203 / 380 (53.4%)
Piperacillin-tazobactam	117 / 719 (16.3%)	331 / 1876 (17.6%)	254 / 1376 (18.5%)
Trimethoprim-sulfamethoxazole	13 / 50 (26%)	88 / 296 (29.7%)	104 / 366 (28.4%)

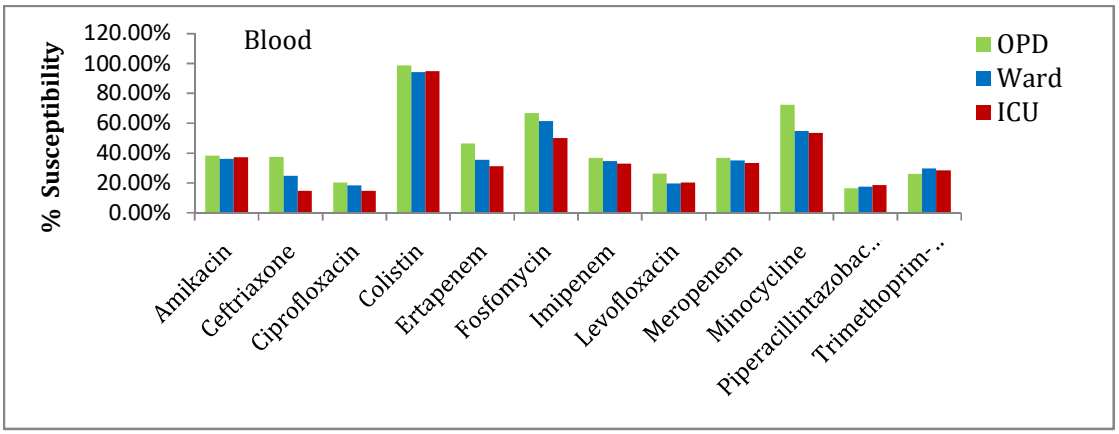


Figure 2.3: Susceptibility pattern of *Klebsiella pneumoniae* from blood samples

Table 2.9: % Susceptibility of *Acinetobacter baumannii* isolates from blood

AMA	*Acinetobacter baumannii*		
	OPD n=237	Ward n=1098	ICU n=1077
Amikacin	79 / 234 (33.8%)	275 / 1087 (25.3%)	164 / 1040 (15.8%)
Cefepime	71 / 235 (30.2%)	202 / 1085 (18.6%)	112 / 1053 (10.6%)
Ceftazidime	69 / 227 (30.4%)	165 / 1044 (15.8%)	88 / 1043 (8.4%)
Colistin	173 / 179 (96.6)	787 / 817 (96.3)	658 / 670 (98.2)
Imipenem	70 / 236 (29.7%)	224 / 1095 (20.5%)	115 / 1072 (10.7%)
Levofloxacin	69 / 197 (35%)	230 / 850 (27.1%)	149 / 844 (17.7%)
Meropenem	73 / 235 (31.1%)	237 / 1088 (21.8%)	146 / 1074 (13.6%)
Minocycline	151 / 219 (68.9%)	610 / 942 (64.8%)	593 / 964 (61.5%)
Piperacillin-tazobactam	69 / 237 (29.1%)	234 / 1098 (21.3%)	131 / 1078 (12.2%)

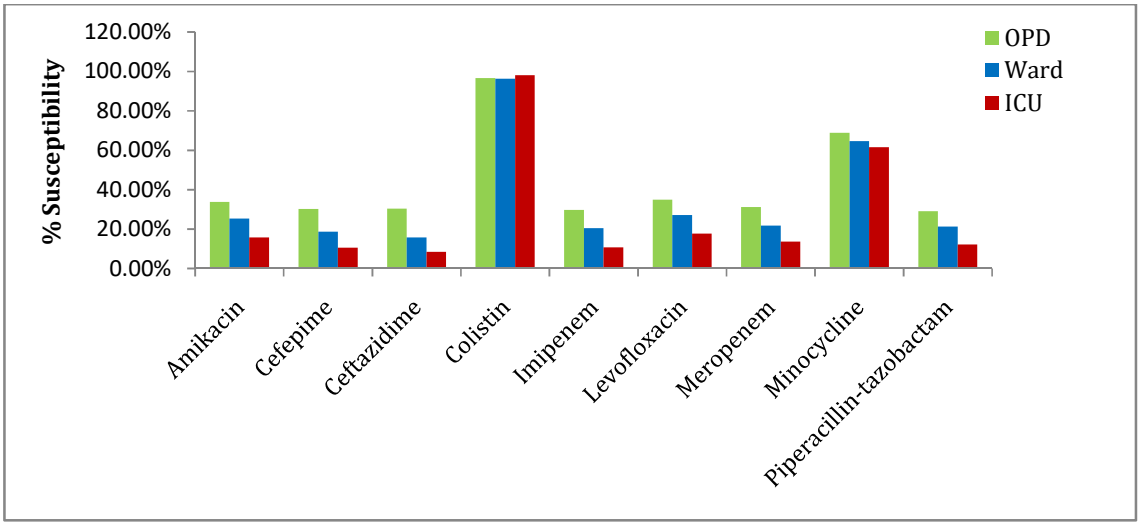


Figure 2.4: Susceptibility pattern of *Acinetobacter baumannii* from blood samples

Table 2.10: % Susceptibility of *P. aeruginosa* isolates from blood

AMA	*P. aeruginosa*		
	OPD n=244	Ward n=800	ICU n=435
Amikacin	199 / 244 (81.6%)	530 / 800 (66.3%)	247 / 434 (56.9%)
Cefepime	196 / 237 (82.7%)	472 / 789 (59.8%)	219 / 418 (52.4%)
Ceftazidime	187 / 237 (78.9%)	457 / 780 (58.6%)	214 / 427 (50.1%)
Ciprofloxacin	139 / 236 (58.9%)	326 / 756 (43.1%)	180 / 415 (43.4%)
Colistin	148 / 152 (97.4)	417 / 425 (98.1)	245 / 247 (99.2)
Gentamicin	139 / 182 (76.4%)	357 / 575 (62.1%)	196 / 347 (56.5%)
Imipenem	183 / 240 (76.3%)	471 / 782 (60.2%)	222 / 423 (52.5%)
Levofloxacin	149 / 205 (72.7%)	331 / 627 (52.8%)	165 / 365 (45.2%)
Meropenem	196 / 243 (80.7%)	465 / 781 (59.5%)	230 / 427 (53.9%)
Piperacillin-tazobactam	202 / 242 (83.5%)	515 / 797 (64.6%)	257 / 437 (58.8%)
Tobramycin	89 / 117 (76.1%)	209 / 318 (65.7%)	116 / 225 (51.6%)

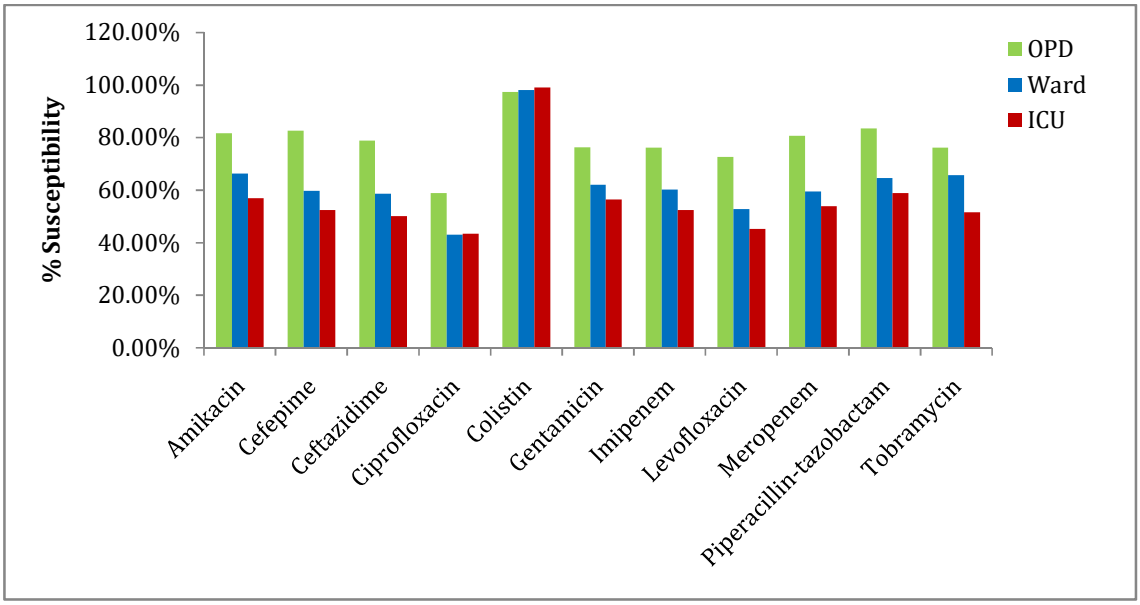


Figure 2.5: Susceptibility pattern of *P. aeruginosa from* blood samples

Table 2.11: % Susceptibility of *S. aureus* isolates from blood

AMA	*Staphylococcus aureus*		
	OPD n=363	Ward n=997	ICU n=424
Cefoxitin	134 / 240 (55.8%)	423 / 791 (53.5%)	185 / 370 (50%)
Ciprofloxacin	67 / 329 (20.4%)	207 / 897 (23.1%)	109 / 411 (26.5%)
Clindamycin	230 / 348 (66.1%)	675 / 980 (68.9%)	258 / 420 (61.4%)
Daptomycin	17 / 17 (100%)	55 / 58 (94.8%)	43 / 45 (95.6%)
Erythromycin	140 / 362 (38.7%)	408 / 988 (41.3%)	138 / 419 (32.9%)
Linezolid	265 / 267 (99.3%)	834 / 846 (98.6%)	389 / 398 (97.7%)
Oxacillin	123 / 181 (68%)	243 / 374 (65%)	84/ 183 (45%)
Teicoplanin	159 / 159 (100%)	419 / 421 (99.5%)	207 / 209 (99%)
Tetracycline	205 / 232 (88.4%)	625 / 745 (83.9%)	281 / 351 (80.1%)
Tigecycline	65 / 65 (100%)	206/ 206 (100%)	131 / 131 (100%)
Trimethoprim-sulfamethoxazole	179 / 239 (74.9%)	591 / 803 (73.6%)	269 / 387 (69.5%)
Vancomycin	315 / 315 (100%)	778 / 778 (100%)	288 / 288 (100%)

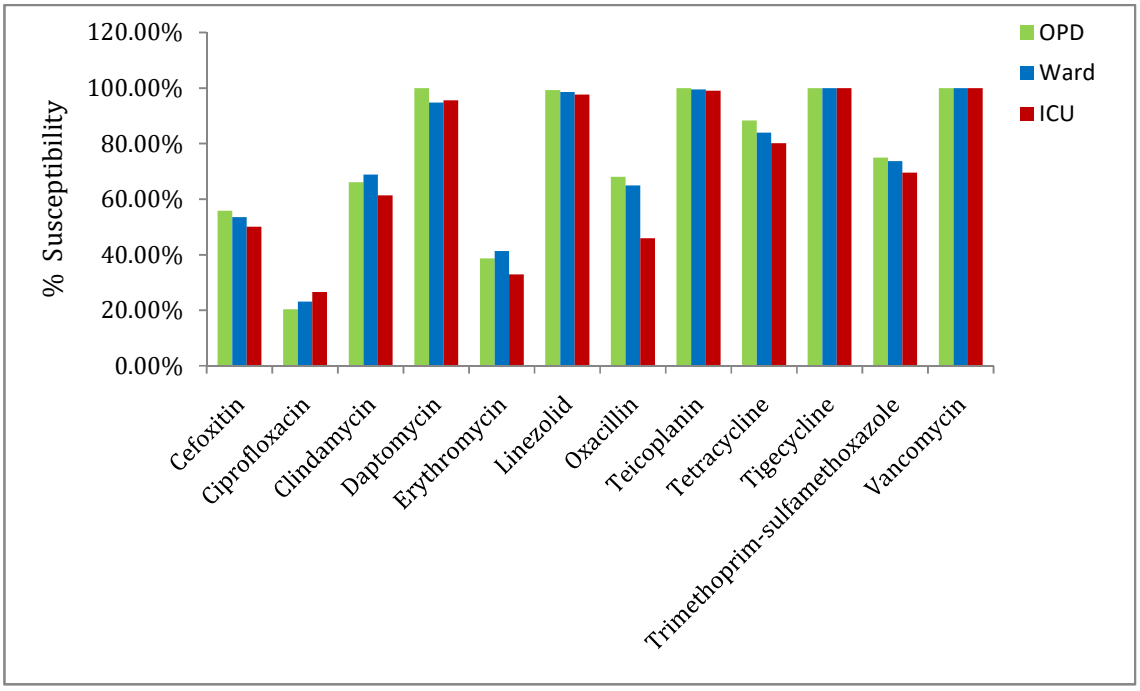


Figure 2.6: Susceptibility pattern of *S. aureus* from blood samples

Table 2.12: % Susceptibility of Salmonella Typhi isolates from blood

AMA	Salmonella Typhi	
	OPD n=317	Ward n=245
Ampicillin	285 / 299 (95.3%)	208 / 223 (93.3%)
Azithromycin	298 / 306 (97.4%)	204 / 213 (95.8%)
Cefixime	244 / 257 (94.9%)	159 / 169 (94.1%)
Cefotaxime	117 / 124 (94.4%)	63 / 73 (86.3%)
Ceftriaxone	299 / 311 (96.1%)	216 / 236 (91.5%)
Chloramphenicol	264 / 278 (95%)	190 / 200 (95%)
Ciprofloxacin	7 / 323 (2.2%)	9 / 244 (3.7%)
Levofloxacin	3 / 67 (4.5%)	4 / 39 (10.3%)
Trimethoprim-sulfamethoxazole	286 / 311 (92%)	232 / 245 (94.7%)

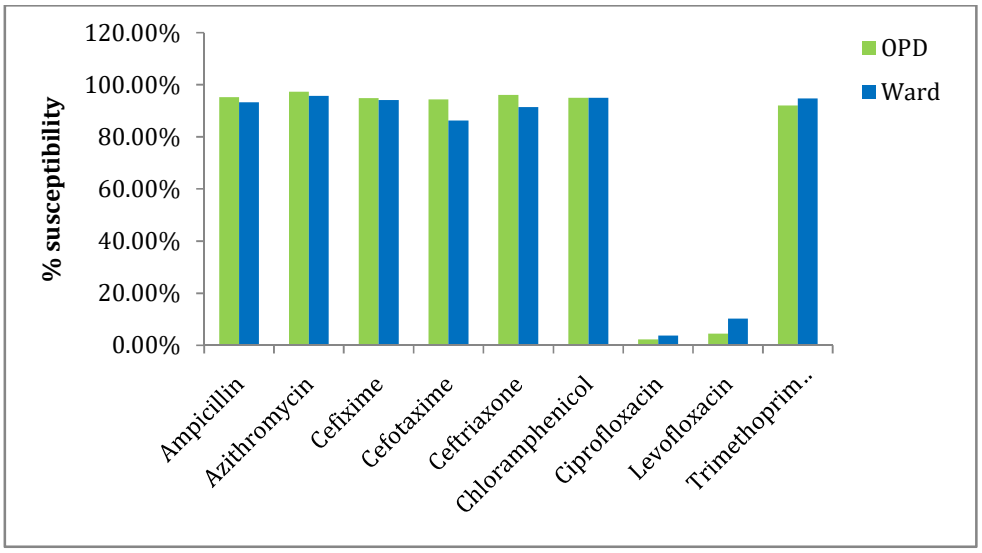


Figure 2.7: Susceptibility pattern of Salmonella Typhi from blood samples

Urine

Table 2.13: % Susceptibility of *E. coli isolates* from urine

AMA	*Escherichia coli*		
	OPD n=6691	Ward n=4537	ICU n=553
Amikacin	5964 / 6666 (89.5%)	3667 / 4527 (81%)	427 / 550 (77.6%)
Cefazolin	620 / 2520 (24.6%)	322 / 2102 (15.3%)	22 / 172 (12.8%)
Ceftriaxone	585 / 1959 (29.9%)	262 / 1476 (17.8%)	50 / 230 (21.7%)
Ciprofloxacin	1394 / 6630 (21%)	687 / 4503 (15.3%)	70 / 547 (12.8%)
Colistin	2565 / 2574 (99.7%)	1521 / 1527 (99.6%)	253 / 254 (99.6%)
Ertapenem	4426 / 5476 (80.8%)	2292 / 3384 (67.7%)	279 / 446 (62.6%)
Fosfomycin	3789 / 3911 (96.9%)	2794 / 2898 (96.4%)	279 / 292 (95.5%)
Imipenem	5521 / 6591 (83.8%)	3220 / 4445 (72.4%)	364 / 541 (67.3%)
Levofloxacin	744 / 2742 (27.1%)	431 / 2208 (19.5%)	17 / 201 (8.5%)
Meropenem	5773 / 6586 (87.7%)	3369 / 4436 (75.9%)	371 / 542 (68.5%)
Minocycline	1392 / 1652 (84.3%)	690 / 941 (73.3%)	93 / 119 (78.2%)
Nitrofurantoin	5259 / 5762 (91.3%)	3625 / 4056 (89.4%)	398 / 469 (84.9%)
Piperacillin-tazobactam	4188 / 6649 (63%)	2147 / 4524 (47.5%)	265 / 550 (48.2%)
Trimethoprim-sulfamethoxazole	2775 / 5879 (47.2%)	1467 / 4007 (36.6%)	191 / 497 (38.4%)

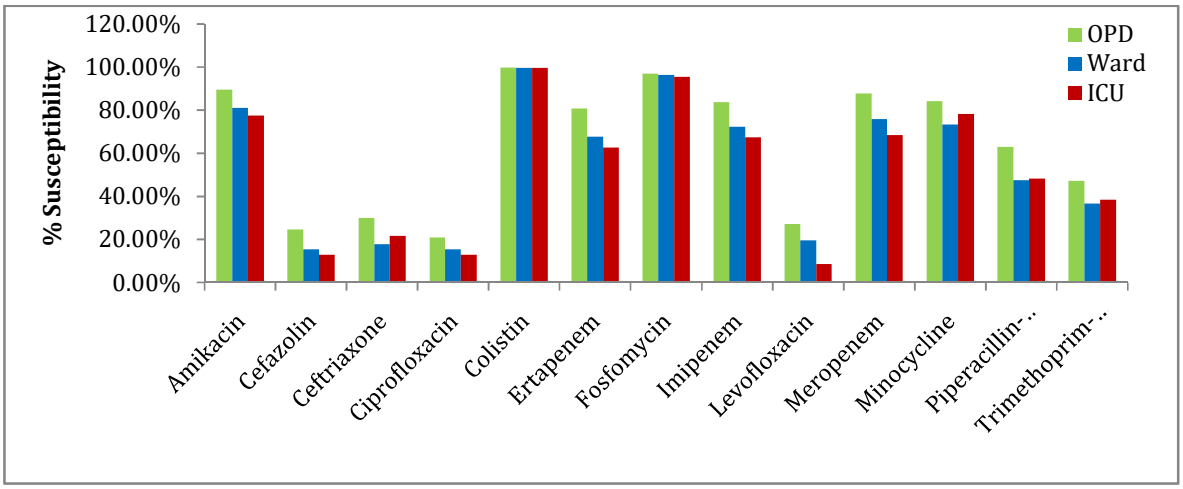


Figure 2.8: Susceptibility pattern of *E. coli* from urine

Table 2.14:% Susceptibility of *Klebseilla pneumoniae* isolates from urine

	Klebsiella pneumoniae		
	OPD n=1650	Ward n=1846	ICU n=329
Amikacin	1114 / 1640 (67.9%)	938 / 1841 (51%)	113 / 327 (34.6%)
Cefazolin	193 / 622 (31%)	144 / 793 (18.2%)	10 / 106 (9.4%)
Ceftriaxone	206 / 527 (39.1%)	169 / 653 (25.9%)	20 / 152 (13.2%)
Ciprofloxacin	515 / 1634 (31.5%)	393 / 1829 (21.5%)	36 / 324 (11.1%)
Colistin	656 / 674 (97.3%)	708 / 737 (96.1%)	170 / 180 (94.4%)
Ertapenem	822 / 1378 (59.7%)	620 / 1375 (45.1%)	62 / 265 (23.4%)
Fosfomycin	723 / 957 (75.5%)	798 / 1134 (70.4%)	117 / 167 (70.1%)
Imipenem	1051 / 1623 (64.8%)	874 / 1799 (48.6%)	94 / 319 (29.5%)
Levofloxacin	269 / 724 (37.2%)	217 / 911 (23.8%)	17 / 136 (12.5%)
Meropenem	1102 / 1625 (67.8%)	897 / 1789 (50.1%)	97 / 322 (30.1%)
Minocycline	266 / 417 (63.8%)	246 / 434 (56.7%)	34 / 69 (49.3%)
Nitrofurantoin	663 / 1412 (47%)	569 / 1586 (35.9%)	65 / 274 (23.7%)
Piperacillin-tazobactam	757 / 1637 (46.2%)	574 / 1840 (31.2%)	65 / 329 (19.8%)
Trimethoprim-sulfamethoxazole	729 / 1483 (49.2%)	600 / 1659 (36.2%)	77 / 285 (27%)

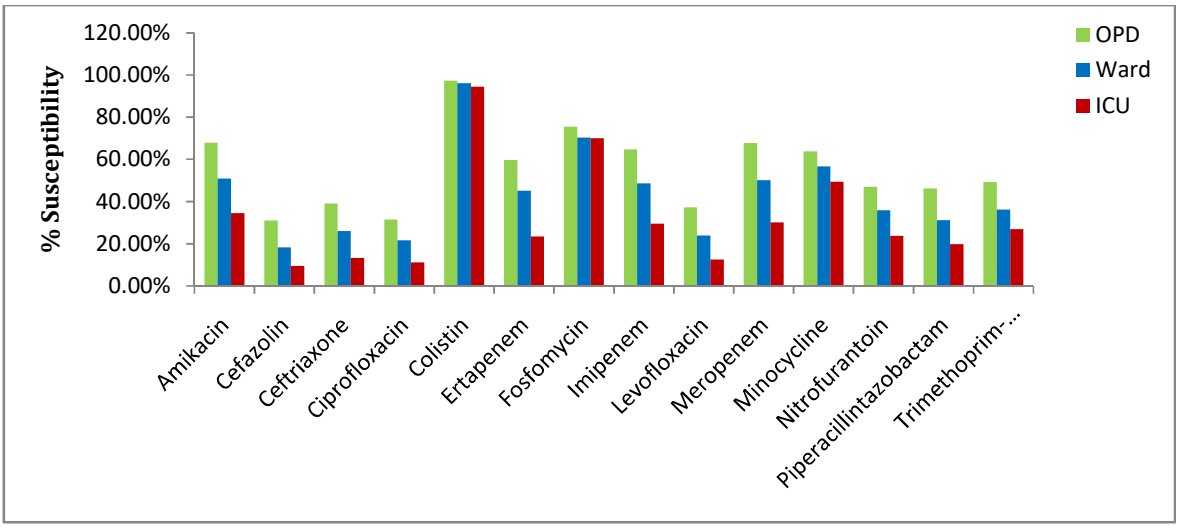


Figure 2.9: Susceptibility pattern of *Klebsiella pneumoniae* from urine

Table 2.15: % Susceptibility of *Pseudomonas aeruginosa* isolates from urine

	Pseudomonas aeruginosa		
	OPD n=595	Ward n=808	ICU n=191
Amikacin	360 / 593 (60.7%)	388 / 810 (47.9%)	70 / 192 (36.5%)
Cefepime	322 / 545 (59.1%)	311 / 748 (41.6%)	45 / 177 (25.4%)
Ceftazidime	305 / 589 (51.8%)	304 / 800 (38%)	39 / 185 (21.1%)
Ciprofloxacin	256 / 593 (43.2%)	269 / 803 (33.5%)	43 / 188 (22.9%)
Colistin	356 / 373 (95.4%)	482 / 503 (95.8%)	144 / 148 (97.3%)
Gentamicin	278 / 511 (54.4%)	298 / 650 (45.8%)	64 / 166 (38.6%)
Imipenem	355 / 590 (60.2%)	398 / 803 (49.6%)	49 / 187 (26.2%)
Levofloxacin	185 / 499 (37.1%)	217 / 654 (33.2%)	33 / 155 (21.3%)
Meropenem	373 / 591 (63.1%)	419 / 798 (52.5%)	58 / 189 (30.7%)
Piperacillin-tazobactam	393 / 588 (66.8%)	440 / 803 (54.8%)	69 / 191 (36.1%)
Tobramycin	127 / 210 (60.5%)	134 / 279 (48%)	26 / 84 (31%)

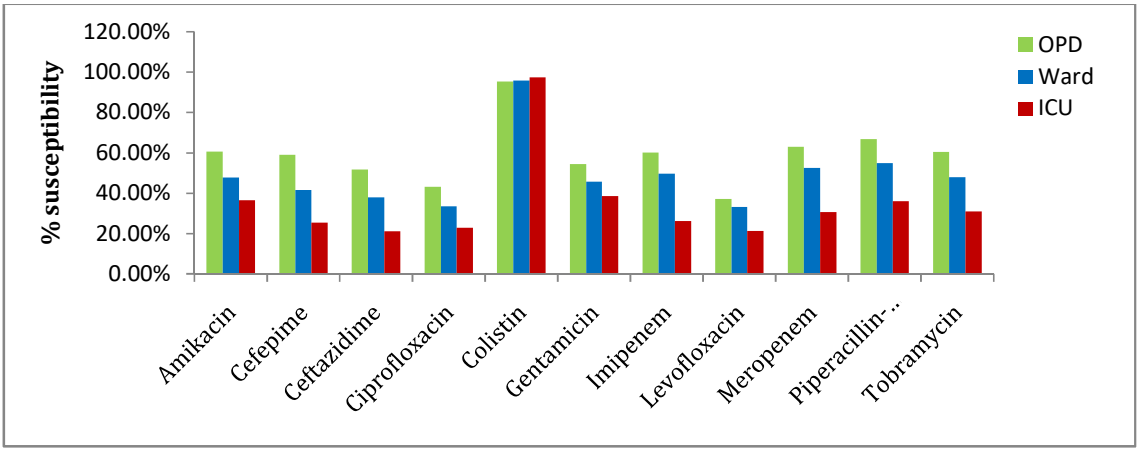


Figure 2.10: Susceptibility pattern of *Pseudomonas aeruginosa* from urine

Table 2.16: % Susceptibility of *Enterococcus faecalis* isolates from urine

	Enterococcus faecalis		
	OPD n=574	Ward n=693	ICU n=95
Ampicillin	391 / 509 (76.8%)	318 / 586 (54.3%)	49 / 87 (56.3%)
Ciprofloxacin	195 / 547 (35.6%)	137 / 667 (20.5%)	16 / 91 (17.6%)
Fosfomycin	299 / 351 (85.2%)	366 / 486 (75.3%)	48 / 68 (70.6%)
Gentamicin_HL	286 / 438 (65.3%)	283 / 565 (50.1%)	38 / 80 (47.5%)
Linezolid	535 / 553 (96.7%)	666 / 687 (96.9%)	92 / 93 (98.9%)
Nitrofurantoin	522 / 554 (94.2%)	563 / 674 (83.5%)	74 / 89 (83.1%)
Penicillin	114 / 169 (67.5%)	67 / 204 (32.8%)	17 / 35 (48.6%)
Teicoplanin	528 / 544 (97.1%)	621 / 657 (94.5%)	87 / 94 (92.6%)
Vancomycin	546 / 563 (97%)	656 / 689 (95.2%)	86 / 95 (90.5%)

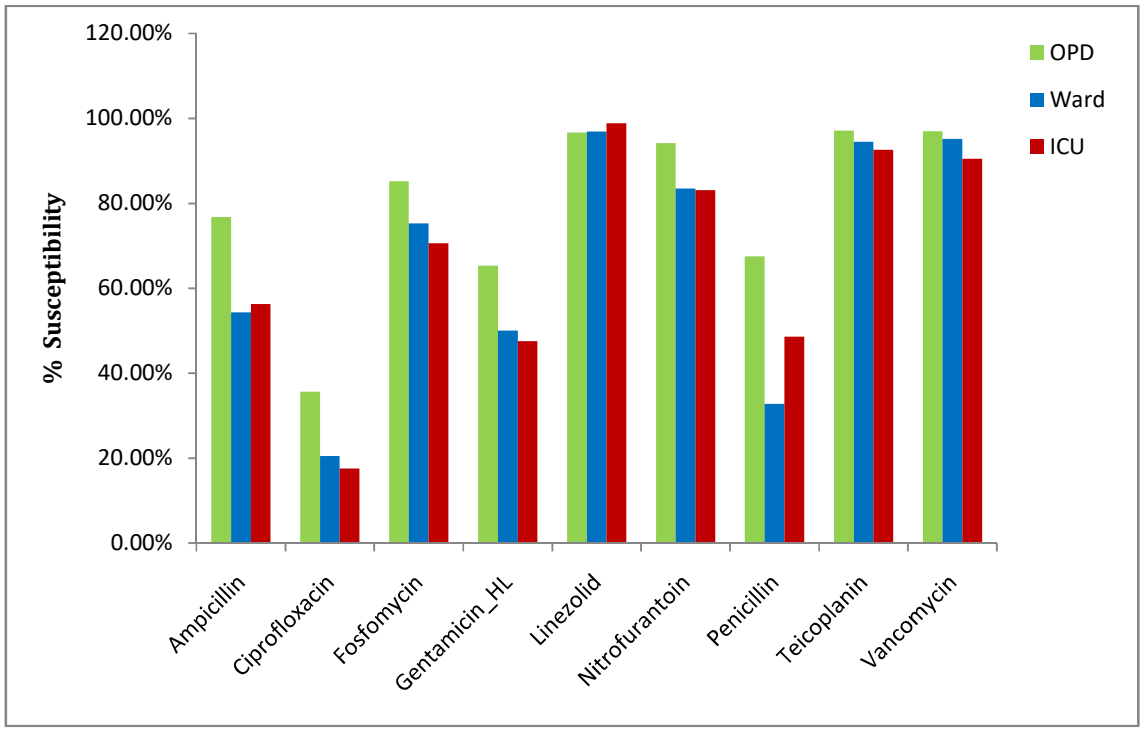


Figure 2.11: Susceptibility pattern of *Enterococcus faecalis* from urine

Table 2.17: % Susceptibility of *Enterococcus faecium* isolates from urine

	Enterococcus faecium		
	OPD n=197	Ward n=596	ICU n=145
Ampicillin	59 / 179 (33%)	68 / 516 (13.2%)	11 / 120 (9.2%)
Ciprofloxacin	42 / 188 (22.3%)	65 / 560 (11.6%)	12 / 137 (8.8%)
Fosfomycin	100 / 124 (80.6%)	181 / 253 (71.5%)	34 / 46 (73.9%)
Gentamicin_HL	94 / 172 (54.7%)	189 / 493 (38.3%)	37 / 95 (38.9%)
Linezolid	185 / 195 (94.9%)	541 / 583 (92.8%)	119 / 143 (83.2%)
Nitrofurantoin	119 / 190 (62.6%)	282 / 562 (50.2%)	37 / 136 (27.2%)
Penicillin	6 / 44 (13.6%)	15 / 156 (9.6%)	4 / 53 (7.5%)
Teicoplanin	162 / 188 (86.2%)	444 / 560 (79.3%)	85 / 137 (62%)
Vancomycin	164 / 196 (83.7%)	477 / 590 (80.8%)	91 / 144 (63.2%)

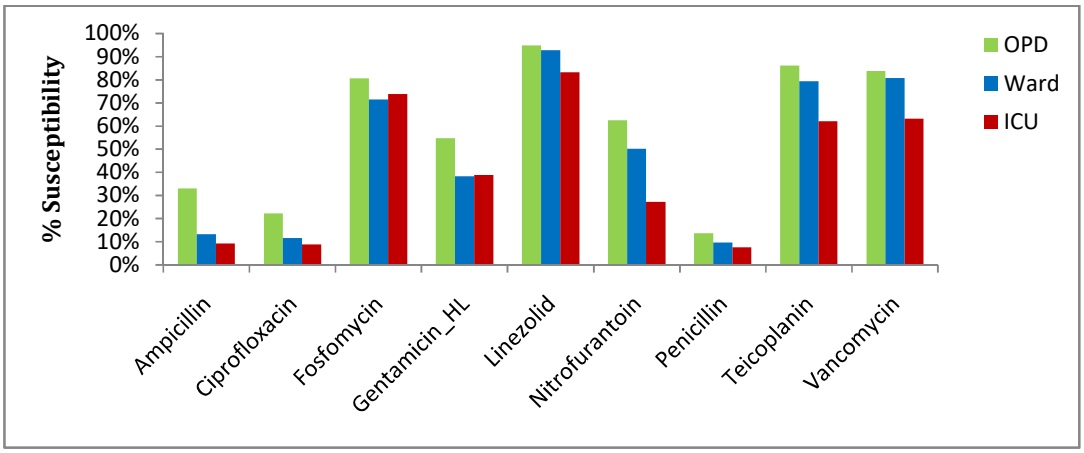


Figure 2.12: Susceptibility pattern of *Enterococcus faecium* from urine

Pus/Exudates

Table 2.18: % Susceptibility of *E.coli* isolates from Pus/exudates

	Escherichia coli		
	OPD n=622	Ward n=1248	ICU n=164
Amikacin	493 / 619 (79.6%)	926 / 1243 (74.5%)	126 / 164 (76.8%)
Ceftriaxone	31 / 129 (24%)	50 / 397 (12.6%)	2 / 57 (3.5%)
Ciprofloxacin	90 / 619 (14.5%)	131 / 1243 (10.5%)	13 / 164 (7.9%)
Colistin	194 / 196 (99.0%)	455 / 460 (98.9%)	84 / 86 (97.7%)
Ertapenem	346 / 515 (67.2%)	577 / 1032 (55.9%)	65 / 139 (46.8%)
Fosfomycin	31 / 34 (91.2%)	30 / 30 (100%)	1 / 1 (100%)
Imipenem	446 / 621 (71.8%)	751 / 1237 (60.7%)	85 / 164 (51.8%)
Levofloxacin	92 / 393 (23.4%)	102 / 786 (13%)	8 / 121 (6.6%)
Meropenem	481 / 617 (78%)	819 / 1235 (66.3%)	96 / 164 (58.5%)
Minocycline	66 / 82 (80.5%)	158 / 228 (69.3%)	27 / 36 (75%)
Nitrofurantoin	4 / 7 (-)	18 / 21 (-)	0 / 0 (-)
Piperacillin-tazobactam	281 / 619 (45.4%)	444 / 1241 (35.8%)	36 / 164 (22%)
Trimethoprim-sulfamethoxazole	20 / 60 (33.3%)	45 / 133 (33.8%)	6 / 11 (54.5%)

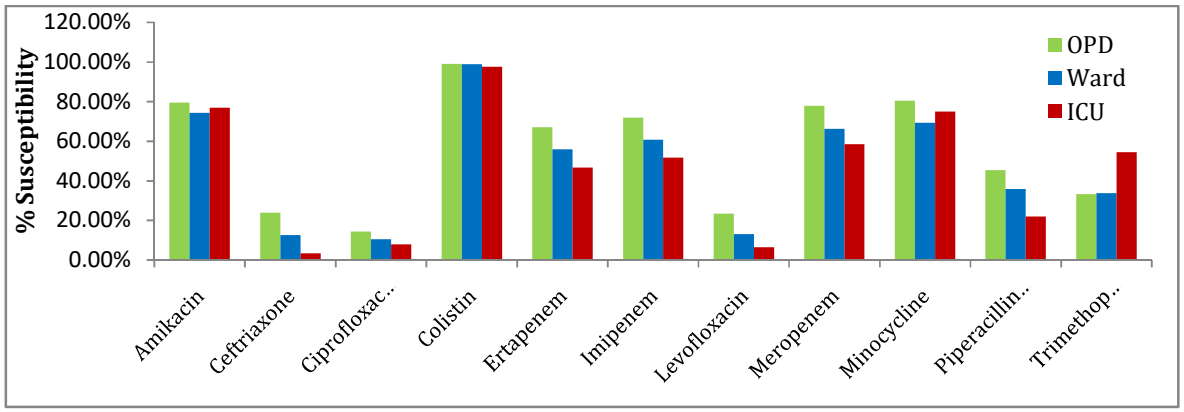


Figure 2.13: Susceptibility pattern of *E. coli* from Pus/exudates samples

Table 2.19: % Susceptibility of *S. aureus* isolates from Pus/exudates

	Staphylococcus aureus		
	OPD n=1196	Ward n=866	ICU n=79
Cefoxitin	696 / 1154 (60.3%)	439 / 805 (54.5%)	30 / 73 (41.1%)
Ciprofloxacin	317 / 1187 (26.7%)	200 / 861 (23.2%)	22 / 80 (27.5%)
Clindamycin	950 / 1199 (79.2%)	686 / 868 (79%)	50 / 80 (62.5%)
Daptomycin	55 / 60 (91.7%)	53 / 55 (96.4%)	5 / 5 (-)
Erythromycin	455 / 1188 (38.3%)	333 / 866 (38.5%)	23 / 79 (29.1%)
Linezolid	1169 / 1194 (97.9%)	835 / 862 (96.9%)	75 / 78 (96.2%)
Oxacillin	160 / 290 (55.2%)	102 / 218 (46.8%)	4 / 20 (-)
Teicoplanin	335 / 337 (99.4%)	231 / 231 (100%)	23 / 23 (-)
Tetracycline	992 / 1163 (85.3%)	704 / 824 (85.4%)	59 / 75 (78.7%)
Tigecycline	294/ 294 (100%)	200 / 200 (100%)	21 / 21 (-)
Trimethoprim-sulfamethoxazole	862 / 1185 (72.7%)	612 / 843 (72.6%)	55 / 77 (71.4%)
Vancomycin	1087 / 1096 (99.2%)	717 / 724 (99%)	60 / 62 (96.8%)

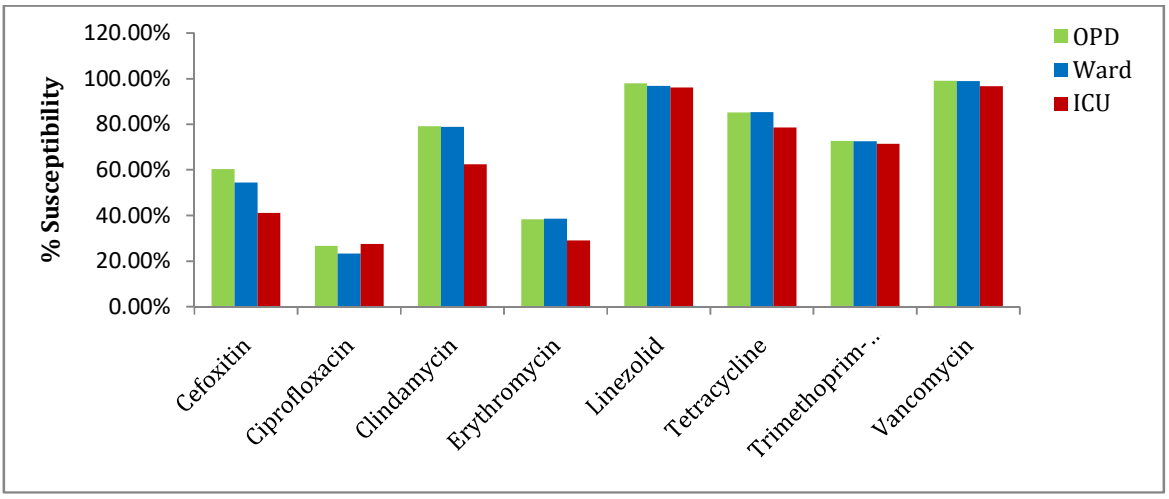


Figure 2.14: Susceptibility pattern of *S. aureus* from Pus/exudates samples

Table 2.20 % Susceptibility of *K. pneumoniae isolates* from Pus/exudates

	Klebsiella pneumoniae		
	OPD n=390	Ward n=779	ICU n=157
Amikacin	247 / 387 (63.8%)	355 / 778 (45.6%)	48 / 157 (30.6%)
Ceftriaxone	30 / 92 (32.6%)	45 / 221 (20.4%)	8 / 55 (14.5%)
Ciprofloxacin	124 / 389 (31.9%)	152 / 777 (19.6%)	20 / 156 (12.8%)
Colistin	141 / 145 (97.2%)	314 / 318 (98.7%)	86 / 88 (97.7%)
Ertapenem	167 / 308 (54.2%)	216 / 607 (35.6%)	28 / 137 (20.4%)
Fosfomycin	17 / 25 (68%)	11 / 14 (78.6%)	1 / 3 (33.3%)
Imipenem	235 / 390 (60.3%)	315 / 775 (40.6%)	44 / 157 (28%)
Levofloxacin	77 / 227 (33.9%)	89 / 476 (18.7%)	15 / 111 (13.5%)
Meropenem	246 / 388 (63.4%)	333 / 777 (42.9%)	40 / 156 (25.6%)
Minocycline	65 / 88 (73.9%)	98 / 160 (61.3%)	26 / 40 (65%)
Piperacillin-tazobactam	155 / 388 (39.9%)	187 / 778 (24%)	17 / 156 (10.9%)
Trimethoprim-sulfamethoxazole	18 / 41 (43.9%)	27 / 75 (36%)	6 / 15 (40%)

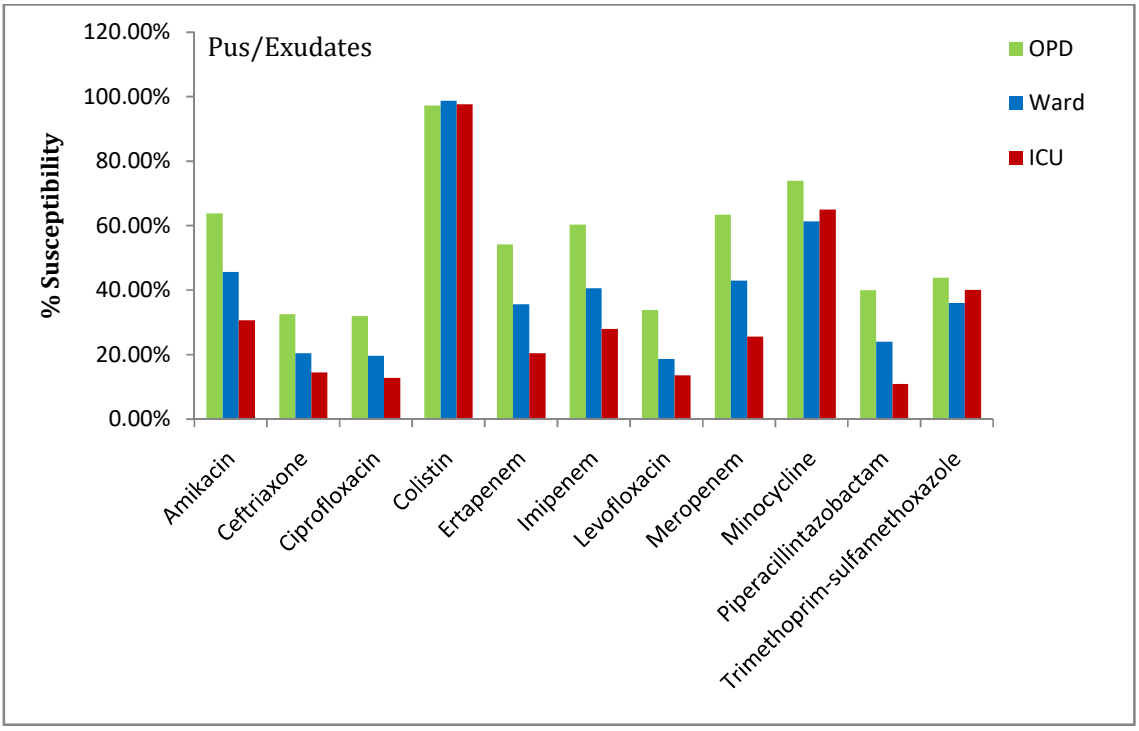


Figure 2.15: Susceptibility pattern of *Klebsiella pneumoniae* from Pus/exudates samples

Table 2.21: % Susceptibility of *A. baumannii* isolates from Pus/exudates

	Acinetobacter baumannii		
	OPD n=157	OPD n=157	OPD n=157
Amikacin	36 / 157 (22.9%)	51 / 363 (14%)	7 / 85 (8.2%)
Cefepime	35 / 157 (22.3%)	23 / 374 (6.1%)	3 / 87 (3.4%)
Ceftazidime	29 / 157 (18.5%)	17 / 375 (4.5%)	2 / 86 (2.3%)
Colistin	130 / 133 (97.7%)	285 / 299 (95.3%)	61 / 64 (95.3%)
Imipenem	35 / 157 (22.3%)	35 / 376 (9.3%)	3 / 87 (3.4%)
Levofloxacin	35 / 155 (22.6%)	40 / 357 (11.2%)	5 / 84 (6%)
Meropenem	40 / 157 (25.5%)	47 / 376 (12.5%)	8 / 87 (9.2%)
Minocycline	108 / 152 (71.1%)	213 / 329 (64.7%)	42 / 75 (56%)
Piperacillin-tazobactam	38 / 157 (24.2%)	43 / 376 (11.4%)	3 / 87 (3.4%)

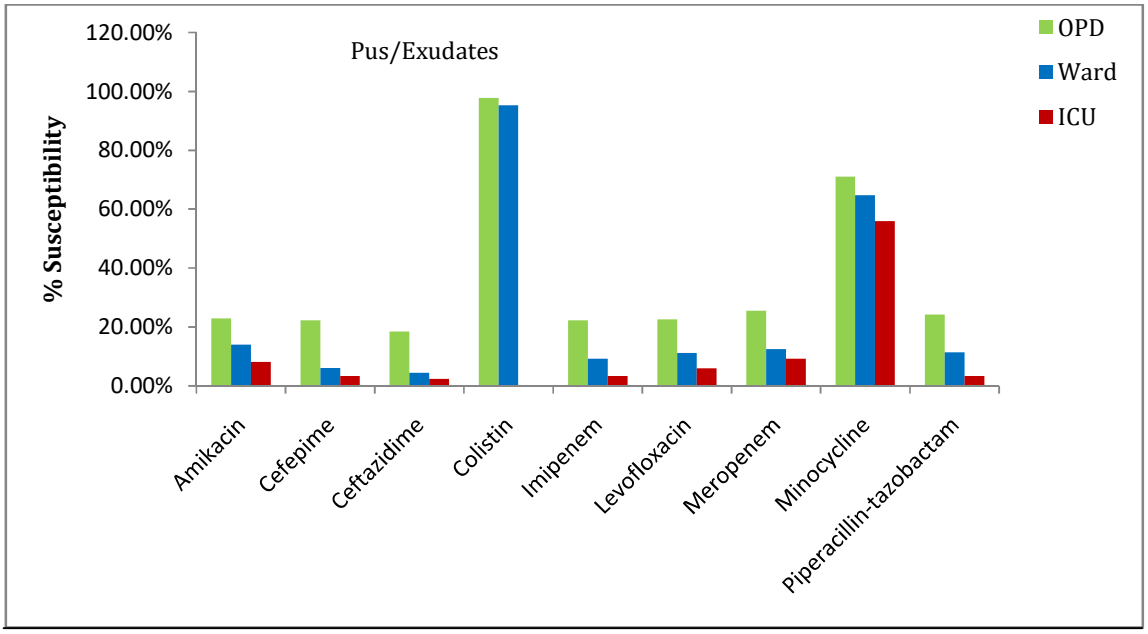


Figure 2.16: Susceptibility pattern of *A. baumannii* from Pus/exudates samples

Table 2.22: % Susceptibility of *P. aeruginosa* isolates from Pus/exudates

	Pseudomonas aeruginosa		
	OPD n=639	OPD n=639	OPD n=639
Amikacin	482 / 634 (76%)	376 / 536 (70.1%)	52 / 87 (59.8%)
Cefepime	424 / 588 (72.1%)	321 / 532 (60.3%)	36 / 87 (41.4%)
Ceftazidime	446 / 634 (70.3%)	297 / 532 (55.8%)	38 / 86 (44.2%)
Ciprofloxacin	379 / 635 (59.7%)	278 / 538 (51.7%)	33 / 87 (37.9%)
Colistin	521 / 530 (98.3%)	373 / 385 (96.9%)	63 / 64 (98.4%)
Gentamicin	326 / 469 (69.5%)	238 / 369 (64.5%)	31 / 68 (45.6%)
Imipenem	479 / 635 (75.4%)	349 / 537 (65%)	44 / 86 (51.2%)
Levofloxacin	365 / 599 (60.9%)	254 / 501 (50.7%)	34 / 84 (40.5%)
Meropenem	508 / 633 (80.3%)	368 / 538 (68.4%)	42 / 87 (48.3%)
Piperacillin-tazobactam	513 / 633 (81%)	378 / 534 (70.8%)	45 / 87 (51.7%)
Tobramycin	299 / 401 (74.6%)	268 / 369 (72.6%)	31 / 57 (54.4%)

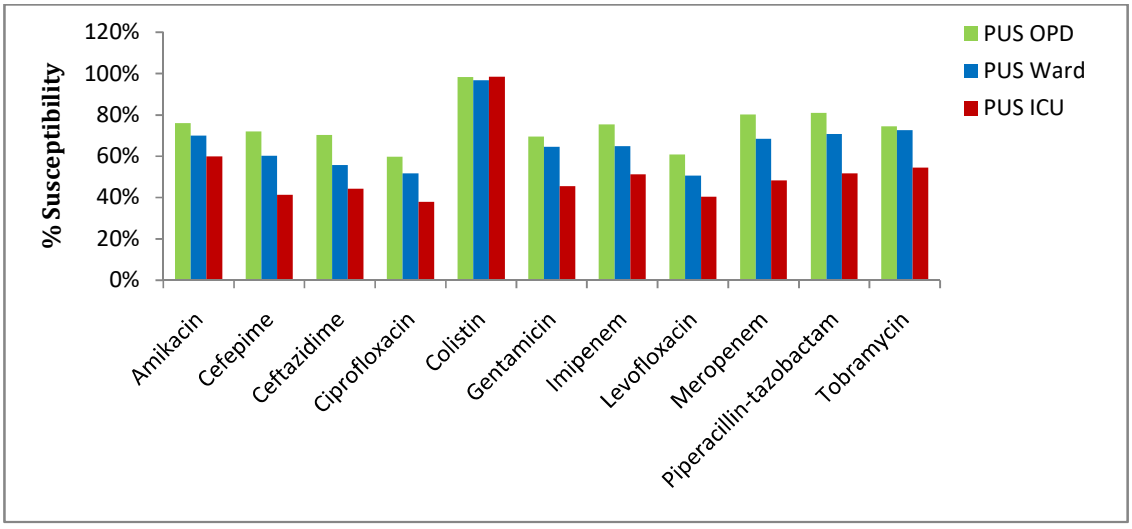


Figure 2.17: Susceptibility pattern of *P. aeruginosa* from Pus/exudates

Faecal samples

Table 2.23: % Susceptibility of *Salmonella spp faecal* isolates from faecal samples

	Salmonella spp. Faecal	
	OPD n=30	Ward n=75
Ampicillin	22 / 30 (73.3%)	59 / 75 (78.7%)
Chloramphenicol	28 / 30 (93.3%)	75 / 75 (100%)
Ciprofloxacin	14 / 30 (46.7%)	47 / 75 (62.7%)
Trimethoprim-sulfamethoxazole	26 / 30 (86.7%)	65 / 75 (86.7%)

Table 2.24: % Susceptibility of *Aeromonas spp*. isolates from faecal samples

	Aeromonas spp.	
	OPD n=86	Ward n=74
Cefixime	71 / 86 (82.6%)	58 / 74 (78.4%)
Ciprofloxacin	6 / 86 (7%)	8 / 74 (10.8%)
Imipenem	54 / 86 (62.8%)	47 / 74 (63.5%)
Meropenem	75 / 86 (87.2%)	59 / 74 (79.7%)
Tetracycline	76 / 86 (88.4%)	62 / 74 (83.8%)

Table 2.25: % Susceptibility of *Escherichia coli Diarrhoeagenic* isolates from faecal samples

	Escherichia coli Diarrhoeagenic	
	OPD n=146	Ward n=43
Ampicillin	3 / 146 (2.1%)	3 / 43 (7%)
Cefixime	5 / 146 (3.4%)	1 / 43 (2.3%)
Nalidixic acid	14 / 126 (11.1%)	1 / 38 (2.6%)
Trimethoprim-sulfamethoxazole	42 / 143 (29.4%)	14 / 43 (32.6%)

Table 2.26: % Susceptibility of *Shigella flexneri isolates* from faecal

AMA	*Shigella flexneri*	
	OPD n=29	Ward n=21
Ampicillin	*2 / 29	4 / 21
Azithromycin	0 / 1	8 / 8
Cefixime	13 / 28	12 / 19
Ciprofloxacin	0 / 3	0 / 10
Nalidixic acid	0 / 5	0 / 3
Trimethoprim-sulfamethoxazole	17 / 28	9 / 21

Table 2.27: % Susceptibility of Salmonella Typhimurium Faecal isolates from faecal

	Salmonella Typhimurium Faecal	
	OPD n=17	Ward n=35
Ampicillin	15 / 17	32 / 35 (91.4%)
Chloramphenicol	17 / 17	33 / 35 (94.3%)
Ciprofloxacin	8 / 17	14 / 36 (38.9%)
Trimethoprim-sulfamethoxazole	16 / 17	31 / 35 (88.6%)

Chapter 3. Enterobacterlaes

Species wise susceptibility of Enterobacterales isolated from all specimens except urine and faeces.

In the year 2022, a total of 52692 significant clinical isolates belonging to various genera and species of family *Enterobacterales* from 21 participating centers were included in the analysis. The isolates belonged to various specimens including blood (8965), sterile body fluids including cerebrospinal fluid (431), pus (1935), wound swabsand aspirates (3446) and respiratory tract specimens (6780).

Significant clinical isolates from all specimens (except urine and faeces) were tested for susceptibility to 10 antibiotics including aminoglycoside (amikacin), cephalosporins (cefotaxime and ceftazidime), fluoroquinolones (ciprofloxacin and levofloxacin), beta lactam and beta-lactamase inhibitor combination (piperacillin-tazobactam), carbapenems (imipenem, meropenem and ertapenem) and polymyxin (colistin). Susceptibility was tested following CLSI guidelines using disc diffusion or automated systems, except colistin where micro-broth dilution test was used.

Susceptibilities of different species to the antibiotics are presented in table 3.1, figure 3.1 and figure 3.2. Colistin susceptibility (tested in recommended species) overall was 95% (marginally lower than previous 4 years); *Citrobacter koseri* showed 100% susceptibility followed by *Klebsiella oxytoca* (99%), and *Escherichia coli* (97%). *K. pneumoniae* and *Enterobacter cloacae* showed 94% and 92% susceptibility respectively.

Table 3.1: Species wise susceptibility of Enterobacterales isolated from all specimens except urine and faeces

	Pip-taz		Cefotax		Ceftazid		Ertapen		Imipen		Meropen		Colistin		Amikacin		Ciproflox		Levoflox	
	n	%S	n	%S	n	%S	n	%S	n	%S	n	%S	n	%S	n	%S	n	%S	n	%S
C. freundii	115	43	96	33	69	28	99	65	115	55	112	71	32	94	116	71	114	41	56	59
C. koseri	391	61	364	55	294	51	315	73	381	73	388	78	37	100	382	82	390	62	221	48
Citrobacter spp	139	43	101	50	58	40	88	81	104	68	123	74	46	80	125	74	135	50	36	44
K. oxytoca	359	26	324	24	301	24	296	46	349	49	353	56	165	99	352	62	356	29	270	31
K. pneumoniae	14953	22	12919	21	9500	19	9845	40	14474	42	14619	44	7008	94	14888	46	14827	20	6782	25
Klebsiella spp	223	28	219	42	199	43	219	66	130	62	221	66	31	90	195	67	195	47	140	46
Enterobacter cloacae	1533	48	1232	48	813	48	945	73	1502	69	1466	72	626	92	1518	77	1525	50	459	51
Enterobacter spp	319	38	251	26	225	29	176	77	266	71	296	78	65	86	306	72	319	52	116	59
K. (E.) aerogenes	129	49	114	35	107	41	46	59	126	71	128	81	28		127	79	125	37	70	59
P. mirabilis	1492	72	1248	49	1120	47	703	79	1436	63	1476	84			1474	67	1483	31	601	28
P. rettgeri	90	40	67	34	58	31	60	45	87	39	90	51			90	51	90	31	44	23
P. stuartii	180	45	122	39	126	31	69	57	173	45	172	62			179	57	180	32	71	24
E. coli	14729	35	12718	18	8988	19	9965	63	13921	67	14304	70	5597	97	14477	77	14564	12	6199	16
M. morganii	445	68	385	60	277	57	242	88	401	64	433	86			432	85	442	34	114	39
S. marcescens	346	53	327	50	302	47	252	80	385	72	435	77			447	78	448	61	220	64
Overall	35443	**33**	30487	**24**	22437	**24**	23320	**55**	33850	**56**	34616	**60**	13635	**95**	35108	**63**	35193	**21**	15399	**24**

** 'n' denotes the denominator*

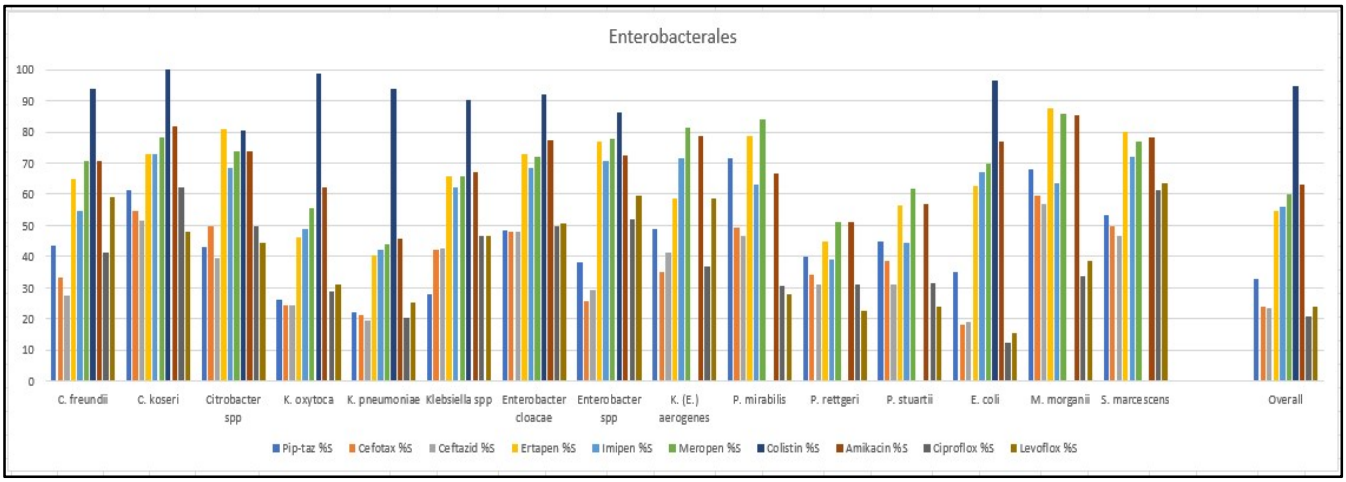


Figure 3.1: Species wise susceptibility of Enterobacterales isolated from of all specimens except urine and faeces.

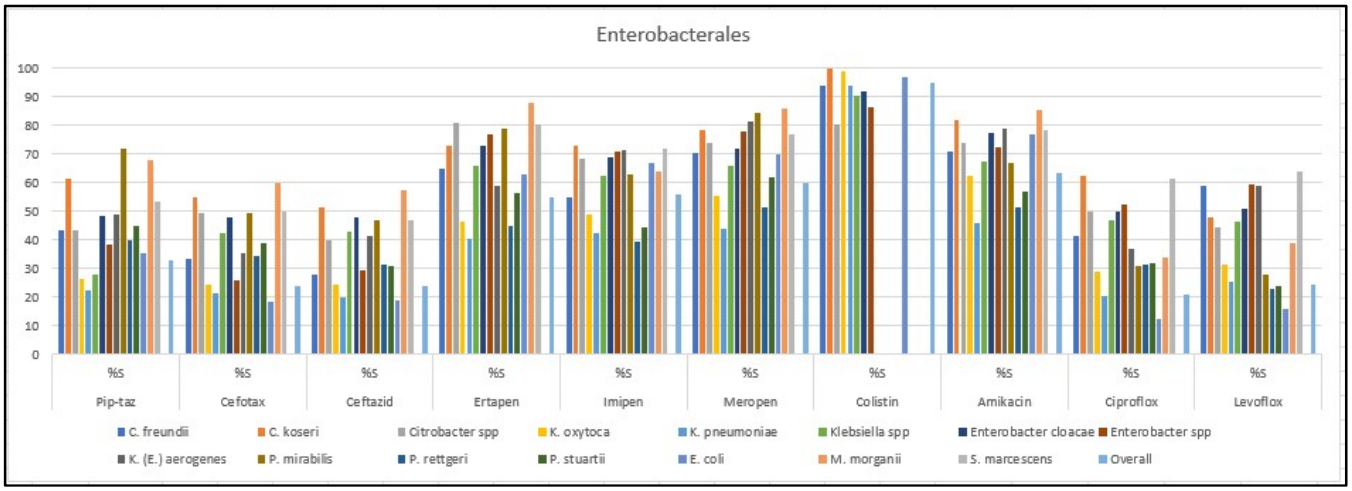


Figure 3.2: Antibiotic wise susceptibility of species of Enterobacterales isolated from of all specimens except urine and faeces.

Out of the carbapenems, overall, meropenem showed 60% susceptibility followed by ertapenem (56%) and imipenem (55%). *M. morganii* (86%), *P. mirabilis* (84%), and *K. aerogenes* (81%) showed highest susceptibility to meropenem followed by *C. koseri* (78%), *Enterobacter* spp. (78%), *S. marcescens* (77%), *Citrobacter* spp (74%), *E. cloacae* (72%), *C. freundii* (71%), and *E. coli* (70%). Least susceptibility was shown by *K. pneumoniae* (44%) and *P. rettgeri* (51%).

Piperacillin-tazobactam susceptibility was overall 33% (significantly lower than last year). Maximum susceptibility was found in *Proteus mirabilis* (72%), *Morganella morganii* (68%), *Citrobacter koseri* (61%) and *Serratia marcescens* (53%). *C. freundii,*

Citrobacter spp., *E. cloacae, K. aerogenes*, *P. stuartii*, and *P. rettgeri* showed susceptibilities between 40% and 50% with *K. pneumoniae* (22%) and *E. coli* (35%) showing the least.

Overall, less than one fourth (21-24%) of isolates showed fluoroquinolone susceptibility. *S. marcescens* (64%) showed maximum susceptibility to levofloxacin followed by *C. freundii*, *Enterobacter* spp, *K. aerogenes* (59% each) and *E. cloacae* (51%). *E. coli* showed the lowest susceptibility to levofloxacin (16%). Ciprofloxacin and levofloxacin showed similar susceptibility for most species tested.

Third generation cephalosporins, cefotaxime and ceftazidime showed comparable susceptibility of 24% of isolates overall. *M. morganii* (60%), *C. koseri* (55%), and *S. marcescens* (50%) showed susceptibility in half of the isolates or more. Overall, two thirds (63%) of the isolates were susceptible to amikacin. *M. morganii* (85%), followed by *C. koseri* (82%), *K. aerogenes* (79%), *S. marcescens* (78%), *E. coli* (77%), and *E. cloacae* (77%) showed better susceptibility than other species. *K. pneumoniae* (46%) showed the lowest susceptibility of all species tested.

Comparison of susceptibility of isolates from OPD, ward and ICU

Overall, for all drugs tested; *Escherichia coli*, *Klebsiella pneumoniae*, *Citrobacter koseri* and *Enterobacter cloacae* isolated from out-patients were more susceptible than those from in-patients and among in-patients, isolates from wards were more susceptible than those from ICU (Tables 3.2 to 3.5, Figures 3.3 to 3.6). The differences were more marked for *E. coli*, and *K. pneumoniae* and *Enterobacter cloacae*, and *Citrobacter koseri*.

Table 3.2: Comparison of susceptibility of *Escherichia coli* isolated from OPD, ward and ICU

	OPD		Ward		ICU		Total	
	n	%S	n	%S	n	%S	n	%S
Amikacin	3244	81	9273	77	1969	72	14486	77
Cefotaxime	2796	22	8248	17	1674	16	12718	18
Ceftazidime	2037	27	5879	17	1071	15	8987	19
Ciprofloxacin	3233	15	9370	12	1961	11	14564	12
Colistin	1247	95	3514	97	836	98	5597	97
Ertapenem	2270	71	6240	61	1455	56	9965	63
Imipenem	3078	74	8961	65	1882	60	13921	66
Levofloxacin	1407	21	4039	14	753	13	6199	16
Meropenem	3094	78	9246	69	1964	62	14304	70
Pip-taz	3253	41	9493	33	1983	34	14729	35

'n' denotes the denominator

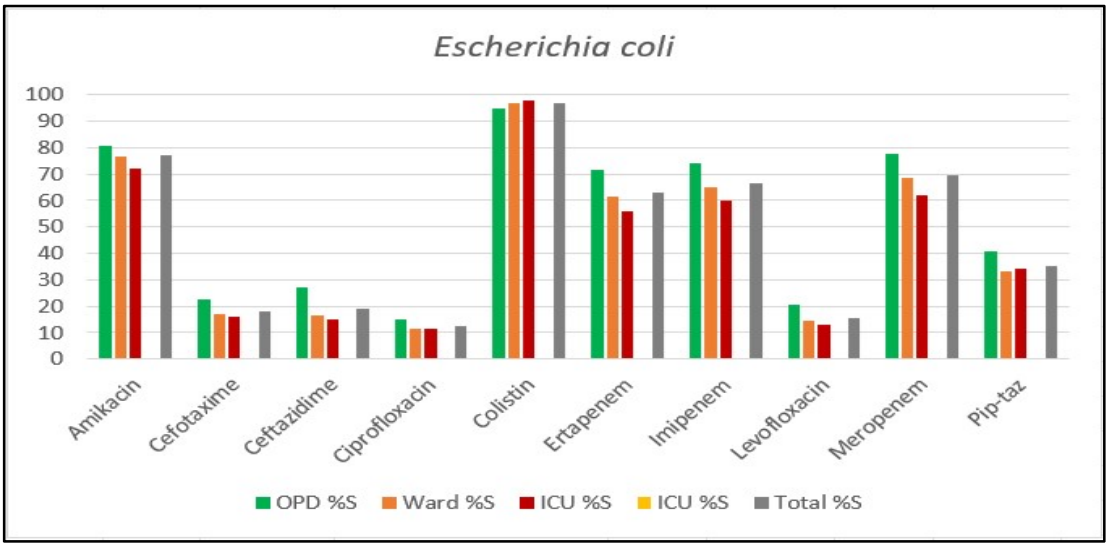


Figure 3.3: Comparison of susceptibility of *Escherichia coli* isolated from OPD, ward and ICU

Table 3.3: Comparison of susceptibility of *Klebsiella pneumonia* isolated from OPD, ward and ICU

	OPD		Ward		ICU		Total	
	n	%S	n	%S	n	%S	n	%S
Amikacin	3000	61	8037	46	3850	34	14887	46
Cefotaxime	2633	36	6948	20	3337	12	12918	21
Ceftazidime	2013	35	5344	17	2242	10	9599	19
Ciprofloxacin	2989	33	8030	19	3807	13	14826	20
Colistin	1286	94	3724	94	1998	93	7008	94
Ertapenem	1983	59	5188	40	2673	26	9844	40
Imipenem	2900	57	7841	42	3732	30	14473	42
Levofloxacin	1414	44	3640	23	1727	15	6781	25
Meropenem	2895	61	7890	44	3833	30	14618	44
Pip-taz	3004	30	8088	22	3860	15	14952	22

'n' denotes the denominator

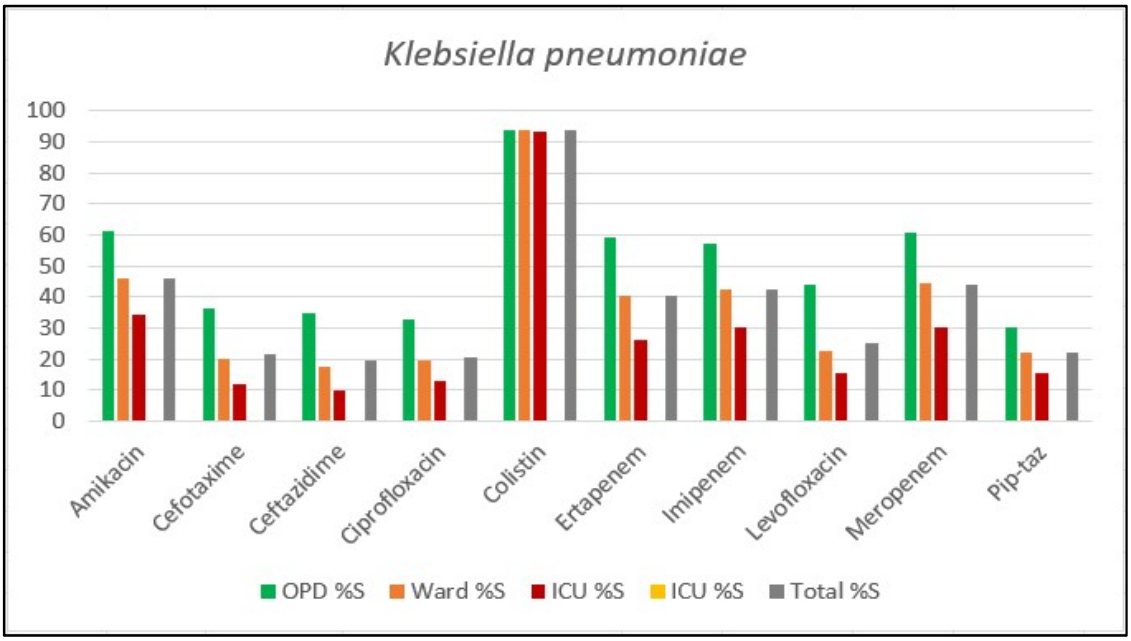


Figure 3.4: Comparison of susceptibility of *Klebsiella pneumoniae* isolated from OPD, ward and ICU

Table 3.4: Comparison of susceptibility of *Citrobacter koseri* isolated from OPD, ward and ICU

	OPD		Ward		ICU		Total	
	n	%S	n	%S	n	%S	n	%S
Amikacin	116	92	153	83	113	69	382	82
Cefotaxime	110	76	142	56	112	32	364	55
Ceftazidime	74	76	117	52	103	33	294	51
Ciprofloxacin	118	81	157	61	115	45	390	62
Ertapenem	90	92	120	72	105	58	315	73
Imipenem	116	89	152	74	113	55	381	73
Levofloxacin	46	65	82	44	93	43	221	48
Meropenem	117	92	156	79	115	62	388	78
Pip-taz	117	80	159	57	115	48	391	61

'n' denotes the denominator

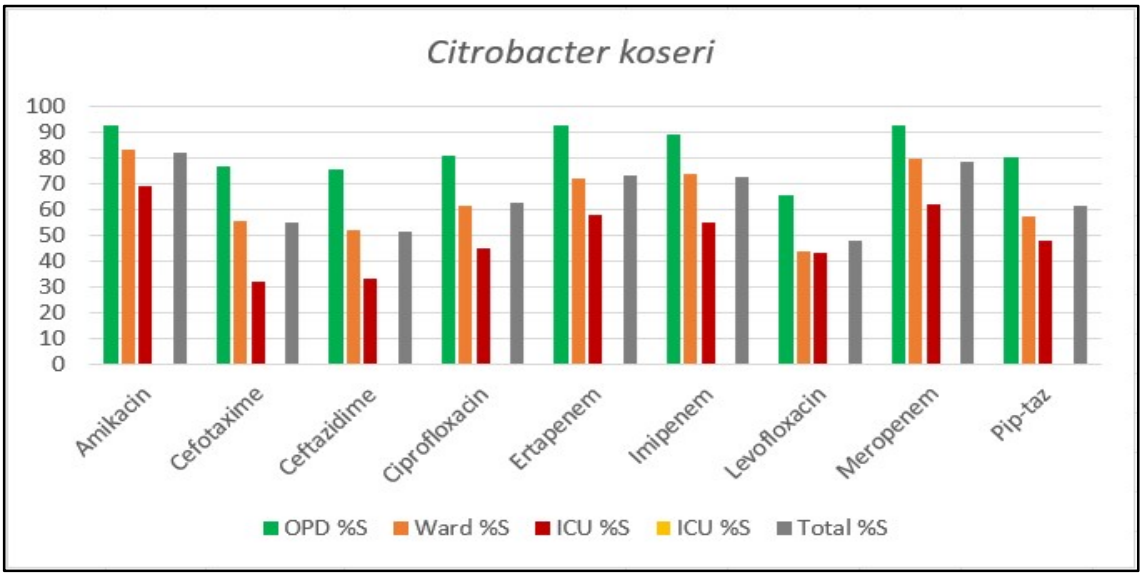


Figure 3.5: Comparison of susceptibility of *Citrobacter koseri* isolated from OPD, ward and ICU

Table 3.5: Comparison of susceptibility of *Enterobacter cloacae* isolated from OPD, ward and ICU

	OPD		Ward		ICU		Total	
	n	%S	n	%S	n	%S	n	%S
Amikacin	417	87	861	75	240	71	1518	77
Cefotaxime	364	62	682	44	186	34	1232	48
Ceftazidime	225	66	477	43	111	32	813	48
Ciprofloxacin	421	63	865	46	239	41	1525	50
Ertapenem	265	82	535	69	145	70	945	73
Imipenem	409	82	854	65	239	58	1502	69
Levofloxacin	109	68	283	45	67	46	459	51
Meropenem	397	84	831	69	238	63	1466	72
Pip-taz	420	56	872	47	241	40	1533	48

'n' denotes the denominator

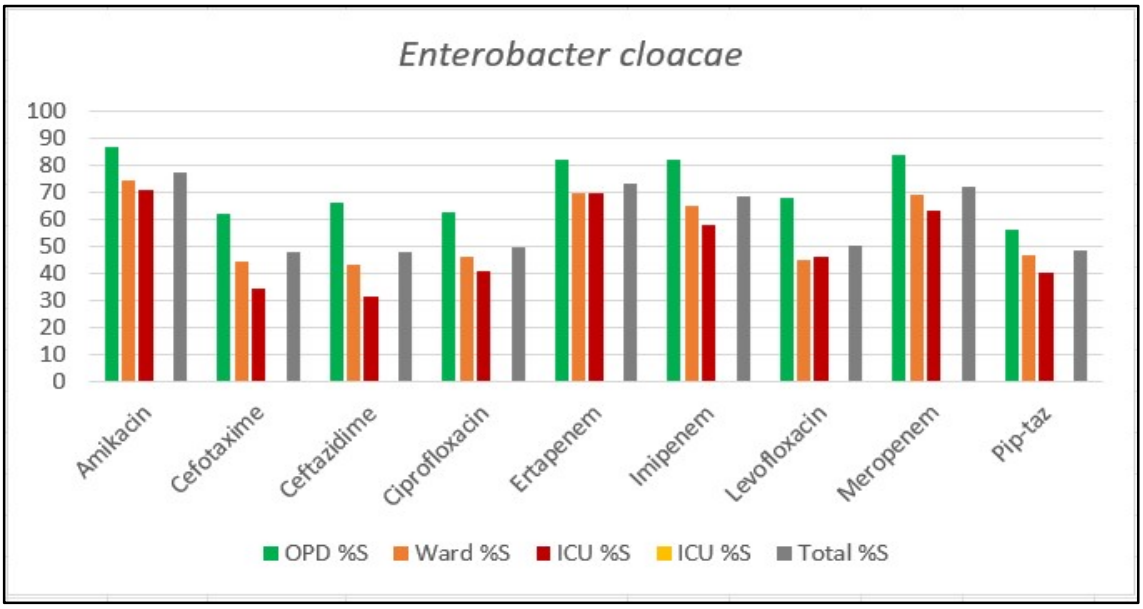


Figure 3.6: Comparison of susceptibility of *Enterobacter cloacae* isolated from OPD, ward and ICU

Susceptibility trends of various species over time

Over the last six years, imipenem susceptibility of *E. coli* dropped from 81% in 2017 to 66% in 2022 (table 3.6, figure 3.7) and that of *Klebsiella pneumoniae* dropped steadily from 59% in 2017 to 42% in 2022 (table 3.7, figure 3.8). There has been a modest and inconsistent drop in meropenem susceptibility for both *E. coli* and *K. pneumoniae*. In contrast, meropenem susceptibility improved from 66% to 74% for *Citrobacter* spp and from 70% to 78% for *Enterobacter* spp over the last five years. There was an increase in susceptibility of *Citrobacter* species to amikacin from 67% in 2017 to 74% in 2022 (table 3.8, figure 3.9). After an increase in susceptibility of *Enterobacter* species to ciprofloxacin from 53% in 2017 to 70% in 2021, it showed a steep fall to 52% in 2022 (Table 3.9, Figure 3.10). Susceptibility to other antibiotics didn't show much change over the last six years.

Table 3.6: Yearly susceptibility trend of *E. coli* isolated from all samples (except faeces and urine)

AMA	Year-2017	Year-2018	Year-2019	Year-2020	Year-2021	Year-2022
	Total n=6282	Total n=9187	Total n=13133	Total n=8198	Total n=13533	Total n=14728
Piperacillin-tazobactam	3424/6030 (56.8)	4857/8961 (54.2)	6620/12121 (54.6)	4211/7890 (53.4)	6126/12935 (47.4)	5170 / 14729 (35.10)
Cefazolin	*0/8	*2/6	*0/1	*0/4	*0/1	5/22 (22.7)
Cefotaxime	879/5747 (15.3)	1274/7817 (16.3)	1537/10646 (14.4)	1063/6835 (15.6)	1656/10613 (15.6)	2311 / 12718 (18.1)
Ceftazidime	1295/5513 (23.5)	1398/5956 (23.5)	1501/7540 (19.9)	943/5072 (18.6)	1220/6786 (18)	1697 / 8988 (18.8)
Ertapenem	3104/4605 (67.4)	4528/6877 (65.8)	6633/9335 (71.1)	4067/5729 (71)	5334/7933 (67.2)	6257 / 9965 (62.7)
Imipenem	4699/5773 (81.4)	6453/8874 (72.7)	6497/10254 (63.4)	5176/7191 (72)	7903/12338 (64.1)	9211 / 13921 (66.1)
Meropenem	4158/5678 (73.2)	5873/8404 (69.9)	9110/12167 (74.9)	5683/7499 (75.8)	8872/12774 (69.5)	9980 / 14304 (69.7)
Amikacin	4788/6048 (79.2)	7071/8912 (79.3)	9936/12549 (79.2)	6451/7935 (81.3)	10326/13209 (78.2)	11138 / 14477 (76.9)
Ciprofloxacin	1028/5368 (19.2)	1889/8451 (22.4)	2427/11700 (20.7)	1580/7092 (22.3)	2287/12013 (19)	1797 / 14564 (12.3)
Levofloxacin	140/889 (15.7)	600/3493 (17.2)	1145/6050 (18.9)	717/3762 (19.1)	866/5143 (16.8)	969 / 6199 (15.6)

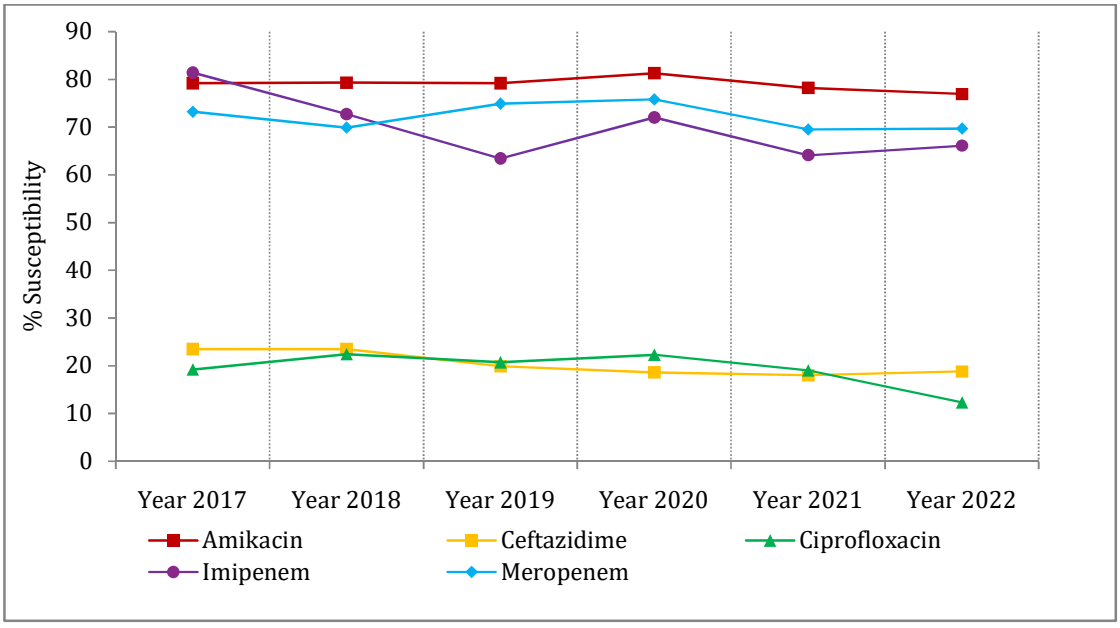


Figure 3.7: Yearly susceptibility trend of *E. coli* isolated from all samples (except faeces and urine)

Table 3.7: Yearly susceptibility trend of *Klebsiella pneumonia* isolated from all samples (except faeces and urine)

AMA	Year-2017	Year-2018	Year-2019	Year-2020	Year-2021	Year-2022
	Total n=5389	Total n=8394	Total n=13381	Total n=8932	Total n=13633	Total n=15008
Piperacillin-tazobactam	2207/5179 (42.6)	3256/8223 (39.6)	4872/12502 (39)	3165/8669 (36.5)	4393/13185 (33.3)	3300 / 14953 (22.0)
Cefazolin	*0/3	*0/0	*0/1	*0/3	*1/3	5/16 (31.3)
Cefotaxime	1109/5092 (21.8)	1577/7158 (22)	2400/11292 (21.3)	1472/7658 (19.2)	2217/10879 (20.4)	2754 / 12919 (21.3)
Ceftazidime	1320/4790 (27.6)	1488/5503 (27)	1985/7908 (25.1)	1147/5334 (21.5)	1452/7507 (19.3)	1852 / 9500 (19.4)
Ertapenem	2022/4456 (45.4)	3189/6667 (47.8)	4362/9650 (45.2)	2560/6255 (40.9)	3526/8298 (42.5)	3978 / 9845 (40.4)
Imipenem	3136/5360 (58.5)	4257/8223 (51.8)	5039/11031 (45.7)	3771/8392 (44.9)	5474/12660 (43.2)	6115 / 14474 (42.2)
Meropenem	2478/5147 (48.1)	3832/7591 (50.5)	6081/12164 (50)	3660/7771 (47.1)	5707/12678 (45)	6404 / 14619 (43.8)
Amikacin	2583/5286 (48.9)	4204/8276 (50.8)	6507/13018 (50)	4171/8828 (47.2)	6174/13451 (45.9)	6838 / 14888 (45.9)
Ciprofloxacin	1667/5213 (32)	2766/7688 (36)	4144/11560 (35.8)	2420/7218 (33.5)	3621/11712 (30.9)	3016 / 14827 (20.3)
Levofloxacin	254/898 (28.3)	967/3333 (29)	2596/7432 (34.9)	1391/4913 (28.3)	1830/6101 (30)	1712 / 6782 (25.2)

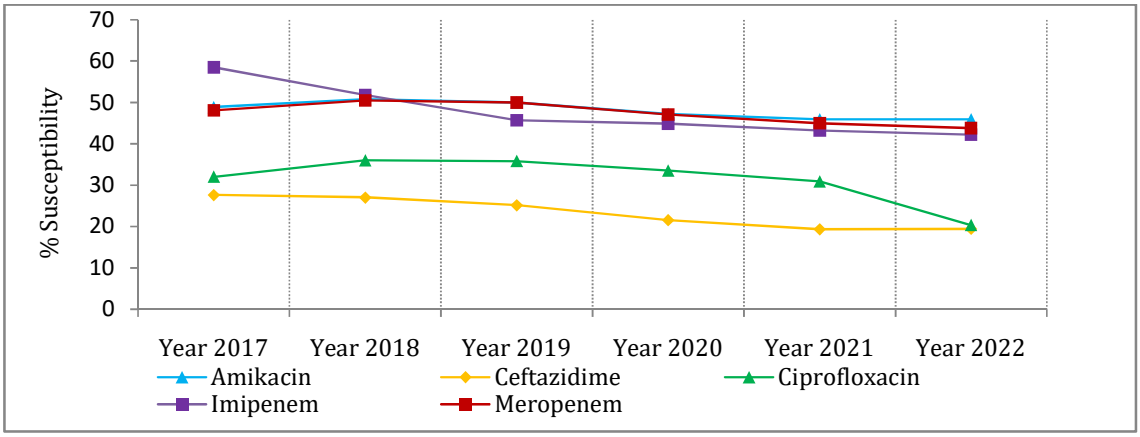


Figure 3.8: Yearly susceptibility trend of *Klebsiella pneumonia* isolated from all samples (except faeces and urine)

Table 3.8: Yearly susceptibility trend of *Citrobacter* species isolated from all samples (except faeces and urine)

AMA	Year-2017	Year-2018	Year-2019	Year-2020	Year-2021	Year-2022
	Total n=321	Total n=613	Total n=796	Total n=447	Total n=136	Total n=139
Piperacillin-tazobactam	178/308 (57.8)	365/603 (60.5)	458/760 (60.3)	252/427 (59)	73/114 (64.0)	60 / 139 (43.2)
Cefazolin	*0/0	*0/0	*0/0	*0/0	*0/0	*0/0
Cefotaxime	94/306 (30.7)	193/556 (34.7)	228/654 (34.9)	144/388 (37.1)	35/87 (40.2%)	50 / 101 (49.5)
Ceftazidime	110/285 (38.6)	168/474 (35.4)	201/577 (34.8)	105/295 (35.6)	15/48 (31.3)	23 / 58 (39.6)
Ertapenem	161/263 (61.2)	336/522 (64.4)	381/597 (63.8)	224/334 (67.1)	81/93 (87.1)	71 / 88 (80.6)
Imipenem	198/303 (65.3)	369/594 (62.1)	403/679 (59.4)	270/421 (64.1)	71/111 (64)	71 / 104 (68.2)
Meropenem	187/284 (65.8)	396/580 (68.3)	505/765 (66)	299/427 (70)	81/131 (61.8)	91 / 123 (73.9)
Amikacin	212/318 (66.7)	416/604 (68.9)	509/763 (66.7)	312/438 (71.2)	89/128 (69.5)	92 / 125 (73.6)
Ciprofloxacin	138/295 (46.8)	324/599 (54.1)	430/740 (58.1)	256/410 (62.4)	72/121 (59.5)	67 / 135 (49.6)
Levofloxacin	44/86 (51.2)	145/319 (45.5)	296/512 (57.8)	132/236 (55.9)	27/34 (79.4)	16 / 36 (44.4)

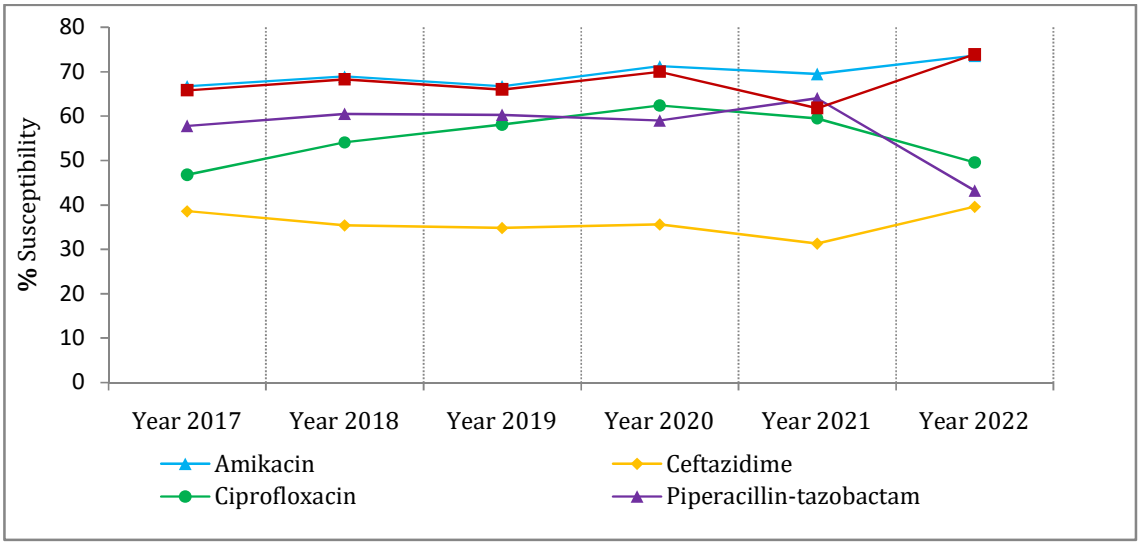


Figure 3.9: Yearly susceptibility trend of *Citrobacter* species isolated from all samples (except faeces and urine)

Table 3.9: Yearly susceptibility trend of *Enterobacter* species isolated from all samples (except faeces and urine)

AMA	Year-2017	Year-2018	Year-2019	Year-2020	Year-2021	Year-2022
	Total n=1140	Total n=1600	Total n=2071	Total n=1287	Total n=393	Total n=324
Piperacillin-tazobactam	682/1092 (62.5)	961/1567 (61.3)	1253/1908 (65.7)	781/1225 (63.8)	234/369 (63.4)	122 / 319 (38.2)
Cefazolin	*0/0	*0/0	*0/0	*0/0	*0/0	*0/0
Cefotaxime	310/1093 (28.4)	448/1423 (31.5)	576/1590 (36.2)	391/1094 (35.7)	78/290 (26.9)	65 / 251 (25.9)
Ceftazidime	363/1013 (35.8)	424/1159 (36.6)	494/1305 (37.9)	281/823 (34.1)	69/251 (27.5)	66 / 225 (29.3)
Ertapenem	613/929 (66)	855/1170 (73.1)	950/1281 (74.2)	562/783 (71.8)	171/216 (79.2)	135 / 176 (76.7)
Imipenem	851/1133 (75.1)	1111/1575 (70.5)	1117/1662 (67.2)	826/1148 (72)	191/281 (68)	188 / 266 (70.6)
Meropenem	735/1051 (69.9)	1068/1503 (71.1)	1497/1990 (75.2)	918/1211 (75.8)	262/378 (69.3)	230 / 296 (77.7)
Amikacin	734/1059 (69.3)	1119/1572 (71.2)	1446/1965 (73.6)	948/1250 (75.8)	267/371 (72)	221 / 306 (72.2)
Ciprofloxacin	578/1088 (53.1)	837/1369 (61.1)	1147/1836 (62.5)	699/1080 (64.7)	189/272 (69.5)	166 / 319 (52.0)
Levofloxacin	93/150 (62)	289/550 (52.5)	587/959 (61.2)	334/554 (60.3)	113/170 (66.5)	69 / 116 (59.4)

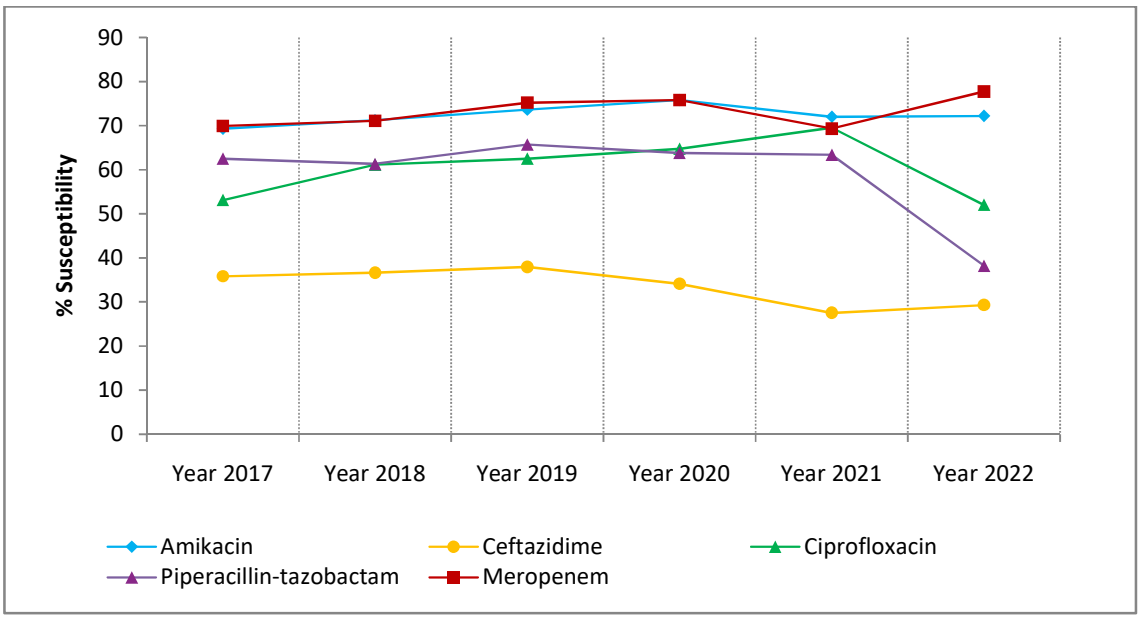


Figure 3.10: Yearly susceptibility trend of *Enterobacter* species isolated from all samples (except faeces and urine)

Relative susceptibilities of carbapenem susceptible and carbapenem resistant isolates of *E. coli* and *K. pneumoniae*

Overall, carbapenem susceptible isolates showed higher susceptibility to all the antibiotics tested, than carbapenem resistant (resistant to at least one of the carbapenems tested) isolates (table 3.10 and figure 3.11). The difference was more marked in *K. pneumoniae* than *E. coli* indicating that carbapenem resistant *K. pneumoniae* isolates were more resistant to all the antibiotics than carbapenem resistant *E. coli* isolates. In *E. coli*, the differences in susceptibility were high for carbapenems and amikacin (range of differences 40-89%) and moderate for other antibiotics (range of differences 13-39%). In *K. pneumoniae*, the differences were high for all the antibiotics tested (range of differences 29-97%).

Table 3.10: Susceptibilities of carbapenem susceptible (CS) and carbapenem resistant (CR) isolates of *E. coli* and *K. pneumoniae* to all antibiotics

	E. coli	*E. coli*		*K. pneumoniae*	*K. pneumoniae*		
	CS	CR		CS	CR		
Pip-taz	35	4		30	1	31	29
Cefotaxime	23	2		55	1	22	54
Ceftazidime	25	2		66	1	23	65
Ertapen	96	7		99	2	89	97
Imipen	95	16		92	8	79	84
Meropen	98	21		96	7	77	89
Amikacin	92	52		93	16	40	77
Ciproflox	15	2		46	2	13	44
Levoflox		5			5	-5	-5
Co-trimox	42	17					
NFT	94	79					

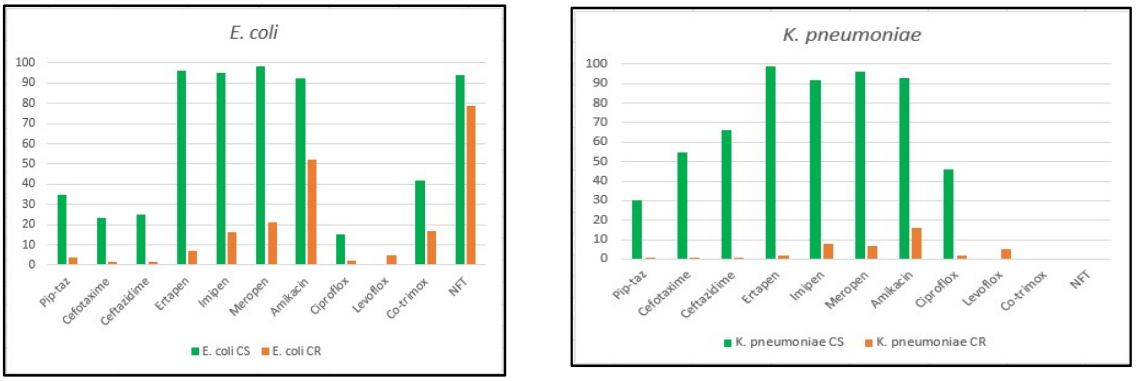


Figure 3.11: Susceptibilities of carbapenem susceptible (CS) and carbapenem resistant (CR) isolates of *E. coli* and *K. pneumoniae* to all antibiotics

Analysis of results from individual Regional Centers

21 Regional Centers (RCs) from various parts of the country, both public and private sectors, participated in surveillance. The results of all centers for the designated organisms and the designated antibiotics were used for overall susceptibility but only those drug-pathogen combinations where the number tested was 30 or more were used for RC wise analyses. The susceptibility profiles showed considerable variation between the RCs.

Species wise susceptibility of Enterobacterales isolated from urine

Fosfomycin showed 97% susceptibility to *E. coli* isolated from urine (Table 3.11 and figure 3.12 and 3.13). Overall, the isolates from urine showed good susceptibility to amikacin (79%), meropenem (76%), nitrofurantoin (76%), imipenem (72%) and ertapenem (69%), followed by and piperacillin-tazobactam (52%). Species wise, *C. koseri* was the most susceptible followed by *E. cloacae* and *M. morganii*. *P. rettgeri* was the least susceptible showing susceptibility of 40 percent or less to all antibiotics tested except imipenem (61%). Comparison of overall susceptibilities of urinary isolates and non-urinary isolates of Enterobacterales showed marginally better susceptibility in the former (Figure 3.14).

Table 3.11: Susceptibility of species of Enterobacterales isolated from urine to antibiotics, overall and species wise

	E. coli		K. pneumoniae		K. oxytoca		Klebsiella spp		E. cloacae		Enterobacter spp		P. mirabilis		C. koseri		C. freundii		M. morganii		P. rettgeri		Overall	
	n	%S	n	%S	n	%S	n	%S	n	%S	n	%S	n	%S	n	%S	n	%S	n	%S	n	%S	n	%S
Pip-taz	11723	56	3806	37	131	20	25		243	69	15		274	82	76	76	35	34	133	79	59	17	16683	52
Cefazolin	4794	20	1521	23	118	3	3		1		4		88	34	20		19		27		13		6688	20
Cefotaxim	11123	29	3490	29	130	18	21		212	61	15		244	54	66	66	32	31	116	66	45	11	15647	30
Ceftazid	3222	22	1202	23	95	18	5		62	48	3		95	32	52	52	18		41	61	22		4844	23
Ertapener	9306	75	3018	50	129	52	15		167	76	7		197	82	86	86	32	75	98	85	46	13	13209	69
Imipenem	11577	79	3741	54	133	47	25		238	80	16		263	65	82	82	34	62	127	61	127	61	16514	72
Meropene	11564	82	3736	56	133	55	24		237	83	15		271	86	88	88	34	85	131	87	58	21	16436	76
Amikacin	11743	86	3808	57	133	77	24		243	82	15		279	72	91	91	35	86	133	89	59	19	16711	79
Ciprofloxa	11680	18	3787	25	133	23	23		242	60	14		272	32	67	67	35	29	134	41	59	12	16615	22
Levofloxa	5151	23	1771	28	122	21	9		53	55	8		126	30	50	50	22		60	40	34	0	7467	25
Cotrimoxa	10383	43	3427	41	129	40	23		181	62	15		236	38	69	69	33	48	108	57	56	9	14789	43
Fosfomyc	7101	97	2258	73	123	76	14		93	67	9		150	79	89	89	27		60	52	41	39	10005	90
NFT	10287	90	3272	40	126	71	23		193	54	12		129	0	80	80	30	83	49	0	31	0	14348	76

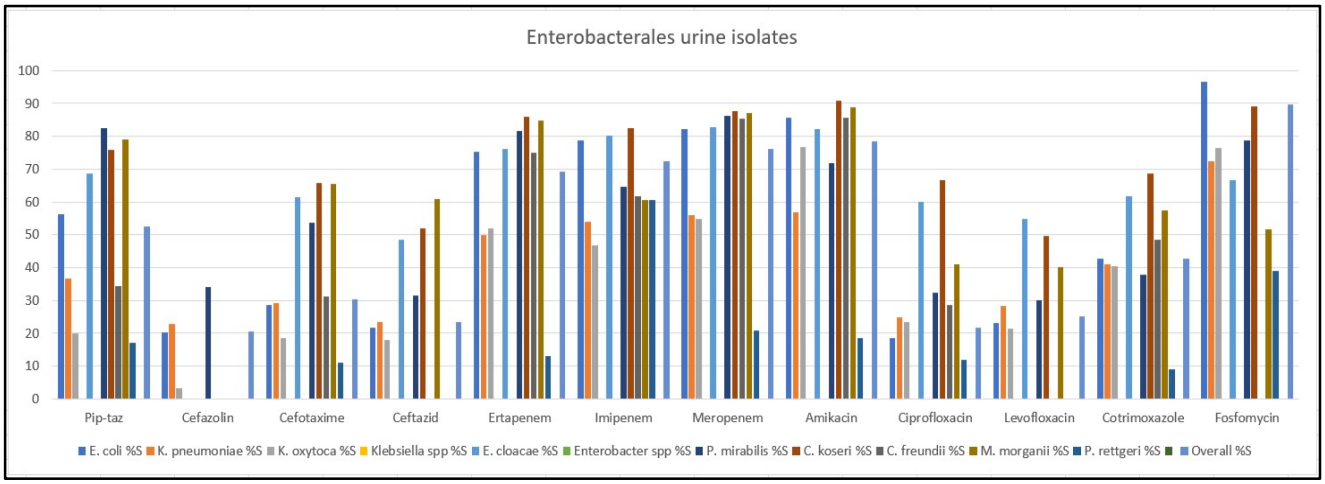


Figure 3.12: Susceptibility of Enterobacterales isolated from urine, antibiotic wise

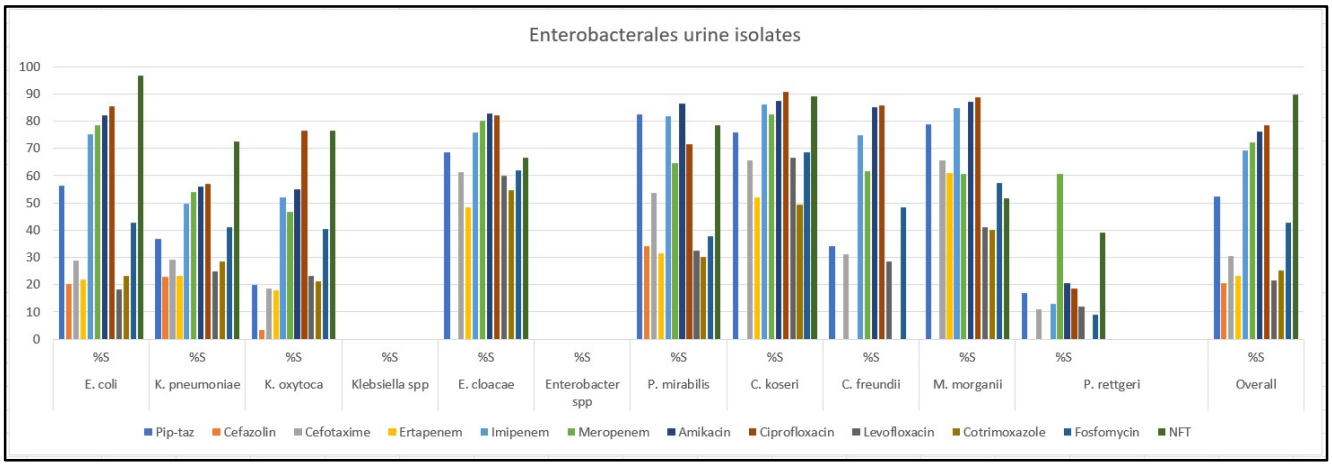


Figure 3.13: Susceptibility of Enterobacterales isolated from urine, overall and species wise

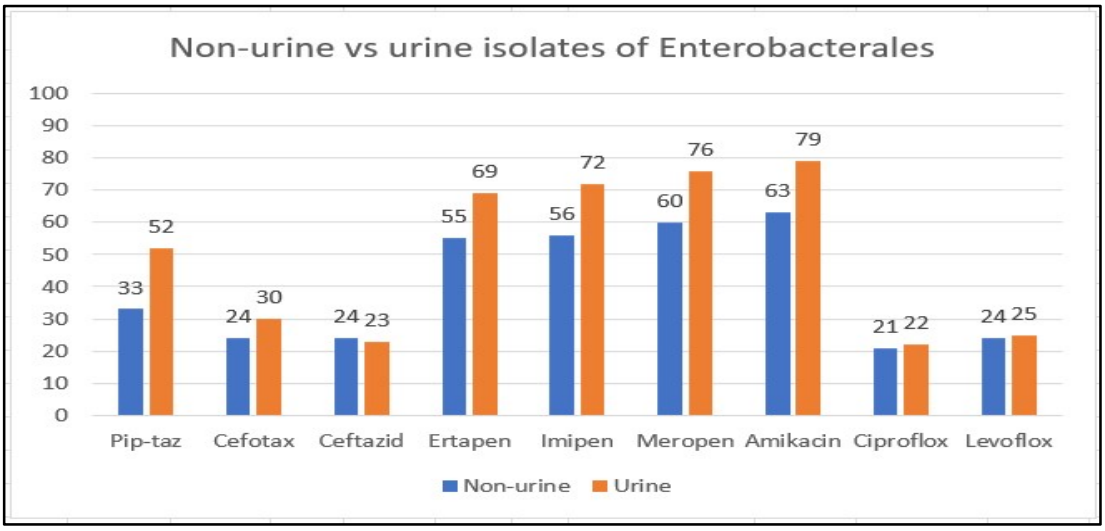


Figure 3.14: Overall susceptibility of non-urinary versus urinary isolates of Enterobacterales to the common antibiotics tested

Comparison of susceptibilities of *E. coli* and *K. pneumoniae* showed that the former is more susceptible than the latter to all antibiotics except cefazolin and fluoroquinolones (table 3.12 and figure 3.15).

Table 3.12: Comparison of susceptibility of *E. coli* and *K. pneumoniae* from urine

	E. coli	K. pneumoniae
Pip-taz	56	37
Cephazolin	20	23
Cefotaxime	29	29
Ceftazidime	22	23
Ertapen	75	50
Imipen	79	54
Meropen	82	56
Amikacin	86	57
Ciproflox	18	25
Levoflox	23	28
Cotrimox	43	43
NFT	90	40

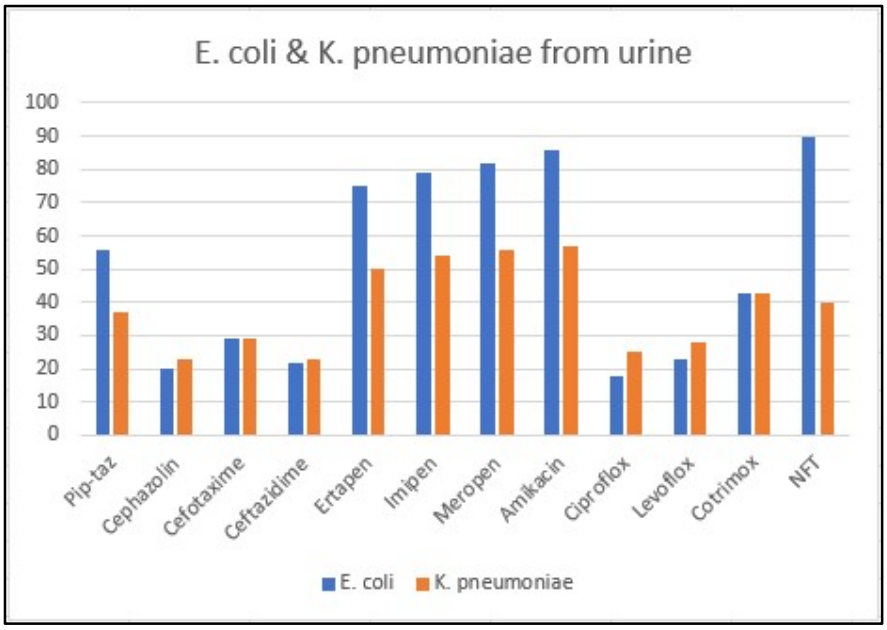


Figure 3.15: Comparison of susceptibility of *E. coli* and *K. pneumoniae* from urine

RC wise susceptibility of *E. coli* and *K. pneumoniae* showed similar variations as the non-urine isolates except in *E. coli* for fosfomycin and nitrofurantoin. RC 21 showed unusually low susceptibility for most antibiotics tested (Table 3.13 and 3.14).

Table 3.13: Susceptibility of *E. coli* isolated from urine, overall and RC wise

	Pip-taz		Cephazolin		Cefotaxime		Ertapen		Imipen		Meropen		Amikacin		Ciproflox		Levoflox		Cotrimox		Phosphomycin		NFT	
	n	%S	n	%S	n	%S	n	%S	n	%S	n	%S	n	%S	n	%S	n	%S	n	%S	n	%S	n	%S
RC 01	699	54	687	14	700	19	700	66	699	65	699	66	700	66	700	22	699	25	686	17	674	97	686	93
RC 02																								
RC 03																								
RC 04	1063	62	1		1063	30			1063	89	1063	89	1056	91	1063	26							1025	92
RC 05	462	71	0		182	16	458	84	463	88	463	89	463	95	416	19			417	47	100	100	417	85
RC 06	787	63	0		788	22	789	78	793	81	793	80	793	88	793	5	5		778	35	695	99	749	92
RC 07	310	62	42	38	38	16	220	83	186	72	166	70	306	85	291	16	37	3	281	40	175	95	248	79
RC 08	133	65	0		132	25	131	79	133	83	133	83	133	92	133	11	133	8	133	47	133	99	19	
RC 09	626	82	615	41	628	41	623	87	627	87	626	92	628	94	624	38	618	42	627	52	588	96	620	92
RC 10	740	76	0		741	39	745	91	715	91	726	92	747	94	746	26	0		724	49	422	99	263	83
RC 11	84	44	0		12		49	63	60	60	57	63	73	78	74	14	28		68	46	30	87	71	85
RC 12	321	28	293	9	323	2	320	51	323	54	323	53	323	66	323	2	313	5	310	27	283	94	318	86
RC 13	907	58	1		909	55	257	70	914	81	914	83	914	80	914	12	313	20	831	38	869	98	849	92
RC 14	1476	81	0		1481	34	1481	91	1481	94	1481	94	1481	97	1479	29			1475	58	152	99	966	92
RC 15	357	50	356	13	357	18	3		357	90	357	96	357	83	357	14	65	5	355	34	183	92	360	91
RC 16	852	12	838	17	858	10	854	68	858	52	858	77	858	90	858	15	855	26	850	44	844	93	850	92
RC 17	945	66	3		945	59	829	77	945	89	945	89	946	93	945	11	121	10	902	45	4		895	93
RC 18	552	32	551	26	552	16	552	72	552	65	552	73	552	76	552	26	552	29	551	51	550	94	552	93
RC 19	773	41	773	25	773	11	773	60	773	63	773	68	773	75	773	8	772	21	773	44	772	100	773	92
RC 20	453	31	453	11	458	11	342	65	452	58	452	74	457	82	456	14	457	22	439	26	451	94	444	87
RC 21	183	2	181	3	183	0	180	3	183	88	183	74	183	42	183	0	183	6	183	37	176	100	182	59
Overall	11723	56	4794	20	11123	29	9306	75	11577	79	11564	82	11743	86	11680	18	5151	23	10383	43	7101	97	10287	90

Table 3.14: Susceptibility of *K. pneumoniae* isolated from urine, overall and RC wise

		Pip-taz	Cephazol		Cefotax		Ertapen		Imipen		Meropen		Amikacin		Ciproflox		Levoflox		Cotrimox		NFT
	n	%S	n	%S	n	%S	n	%S	n	%S	n	%S	n	%S	n	%S	n	%S	n	%S	n	%S
RC 01	352	27	316	11	352	16	352	36	352	36	352	37	352	32	352	20	352	21	316	44	316	13
RC 02	0		0		0		0		0		0		0		0		0		0		0	
RC 03	0		0		0		0		0		0		0		0		0		0		0	
RC 04	214	57	0		214	51	0		213	75	214	74	212	73	214	46	0		207	33	0	
RC 05	182	53	0		84	23	181	65	181	68	181	67	183	73	165	32	0		156	16	165	54
RC 06	344	19	1		340	11	344	31	344	33	344	34	344	37	344	8	0		328	22	339	24
RC 07	164	30	12		20		104	48	127	38	116	41	161	52	159	25	11		98	15	126	44
RC 08	76	24	2		67	24	68	29	77	32	76	32	76	36	76	18	76	17	8		76	37
RC 09	99	67	97	48	99	57	99	74	99	71	99	74	99	71	99	61	99	64	97	61	99	52
RC 10	247	47	0		245	38	250	60	234	64	245	62	249	64	250	32	0		120	26	245	49
RC 11	72	21	0		15		38	32	56	23	50	24	73	23	71	15	37	16	60	22	59	32
RC 12	151	23	131	11	149	3	149	34	150	36	150	33	150	35	150	13	141	10	148	26	142	35
RC 13	359	35	1		358	34	72	35	361	54	361	53	362	45	361	11	156	24	325	28	328	31
RC 14	362	73	0		362	58	362	83	362	86	362	88	362	91	361	52	0		238	33	361	68
RC 15	145	39	145	19	145	23	1		145	70	145	74	145	61	144	19	29		147	30	145	35
RC 16	199	11	189	20	199	18	197	55	199	42	199	62	199	70	199	20	196	38	197	61	197	52
RC 17	206	40	0		207	58	186	42	207	55	207	55	206	59	207	19	41	20	197	75	201	35
RC 18	182	26	180	33	182	19	182	64	182	55	182	66	182	75	182	42	182	45	181	68	180	64
RC 19	286	34	284	37	285	15	286	51	286	50	286	55	286	59	286	15	285	30	286	60	285	52
RC 20	98	16	96	15	99	18	79	33	98	39	99	42	99	44	99	18	98	31	96	45	95	16
RC 21	68	4	67	0	68	0	68	1	68	74	68	56	68	49	68	1	68	13	67	21	68	31
Overall	3806	37	1521	23	3490	29	3018	50	3741	54	3736	56	3808	57	3787	25	1771	28	3272	40	3427	41

Clinical relevance

The relative frequency of isolation of various species and their susceptibility trends has an important role in deciding empiric antibiotic policies in hospitals. The trends of change in susceptibility indicate behavior of organisms over time and alert us to take appropriate preventive measures.

Colistin, as expected, was the most effective antibiotic with an overall susceptibility of near 95% with most species tested except *Citrobacter* species (80%) and *Enterobacter* species (86%). With increasing use over the last five years, colistin resistance is emerging and the recent removal by CLSI of susceptible category from colistin indicates that there are strains of organisms without any detectable resistance mechanism (wild strains) which may not respond to therapy with this drug. Systemic therapy with colistin has also been mentioned as not adequate for treating respiratory tract infections. The fact that, in tertiary care facilities, many isolates from hospital-acquired and ventilator-associated pneumonias are carbapenem resistant, colistin therapy, if required, should be supplemented with nebulized colistin through inhalation. The removal of susceptible category from colistin also indicates that, in all situations, therapy with colistin may have unpredictable outcome and therefore should be highly restricted.

Carbapenem (meropenem) resistance was very high in *Klebsiella pneumoniae* (44%), *P. rettgeri* (51%), and *K. oxytoca* (56%), with an overall all-species susceptibility of 60%. Carbapenems have been mainstay in empiric therapy in tertiary care ICU settings. Though there was good susceptibility in *M. morganii* (86%), *P. mirabilis* (84%), and *K. aerogenes* (81%), the efficacy of this drug as empiric therapy protocol should depend on relative distribution of the various species in a particular set up. This also demands

regular surveillance of carbapenem resistant Enterobacterales by molecular detection of various genes.

Piperacillin-tazobactam susceptibility overall was alarmingly low at 33%. Though the drug showed reasonable susceptibility in *Proteus mirabilis* (72%), *M. morganii* (68%), and *Citrobacter koseri* (61%), it showed poor susceptibility in commonly isolated species like *Klebsiella pneumoniae* (22%) and *E. coli* (35%) and therefore should be used only when an isolate is tested susceptible. Third generation cephalosporins and fluoroquinolones have susceptibilities far below the level to consider them appropriate for use in serious patients. Extensive use and abuse of these two groups over the last three decades have resulted in high prevalence of extended-spectrum beta lactamases and carbapenemases against oxyimino-cephalosporins and multiple mutations in organisms against fluoroquinolones making them nearly unusable as empiric therapy in seriously ill patients in tertiary care practices.

Amongst the urinary isolates, phosphomycin showed the highest susceptibility (97%) in *E. coli,* the commonest species and the one for which it is recommended by CLSI. The urinary isolates showed marginally better susceptibility than non-urinary isolates to most antibiotics and this fact combined with the concentrating effect of urine on many antibiotics should be considered while treating such infections.

The differences in susceptibility of various organisms isolated from patients in OPD, indoor wards and ICU practices are clearly an outcome of the extent of use of the antibiotics in these areas and the consequent selection pressure. While OPD patients are usually put on oral antibiotics, the indoor patients are frequently on parenteral antibiotics and the ICU patients are usually exposed to the highest and broad-spectrum antibiotics, often multiple.

Resistance of an organism to an antibiotic is a direct outcome of the frequency of isolation of the organism and the selection pressure of the antibiotic load used to treat it. Over the last two decades, use of carbapenems have increased many folds and the same is reflected in imipenem susceptibility of *E. coli* dropping steadily from 81% in 2017 to 66% in 2022 and that of *Klebsiella pneumoniae* dropping steadily from 59% in 2017 to 42% in 2022. The increase in susceptibility to amikacin in *Citrobacter* species and meropenem in *Citrobacter* and *Enterobacter* speciesmay reflect drop in use of the same for these organisms.

Characterisation of resistance mechanism

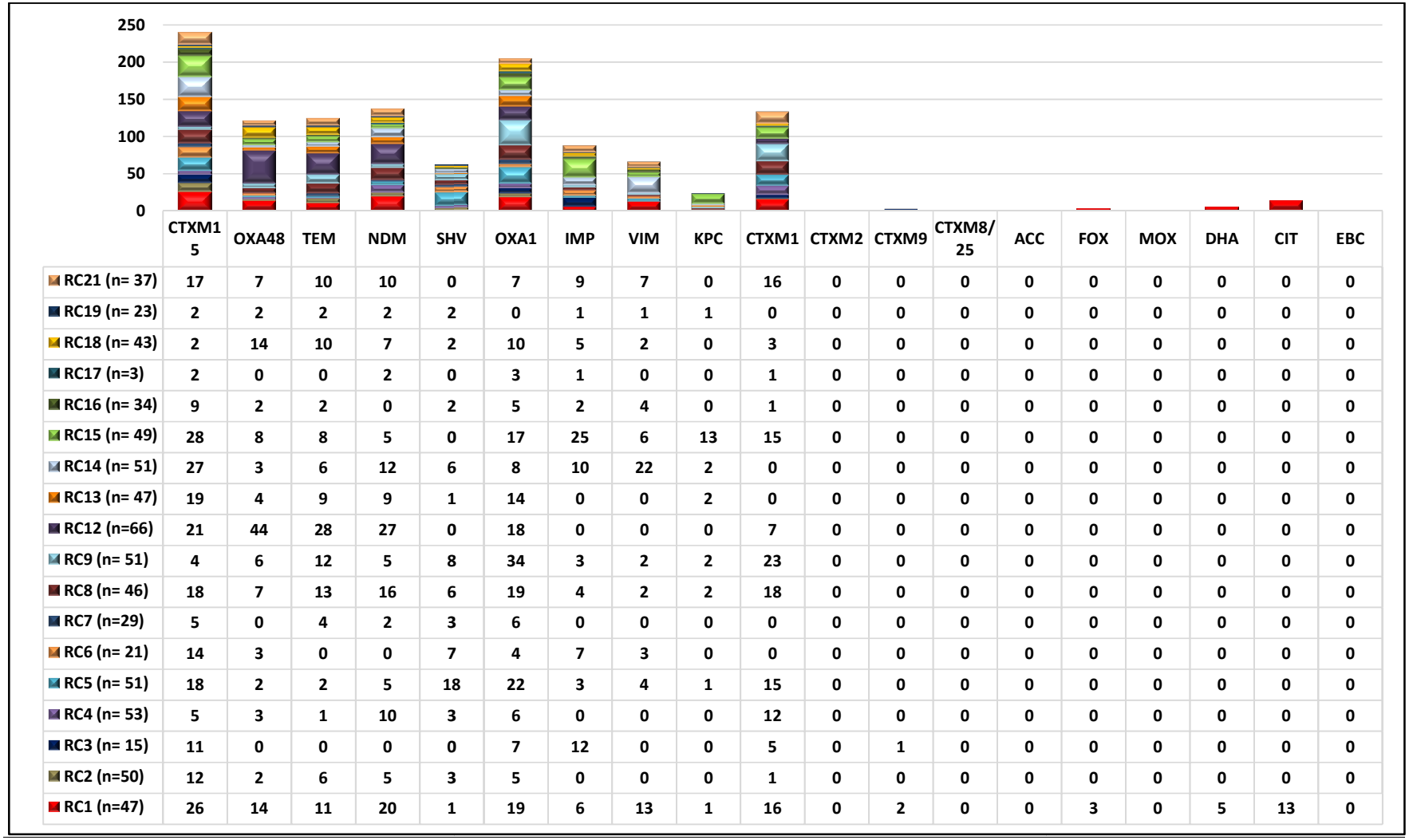
E. coli

A total of seven hundred and sixteen (716) *E. coli* isolates were subjected to four multiplex PCRs and three monoplex PCRs for OXA-48, CTXM-15 and NDM. Overall, CTXM-15 (34%) was the most common, followed by OXA-1 (28%), CTXM-1 and NDM-1 (19% each), TEM and OXA-48 (17% each), IMP (12%), VIM and SHV (9% each) and KPC (3%) (Figures 3.16, Figure 3.17 and Table 3.15). The *E. coli* isolates received from RC1 were positive for CTXM-15 (55%) followed by NDM-1 (43%) and CTXM-1 gene (34%).

The isolates from RC2 showed maximum positivity for CTXM-15 (24%), followed by TEM (12%), NDM and OXA-1 (10% each) and OXA-48, SHV, CTXM-1 less than 10%. The majority of RC3 isolates were positive for IMP (80%) and CTXM-15 (73%) followed by OXA-1 (47%) and CTXM-1 (33%).

The RC4 isolates were majorly positive for CTXM-1 (23%) followed by NDM (19%) and OXA-1 (11%). RC5 isolates showed OXA-1 (43%) followed by SHV (35%), CTX-M15 (35%) and CTXM-1 (29%). RC6 isolates showed CTXM-15(67%) followed by SHV and IMP (33% each). The RC7 isolates were positive for OXA-1 (21%), CTXM-15 (17%), and TEM (14%). In RC8, OXA-1 was detected in 41% isolates and CTXM-15 and CTXM-1 were detected in 39% of the isolates. RC9 showed high positivity for OXA-1 (67%) and CTXM-1 (45%). RC12 isolates were maximally positive for OXA-48 (67%), followed by TEM (42%), NDM (41%), CTXM-15 (32%) and OXA-1 (27%). The RC13 isolates showed positivity for CTXM-15 (40%), OXA-1 (30%), TEM and NDM (19% each) and rest genes showed lesser prevalence (less than 10%). In RC14 isolates, CTXM-15 and VIM were the commonest (53% and 43% respectively) followed by NDM (24%). In RC15 samples, CTXM-15 (57%) and IMP (51%) had the highest prevalence followed by OXA-1(35%). Among the RC16 samples, the CTXM-15 resistance gene was found in 26% of cases; while OXA-1 resistance gene was present in 15% isolates and the rest of the genes had low prevalence. In the RC17 samples, OXA-1 had the highest prevalence at 100%, followed by CTXM-15 and NDM at 67%, other resistance genes, such as IMP and CTXM-1, had a prevalence of 33% each. The predominant resistance genes in RC18 samples were OXA-48 (33%), TEM and OXA-1, with a prevalence of 23% each; IMP and NDM were also present in 12% and 16% of the samples, respectively. The least prevalence resistance genes (less than 10%) were found in RC19 samples. RC21 isolates showed higher prevalence of CTXM-15 (46%) followed by CTXM-1 (43%), TEM and NDM (27% each). The OXA-48, OXA-19 and VIM were found in 19% of isolates whereas 24% carried IMP genes.

As per figure 2, in *E. coli* isolates, CTXM-15 gene was the predominant gene present in 34% of the isolates followed by OXA-1 in 28% of the isolates and NDM and CTXM-1 in 19% of the isolates. The genes encoding for AmpC β-lactamases were the least prevalent genes.



	CTXM15	OXA48	TEM	NDM	SHV	OXA1	IMP	VIM	KPC	CTXM1	CTXM2	CTXM9	CTXM8/25	ACC	FOX	MOX	DHA	CIT	EBC
RC21 (n= 37)	17	7	10	10	0	7	9	7	0	16	0	0	0	0	0	0	0	0	0
RC19 (n= 23)	2	2	2	2	2	0	1	1	1	0	0	0	0	0	0	0	0	0	0
RC18 (n= 43)	2	14	10	7	2	10	5	2	0	3	0	0	0	0	0	0	0	0	0
RC17 (n=3)	2	0	0	2	0	3	1	0	0	1	0	0	0	0	0	0	0	0	0
RC16 (n= 34)	9	2	2	0	2	5	2	4	0	1	0	0	0	0	0	0	0	0	0
RC15 (n= 49)	28	8	8	5	0	17	25	6	13	15	0	0	0	0	0	0	0	0	0
RC14 (n= 51)	27	3	6	12	6	8	10	22	2	0	0	0	0	0	0	0	0	0	0
RC13 (n= 47)	19	4	9	9	1	14	0	0	2	0	0	0	0	0	0	0	0	0	0
RC12 (n=66)	21	44	28	27	0	18	0	0	0	7	0	0	0	0	0	0	0	0	0
RC9 (n= 51)	4	6	12	5	8	34	3	2	2	23	0	0	0	0	0	0	0	0	0
RC8 (n= 46)	18	7	13	16	6	19	4	2	2	18	0	0	0	0	0	0	0	0	0
RC7 (n=29)	5	0	4	2	3	6	0	0	0	0	0	0	0	0	0	0	0	0	0
RC6 (n= 21)	14	3	0	0	7	4	7	3	0	0	0	0	0	0	0	0	0	0	0
RC5 (n= 51)	18	2	2	5	18	22	3	4	1	15	0	0	0	0	0	0	0	0	0
RC4 (n= 53)	5	3	1	10	3	6	0	0	0	12	0	0	0	0	0	0	0	0	0
RC3 (n= 15)	11	0	0	0	0	7	12	0	0	5	0	1	0	0	0	0	0	0	0
RC2 (n=50)	12	2	6	5	3	5	0	0	0	1	0	0	0	0	0	0	0	0	0
RC1 (n=47)	26	14	11	20	1	19	6	13	1	16	0	2	0	0	3	0	5	13	0

Figure 3.16: Various resistance genes found in *E. coli* isolates from different regional centres across India

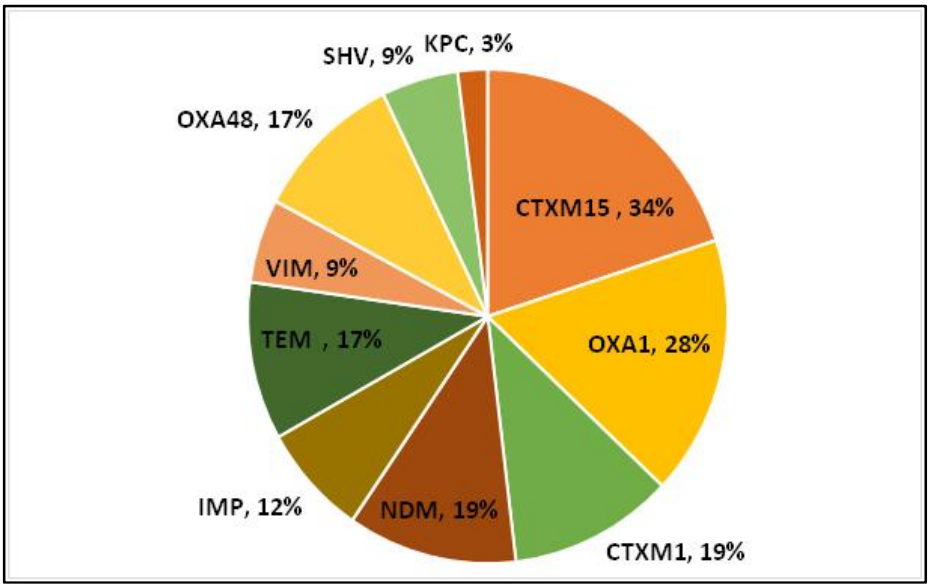


Figure 3.17: Percentage positivity of AMR associated genetic determinants in *E. coli*

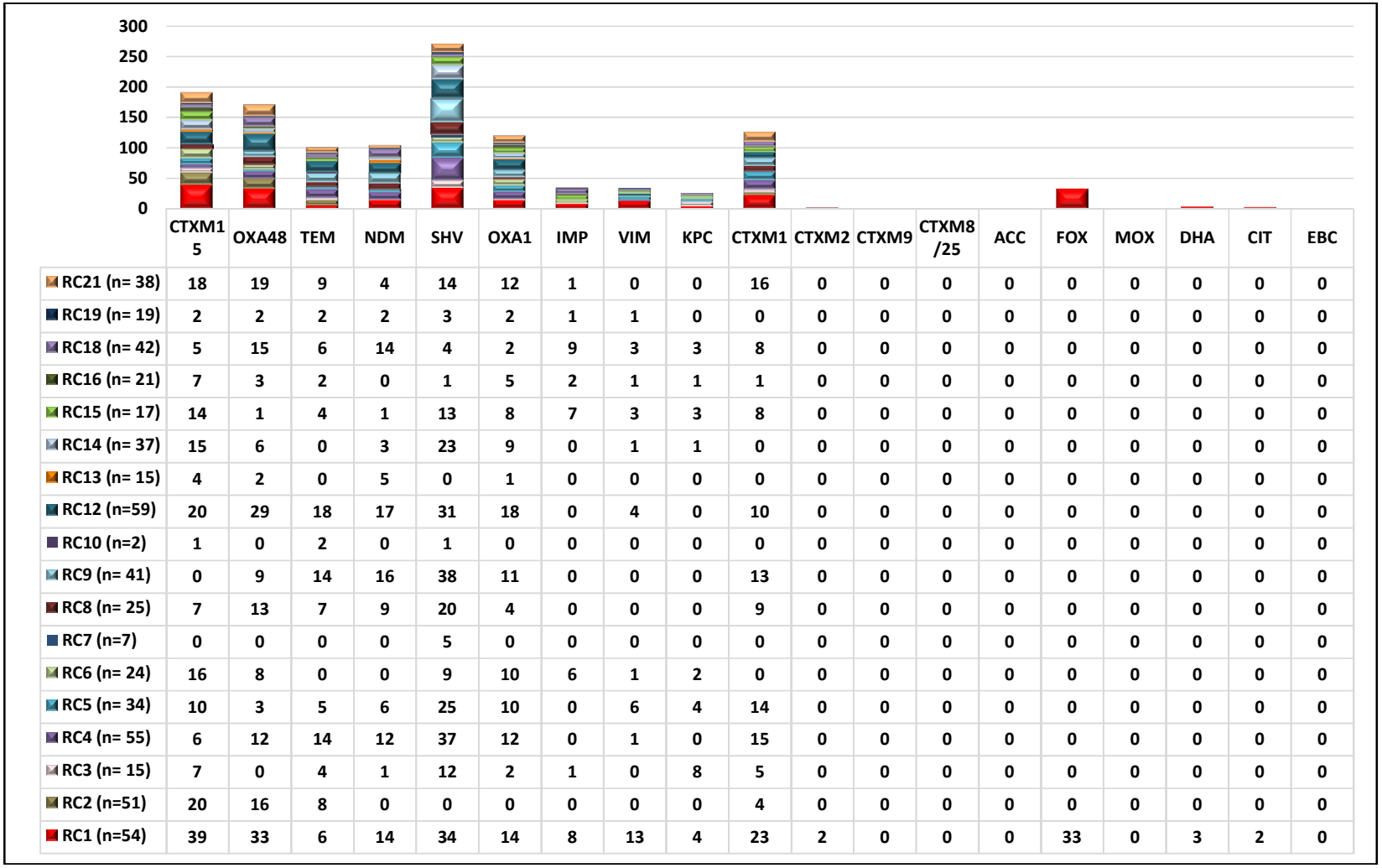
Table 3.15: Percentage positivity of resistant genes in *E. coli* from each centre

Regional Centers	Antimicrobial Resistance Genes									
	CTXM15	OXA48	TEM	NDM	SHV	OXA1	IMP	VIM	KPC	CTXM1
RC1	55%	30%	23%	43%	2%	40%	13%	28%	2%	34%
RC2	24%	4%	12%	10%	6%	10%	0%	0%	0%	2%
RC3	73%	0%	0%	0%	0%	47%	80%	0%	0%	33%
RC4	9%	6%	2%	19%	6%	11%	0%	0%	0%	23%
RC5	35%	4%	4%	10%	35%	43%	6%	8%	2%	29%
RC6	67%	14%	0%	0%	33%	19%	33%	14%	0%	0%
RC7	17%	0%	14%	7%	10%	21%	0%	0%	0%	0%
RC8	39%	15%	28%	35%	13%	41%	9%	4%	4%	39%
RC9	8%	12%	24%	10%	16%	67%	6%	4%	4%	45%
RC12	32%	67%	42%	41%	0%	27%	0%	0%	0%	11%
RC13	40%	9%	19%	19%	2%	30%	0%	0%	4%	0%
RC14	53%	6%	12%	24%	12%	16%	20%	43%	4%	0%
RC15	57%	16%	16%	10%	0%	35%	51%	12%	27%	31%
RC16	26%	6%	6%	0%	6%	15%	6%	12%	0%	3%
RC17	67%	0%	0%	67%	0%	100%	33%	0%	0%	33%
RC18	5%	33%	23%	16%	5%	23%	12%	5%	0%	7%
RC19	9%	9%	9%	9%	9%	0%	4%	4%	4%	0%
RC21	46%	19%	27%	27%	0%	19%	24%	19%	0%	43%

K. pneumoniae

A total of five hundred and fifty-six (556) *K. pneumoniae* isolates were subjected to four multiplex PCRs and three monoplex PCRs for OXA-48, CTXM-15 and NDM. Overall, SHV gene was the predominant present in 49% of the isolates followed by CTXM-15 in 34%, OXA-48 in 31%, OXA-1 in 22%, CTXM-1in 23%, NDM in 19%, TEM in 18%, VIM and IMP in 6% each and KPC in 5% of the isolates (Figure 3.18, Figure 3.19 and Table 3.16). Among the RC1 isolates, the most prevalent resistance genes were CTXM-15 (72%), followed by SHV (63%), OXA-48 (61%) and CTXM-1 (43%). The isolates from RC2 showed maximum positivity for CTXM-15 (39%), followed by OXA-48 (31%), TEM (16%) and CTXM-1 less than 10%. In the RC3 samples, SHV had the highest prevalence at 80%, followed by KPC (53%) and CTXM-15 (47%) and CTXM-1 (33%). The RC4 isolates were majorly positive for SHV (67%) followed by CTXM-1 (27%) and TEM (25%). Within RC5 isolates, SHV (74%) was the predominant resistance gene followed by CTXM-1 (41%), and OXA-1 and CTXM-15 (29% each). RC6 samples exhibited high prevalence for CTXM-15 (67%) and OXA-1 (42%). Additionally, SHV and OXA-48 were present at 38% and 33% isolates respectively. The RC7 isolates were positive only for SHV (71%). Among the RC8 isolates, SHV (80%), OXA-48 (52%) and CTXM-1 (36%) were the most prevalent resistance genes. The RC9 samples showed high prevalence of SHV (93%) and NDM (39%). The RC10 isolates were positive for TEM (100%) and, SHV and CTXM-15 (50% each). The RC12 isolates showed maximum positivity for SHV (53%), OXA-48 (49%), CTXM-15 (34%), TEM and OXA-1 (31% each), and NDM (29%). Within RC13 isolates had lesser genes; NDM (33%) and CTXM-15 (27%) being the most prevalent resistance genes. RC14 samples exhibited high prevalence of SHV (62%) and CTXM-15 (41%). Other resistance genes were present at lower levels or absent. Among the RC15 isolates, CTXM-15 (82%) and SHV (76%) were the most common resistance genes. Other genes, like OXA-1 (47%) and IMP (41%), were also commonly detected. In RC16 samples, CTXM-15 (33%) and SHV (24%) were prevalent, while other resistance genes had prevalence rates less than 10%. The RC18 samples showed varying prevalence for different resistance genes, with OXA-48 (36%), NDM (33%) and IMP (21%) being notable. Others like VIM, KPC and OXA-1 were detected at lower levels (lesser than 10%). Within RC19 isolates, overall lower prevalence of resistance genes was found and SHV (16%) and CTXM-15 (11%) were the most prevalent. In RC21, 50% of the isolates showed the presence of OXA-48, followed by CTXM-15 in 47% of the isolates and CTXM-1 in 42% and SHV in 37% of the isolates. In RC10 (n=2), both the isolates were positive for TEM-1, whereas one strain was positive for CTXM-15 and SHV each.

As per figure 3.19, in *K. pneumoniae* isolates, SHV gene was the predominant gene present in 49% of the isolates followed by CTXM-15 in 34% of the isolates and OXA-48 in 31% of the isolates. The genes encoding for AmpC β-lactamases were the least prevalent genes.



	CTXM15	OXA48	TEM	NDM	SHV	OXA1	IMP	VIM	KPC	CTXM1	CTXM2	CTXM9	CTXM8/25	ACC	FOX	MOX	DHA	CIT	EBC
RC21 (n= 38)	18	19	9	4	14	12	1	0	0	16	0	0	0	0	0	0	0	0	0
RC19 (n= 19)	2	2	2	2	3	2	1	1	0	0	0	0	0	0	0	0	0	0	0
RC18 (n= 42)	5	15	6	14	4	2	9	3	3	8	0	0	0	0	0	0	0	0	0
RC16 (n= 21)	7	3	2	0	1	5	2	1	1	1	0	0	0	0	0	0	0	0	0
RC15 (n= 17)	14	1	4	1	13	8	7	3	3	8	0	0	0	0	0	0	0	0	0
RC14 (n= 37)	15	6	0	3	23	9	0	1	1	0	0	0	0	0	0	0	0	0	0
RC13 (n= 15)	4	2	0	5	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
RC12 (n=59)	20	29	18	17	31	18	0	4	0	10	0	0	0	0	0	0	0	0	0
RC10 (n=2)	1	0	2	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
RC9 (n= 41)	0	9	14	16	38	11	0	0	0	13	0	0	0	0	0	0	0	0	0
RC8 (n= 25)	7	13	7	9	20	4	0	0	0	9	0	0	0	0	0	0	0	0	0
RC7 (n=7)	0	0	0	0	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0
RC6 (n= 24)	16	8	0	0	9	10	6	1	2	0	0	0	0	0	0	0	0	0	0
RC5 (n= 34)	10	3	5	6	25	10	0	6	4	14	0	0	0	0	0	0	0	0	0
RC4 (n= 55)	6	12	14	12	37	12	0	1	0	15	0	0	0	0	0	0	0	0	0
RC3 (n= 15)	7	0	4	1	12	2	1	0	8	5	0	0	0	0	0	0	0	0	0
RC2 (n=51)	20	16	8	0	0	0	0	0	0	4	0	0	0	0	0	0	0	0	0
RC1 (n=54)	39	33	6	14	34	14	8	13	4	23	2	0	0	0	33	0	3	2	0

Figure 3.18: Various resistance genes found in *K. pneumoniae* isolates from different regional centres across India

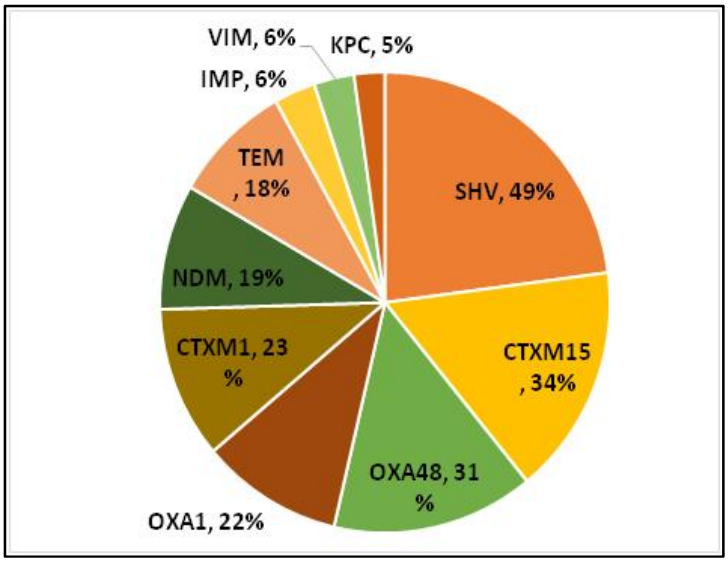


Figure 3.19: Percentage positivity of AMR associated genetic determinants in *K. pneumoniae*

Table 3.16: Percentage positivity of resistant genes in *K. pneumoniae* from each centre

Regional Centers	Antimicrobial Resistance Genes									
	CTXM15	OXA48	TEM	NDM	SHV	OXA1	IMP	VIM	KPC	CTXM1
RC1	72%	61%	11%	26%	63%	26%	15%	24%	7%	43%
RC2	39%	31%	16%	0%	0%	0%	0%	0%	0%	8%
RC3	47%	0%	27%	7%	80%	13%	7%	0%	53%	33%
RC4	11%	22%	25%	22%	67%	22%	0%	2%	0%	27%
RC5	29%	9%	15%	18%	74%	29%	0%	18%	12%	41%
RC6	67%	33%	0%	0%	38%	42%	25%	4%	8%	0%
RC7	0%	0%	0%	0%	71%	0%	0%	0%	0%	0%
RC8	28%	52%	28%	36%	80%	16%	0%	0%	0%	36%
RC9	0%	22%	34%	39%	93%	27%	0%	0%	0%	32%
RC10	50%	0%	100%	0%	50%	0%	0%	0%	0%	0%
RC12	34%	49%	31%	29%	53%	31%	0%	7%	0%	17%
RC13	27%	13%	0%	33%	0%	7%	0%	0%	0%	0%
RC14	41%	16%	0%	8%	62%	24%	0%	3%	3%	0%
RC15	82%	6%	24%	6%	76%	47%	41%	18%	18%	47%
RC16	33%	14%	10%	0%	5%	24%	10%	5%	5%	5%
RC18	12%	36%	14%	33%	10%	5%	21%	7%	7%	19%
RC19	11%	11%	11%	11%	16%	11%	5%	5%	0%	0%
RC21	47%	50%	24%	11%	37%	32%	3%	0%	0%	42%

The comparison between the *E. coli* (n= 716) and *K. pneumoniae* (n=556) isolates received from regional centres (n= 19) in 2022 revealed the presence of resistance genes more in *Klebsiella* isolates than *E. coli* (Figure 3.20).

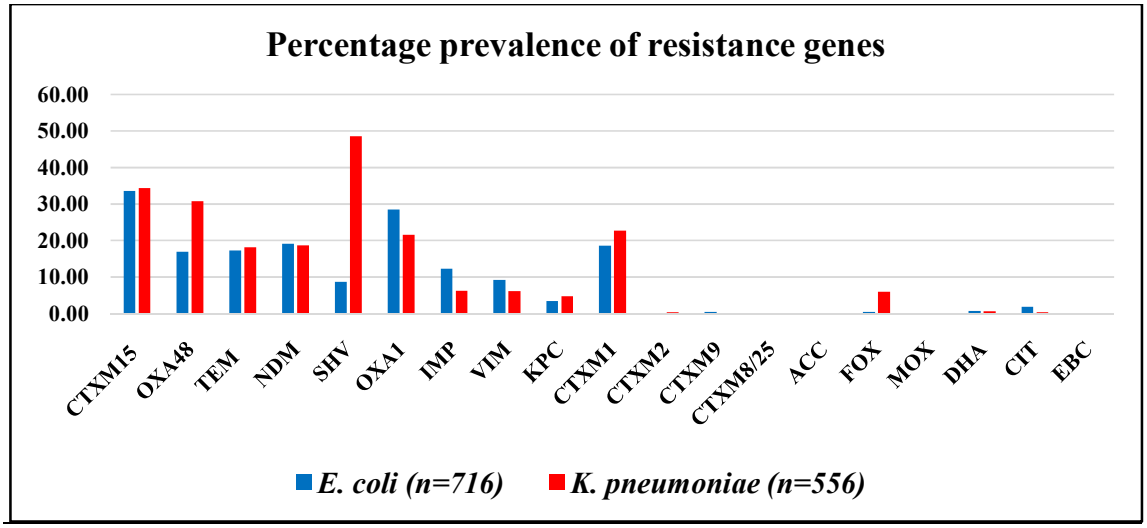


Figure 3.20: Comparison of resistance genes present in *E. coli* and *K. pneumoniae* isolates from regional centres across India

Chapter 4. Typhoidal Salmonella

Typhoid fever poses a significant health burden in developing nations, leading to high rates of illness and death. The problem is exacerbated by the increasing resistance to antibiotics, which complicates the treatment of this disease.

Accurate diagnosis and timely administration of appropriate antibiotics are crucial for effective treatment. The impact of typhoid fever on individuals and communities is profound. However, diagnosing typhoid fever is challenging because its symptoms are similar to those of other febrile illnesses. To determine the most effective treatment, it is essential to rely on culture and susceptibility test results. Understanding the history of antibiotic resistance reveals that the introduction of antibiotics has led to a gradual acquisition of resistance. Initially, multidrug-resistant strains (resistant to chloramphenicol, ampicillin, and co-trimoxazole) emerged, leading to fluoroquinolones being designated as the first-line drugs.

Presently, third-generation cephalosporins and azithromycin are the available treatment options for multidrug-resistant and fluoroquinolone-resistant typhoid fever. However, recent outbreaks of extensively drug-resistant (XDR) strains in Asian countries have severely limited these treatment choices. The emergence of these extensively drug-resistant typhoidal Salmonellae poses a global threat. Therefore, continuous surveillance and focused attention are required to prevent their spread. With the elimination of geographical boundaries due to travel and the dissemination of drug-resistant isolates, addressing this issue has become more crucial than ever.

Overall, Salmonella Typhi, commonly referred to as S. Typhi, is the primary causes of typhoid fever in India, followed by Salmonella Paratyphi A (S. Paratyphi A). In 2017, the highest isolation rate was observed in West India (4.8%), however, in 2018, there was a shift in the highest isolation rate, which moved to Central India with a significant increase to 10.9%. In 2019, the maximum isolation of S. Typhi was once again observed in West India, but the rate had slightly increased to 5.9%. The year 2020, which coincided with the COVID-19 pandemic, saw the highest isolations of S. Typhi reported from West India, constituting 6.2% of the cases. This period may have been influenced by various factors related to the pandemic, impacting disease prevalence. In 2021, Central India experienced the highest isolation rate of S. Typhi at 2.5%, marking a shift from the previous years' trends. Finally, in 2022, the maximum isolation was recorded in North India, indicating a change in the distribution pattern once again.

A total of 702 typhoidal Salmonellae cases were reported across India in 2022 (Table 4.1). Among them, 584 cases were positive for Salmonella Typhi, while 118 cases were positive for Salmonella Paratyphi A. The antimicrobial susceptibility results for Salmonella Typhi revealed that 94% of isolates were susceptible to ampicillin, 93% were susceptible to trimethoprim-sulfamethoxazole, and 95% were susceptible to chloramphenicol. Additionally, 3rd generation cephalosporins exhibited a susceptibility rate of 94% in 2022, whereas fluoroquinolones showed a susceptibility rate of only 3%.

Azithromycin, on the other hand, exhibited a susceptibility rate of 97% during the same period.

Table 4.1: Susceptibility pattern of *Salmonella* species from blood

AMA	*S. Typhi* n=584	*Salmonella Paratyphi A* n=118
Ampicillin	510 / 542 (94.1)	109 / 113 (96.5)
Azithromycin	520 / 537 (96.8)	*0 / 0
Cefixime	416 / 440 (94.5)	72 / 80 (90)
Ceftriaxone	534 / 569 (93.8)	111 / 115 (96.5)
Chloramphenicol	473 / 499 (94.8)	107 / 109 (98.2)
Ciprofloxacin	18 / 590 (3.1)	1 / 121 (0.8)
Levofloxacin	7 / 108 (6.5)	*1 / 6
Ofloxacin	4 / 69 (5.8)	*0 / 0
Pefloxacin	35 / 188 (18.6)	*3 / 23
Trimethoprim-sulfamethoxazole	537 / 578 (92.9)	117 / 118 (99.2)

*Azithromycin sensitivity cut off values are not given in CLSI for *Salmonella Paratyphi A*

Salmonella Paratyphi A exhibited high susceptibility rates to various antimicrobial agents in 2022. Trimethoprim-sulfamethoxazole demonstrated a susceptibility rate of 99%, chloramphenicol had 98%, and ampicillin showed a rate of 97%. Additionally, 3rd generation cephalosporins were effective against Salmonella Paratyphi A with a susceptibility rate of 97%. However, susceptibility to ciprofloxacin, a fluoroquinolone, was notably low at only 1% during the same period. These findings highlight the antimicrobial resistance patterns of Salmonella Paratyphi A and emphasize the limited effectiveness of ciprofloxacin in treating infections caused by this pathogen.

Salmonella Typhi

The susceptibility data reveals the sensitivity patterns of various antimicrobial agents against Salmonella Typhi in different regions of India (Table 4.2). In the South region, ampicillin exhibited a susceptibility rate of 86%, while in the North region; it was 90%. The West region reported 92% susceptibility, and across India the overall susceptibility rate was 94%. For trimethoprim-sulfamethoxazole, the West region showed 94% susceptibility, the South region had a rate of (26/26), the North region had a rate of 92%. Across India, Chloramphenicol demonstrated a susceptibility rate of 95%, in the West region it was 88.2% while in the South region it was 96% and 96.8% in the North region. The susceptibility patterns of cephalosporins varied across different regions of India. Ceftriaxone displayed a susceptibility rate of 93.8% nationwide, with six resistant

strains identified in the South region. However, all S. Typhi isolates from the North and Central regions exhibited 97.9% and 95.4% susceptibility followed by 89.9% susceptibility from West and (25/28) East. Azithromycin, on the other hand, demonstrated 100% susceptibility in the North, and Central, it was (21/26) from South and 94% West region.

Ciprofloxacin susceptibility was found to be (2/27) in the South region and (8/184) in the West region. Across India, the overall ciprofloxacin susceptibility rate was 3%. The observed findings underscore the significance of regional disparities in antimicrobial susceptibility patterns, emphasizing the emergence of resistance, especially in cephalosporins and fluoroquinolones. Accurate understanding of these trends plays a crucial role in guiding effective treatment approaches and facilitating surveillance measures to address antimicrobial resistance in Salmonella Typhi infections.

Table 4.2: Susceptibility pattern of *S.* Typhi from Blood across different regions of India

	National (n=584)	North (n=294)	South (n=26)	West (n=188)	Central (n=45)	East (n=31)
Ceftriaxone	534/569 (93.8)	286/292 (97.9)	*20/26	161/179 (89.9)	42/44 (95.4)	*25/28
Azithromycin	520/537 (96.8)	291/291 (100)	*21/26	158/168 (94.0)	41/41 (100)	*9/11
Cefixime	416/440 (94.5)	280/290 (96.5)	*15/20	99/104 (95.1)	*1/1	*21/25
Ampicillin	510/542 (94.0)	283/292 (90.0)	*19/22	144/156 (92.3)	41/43 (95.3)	*23/29
Chloramphenicol	473/499 (94.7)	279/288 (96.8)	*22/23	105/119 (88.2)	40/40 (100)	*27/29
Trimethoprim-sulfamethoxazole	537/578 (92.9)	268/291 (92.0)	*26/26	173/185 (93.5)	43/44 (97.7)	27/32 (84.3)
Pefloxacin	35/188 (18.6)	13/70 (18.5)	*9/18	10/81 (12.3)	*0/1	*3/18
Levofloxacin	7/108 (6.4)	7/69 (10.1)	*0/2	*0/26	*0/2	*0/9
Ciprofloxacin	18/590 (3.0)	8/302 (2.6)	*2/27	8/184 (4.3)	0/45 (-)	0/32 (-)

Table 4.3 and Fig. 4.1 represent yearly susceptibility trends of Salmonella Typhi isolated from blood. Antimicrobial susceptibility for ampicillin in S. Typhi has increased from 91.9% in 2017 to 94% in 2022. Chloramphenicol susceptibility has increased initially from 2017 to 2020 and then followed by a slight decrease in 2021, where susceptibility was reported 95.7% and 94.7% in 2022. Trimethoprim-sulfamethoxazole susceptibility was 94.4% in 2017 and 96% in 2020- 2021 and further decreased to 92.9% in 2022. Ceftriaxone and cefixime susceptibility were found to be consistent for 5 years i.e. from 98.5% to 99.5% in 2021. During 2022, susceptibility to 3rd generation cephalosporin has decreased in comparison to previous years. It was 93.8% for ceftriaxone and 94.5% for cefixime. Ciprofloxacin sensitivity has decreased from 11.6% in 2017 to 3% in 2022.

Table 4.3: Yearly susceptibility trends of *S.* Typhi from Blood

AMA	Year 2017 Total n=345	Year 2018 Total n=580	Year 2019 Total n=728	Year 2020 Total n=206	Year 2021 Total n=293	Year 2022 Total n=584
Ampicillin	305/332 (91.9)	551/576 (95.7)	658/703 (93.6)	192/197 (97.5)	278/290 (95.9%)	510 / 542 (94.1)
Ceftriaxone	329/334 (98.5)	531/541 (98.2)	645/658 (98)	192/193 (99.5)	280/281 (99.6)	534 / 569 (93.8)
Cefixime	221/223 (99.1)	344/349 (98.6)	434/448 (96.9)	157/158 (99.4)	209/212 (98.6)	416 / 440 (94.5)
Azithromycin	266/278 (95.7)	497/506 (98.2)	547/568 (96.3)	163/166 (98.2)	212/213 (99.5)	520 / 537 (96.8)
Ciprofloxacin	35/302 (11.6)	29/440 (6.6)	35/501 (7)	8/162 (4.9)	40/204 (19.6)	18 / 590 (3.0)
Levofloxacin	*0/3	*5/18	3/35 (8.6)	*4/12	9/30 (30)	7 / 108 (6.4)
Trimethoprim-sulfamethoxazole	322/341 (94.4)	552/575 (96)	693/718 (96.5)	194/202 (96)	266/278 (95.7)	537 / 578 (92.9)
Chloramphenicol	267/278 (96)	541/560 (96.6)	582/611 (95.3)	180/185 (97.3)	246/257 (95.7)	473 / 499 (94.7)

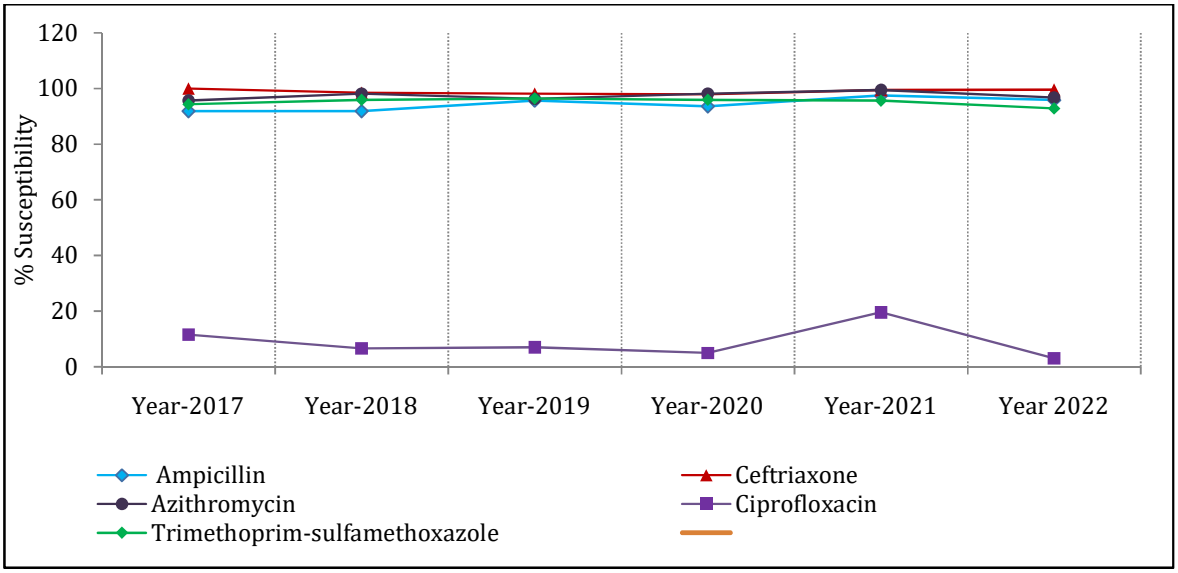


Figure 4.1: Yearly susceptibility trends of *S.* Typhi from blood

To analyse the changing trend of ciprofloxacin minimum inhibitory concentration (MIC) over a period of 9 years, the data was categorized into two groups: 2014-2016 and 2017-2019. Additionally, the individual years of 2020, 2021, and 2022 were examined independently, as shown in Figure 4.2. This division allowed for a more detailed understanding of any variations in ciprofloxacin MIC values over time. Notably, the minimum MIC value (ranging from 0.016 µg/ml to 0.047 µg/ml) was not reported in the strains isolated between 2014 and 2019. However, this minimum MIC value was observed in the strains isolated in 2020. Furthermore, the maximum MIC range of 256

μg/ml was reported from 2020 onwards. It is important to highlight that the number of strains exhibiting higher MIC values has increased in both 2021 and 2022, indicating a potential shift towards reduced susceptibility to ciprofloxacin in recent years.

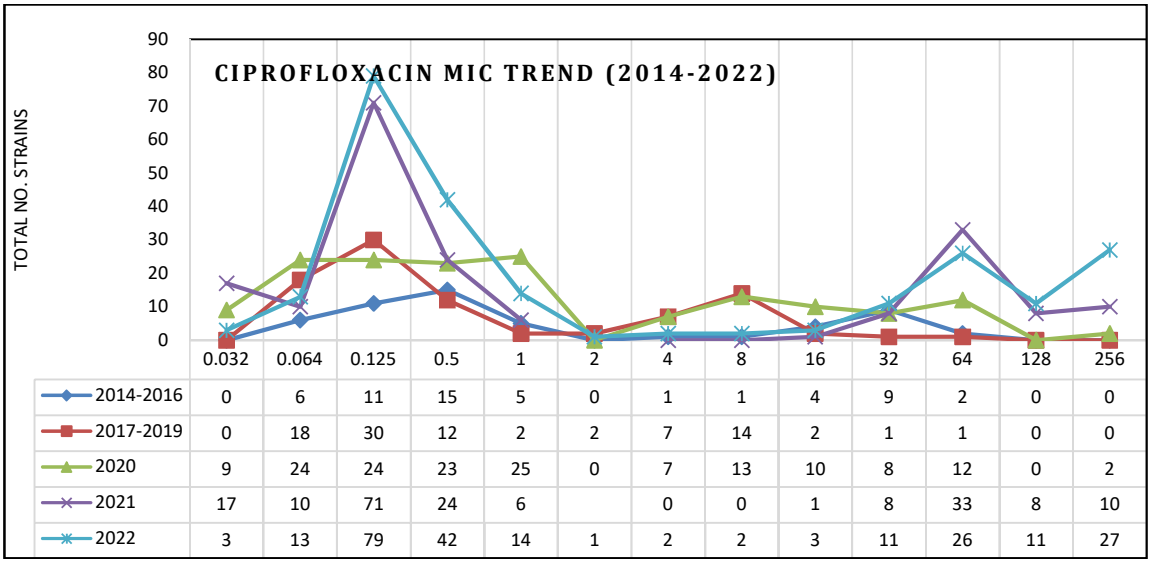
Although the majority of S. Typhi isolates showed intermediate sensitivity to ciprofloxacin in the years 2014-2016 (45/77, 58%) and 2017-2019 (113/160, 71%), these were considered as resistant, resulting in a total ciprofloxacin resistance of 92% (71/77) and 93% (149/160) respectively for those periods. In 2020, the resistance rate increased significantly, with 191/194 (98.4%) typhoidal Salmonella isolates showing resistance to ciprofloxacin. In 2021, 168/263 (63.8%) isolates exhibited intermediate sensitivity, and 66/263 (25%) were classified as resistant, resulting in a total ciprofloxacin resistance of 88.9% (234/263). Notably, there has been a slight increase of 10% in ciprofloxacin susceptibility during this period.

When comparing the data from 2022 to previous years, a significant rise in ciprofloxacin non-susceptibility was observed. In comparison to 2021, there was a decrease in ciprofloxacin susceptibility of 1.4% (5/344) among the isolates. The majority of isolates, 70.3% (242/344), exhibited intermediate MIC, indicating reduced effectiveness of ciprofloxacin. Additionally, 28% (97/344) of the isolates were classified as non-susceptible to ciprofloxacin, indicating high levels of resistance.

In order to examine the trend of ceftriaxone creeping minimum inhibitory concentration (MIC) over a 9-year period, the data was divided into two groups for 6 years: 2014-2016 and 2017-2019 and the individual years of 2020, 2021, and 2022 were analysed separately for any recent change (Fig 4.3). During the period of 2014-2016, maximum number of isolates showed a minimum inhibitory concentration (MIC) range of 0.032-0.064 μg/ml. An equal number of isolates exhibited an MIC range of 0.125-0.19 μg/ml, with a slight increase in isolates having an MIC of 0.25 μg/ml followed by five ceftriaxone resistant Salmonella Typhi reported in 2016 from hospital from, Mumbai. In the subsequent period of 2017-2019, a similar pattern was observed, although there was a slight decrease in the number of isolates with an MIC of 0.19 μg/ml and an increase in isolates with an MIC of 0.25 μg/ml. Three ceftriaxone resistant isolates were observed during 2018 and 2019. In 2020, a notable shift occurred in the distribution of isolates with higher MIC values compared to previous years. The majority of isolates exhibited an MIC range of 0.064 μg/ml to 0.25 μg/ml. None of the ceftriaxone resistant isolate was observed during 2020 and 2021. However, in the following years (2021 and 2022) there was a reversal in this trend, with a shift towards lower MIC values. The maximum number of isolates fell within the range of 0.032-0.064 μg/ml MIC. It is worth noting that in 2022, three isolates were reported as resistant to ceftriaxone.

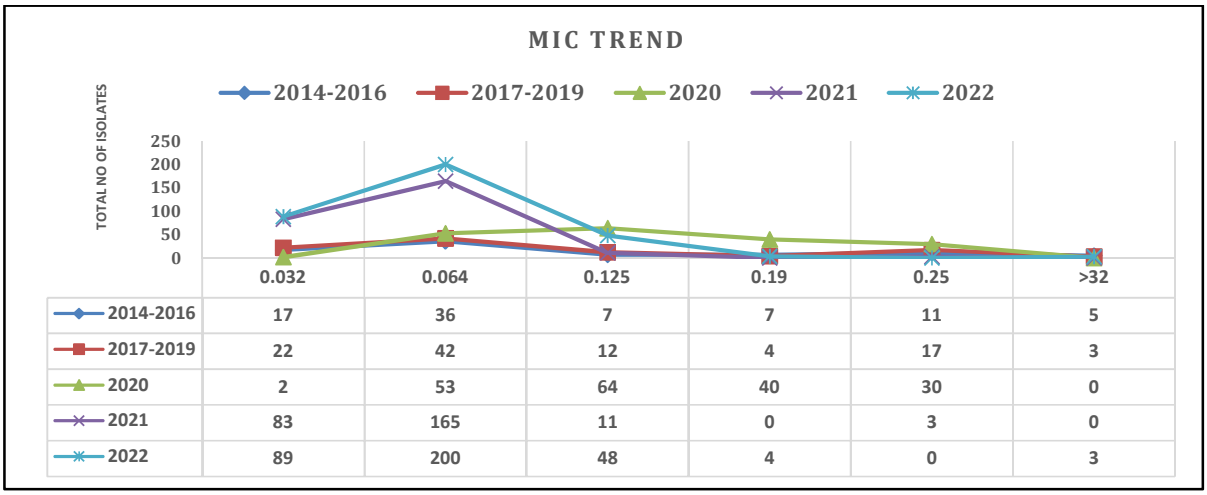
These findings suggest a fluctuation in the MIC values of ceftriaxone over the years, with a notable shift towards higher MIC values in 2020 and a subsequent return to lower MIC values in 2021 and 2022. The emergence of ceftriaxone-resistant isolates during the study period highlights the need for continued monitoring of antimicrobial resistance patterns in *Salmonella* Typhi infections.

To understand the trend of Azithromycin MIC over a 9-year period, the data was divided into two groups: 2014-2016 and 2017-2019. Additionally, the individual years of 2020, 2021, and 2022 were analysed separately (Fig. 4.4) for any recent change. In the years 2014-2016 and 2017-2019, the majority of isolates showed a maximum concentration (MIC) range of 2-4 µg/ml. However, in the subsequent years, there was a shift in the distribution, with the maximum number of isolates falling in the 4-16 µg/ml MIC range. Notably, in 2020 and 2021, there were reports of isolates with a MIC range of 32 µg/ml. While the majority of strains exhibited MIC values ranging from 3 µg/ml to 16 µg/ml, there has also been an emergence of strains with higher MIC values. These findings indicate a changing pattern of azithromycin susceptibility, with an increasing number of isolates exhibiting higher MIC values over time.



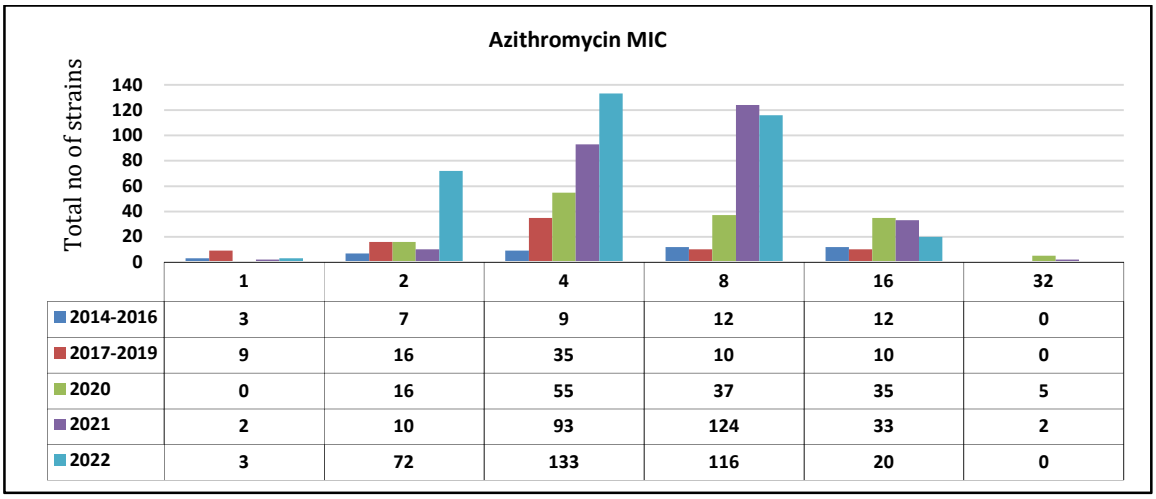
	0.032	0.064	0.125	0.5	1	2	4	8	16	32	64	128	256
2014-2016	0	6	11	15	5	0	1	1	4	9	2	0	0
2017-2019	0	18	30	12	2	2	7	14	2	1	1	0	0
2020	9	24	24	23	25	0	7	13	10	8	12	0	2
2021	17	10	71	24	6		0	0	1	8	33	8	10
2022	3	13	79	42	14	1	2	2	3	11	26	11	27

Figure 4.2: Ciprofloxacin MIC trends in Salmonella Typhi from pan India over a period of nine years



	0.032	0.064	0.125	0.19	0.25	>32
2014-2016	17	36	7	7	11	5
2017-2019	22	42	12	4	17	3
2020	2	53	64	40	30	0
2021	83	165	11	0	3	0
2022	89	200	48	4	0	3

Figure 4.3: MIC trend for Ceftriaxone in S. Typhi from Pan India over a period of nine years



	1	2	4	8	16	32
2014-2016	3	7	9	12	12	0
2017-2019	9	16	35	10	10	0
2020	0	16	55	37	35	5
2021	2	10	93	124	33	2
2022	3	72	133	116	20	0

Figure 4.4: Azithromycin MIC trend in S. Typhi over a period of nine years from Pan India

Salmonella Paratyphi A

The antibiotic susceptibility pattern of S. Paratyphi A from 2017 to 2022 reveals the consistent pattern i.e. from 95% to 96.4% except in 2019 where 90% susceptibility was reported (Table 4.4 and Figure 4.5). Chloramphenicol and trimethoprim - sulmethoxazole susceptible pattern was also consistent from 2017 to 2022.
Ciprofloxacin sensitivity has decreased significantly from 10% in 2017 to 0.8% in 2022. Ceftriaxone antimicrobial susceptibility has increased from 95% in 2017 to 100% in 2021 and further 96.5% in 2022. Cefixime was 96.3% susceptible in 2017 followed by 100% in 2021. During 2022 it was 90% (72/80) susceptible. Azithromycin was not analysed as azithromycin susceptibility cutoff for S. Paratyphi A are not given in CLSI.

Table 4.4: Yearly susceptibility trends of S.Paratyphi A from blood

AMA	Year 2017 Total n=41	Year 2018 Total n=125	Year 2019 Total n=147	Year 2020 Total n=52	Year 2021 Total n=58	Year 2022 Total n=118
Ampicillin	38/40 (95)	122/125 (97.6)	125/138 (90.6)	42/46 (91.3)	55/57 (96.5%)	109 / 113 (96.4)
Ceftriaxone	38/40 (95)	121/124 (97.6)	139/142 (97.9)	47/47 (100)	57/57 (100%)	111 / 115 (96.5)
Cefixime	26/27 (96.3)	105/105 (100)	105/107 (98.1)	32/32 (100)	45/45 (100%)	72 / 80 (90.0)
Ciprofloxacin	4/40 (10)	1/111 (0.9)	1/86 (1.2)	1/31 (3.2)	4/46 (8.7%)	1 / 121 (0.8)
Levofloxacin	*0/2	*0/5	0/25 (0)	*0/9	*0/8	*1 / 6
Trimethoprim-sulfamethoxazole	41/41 (100)	123/123 (100)	144/145 (99.3)	47/49 (95.9)	54/55 (98.2%)	117 / 118 (99.1)
Chloramphenicol	30/30 (100)	121/121 (100)	128/128 (100)	48/49 (98)	54/57 (94.7%)	107 / 109 (98.1)

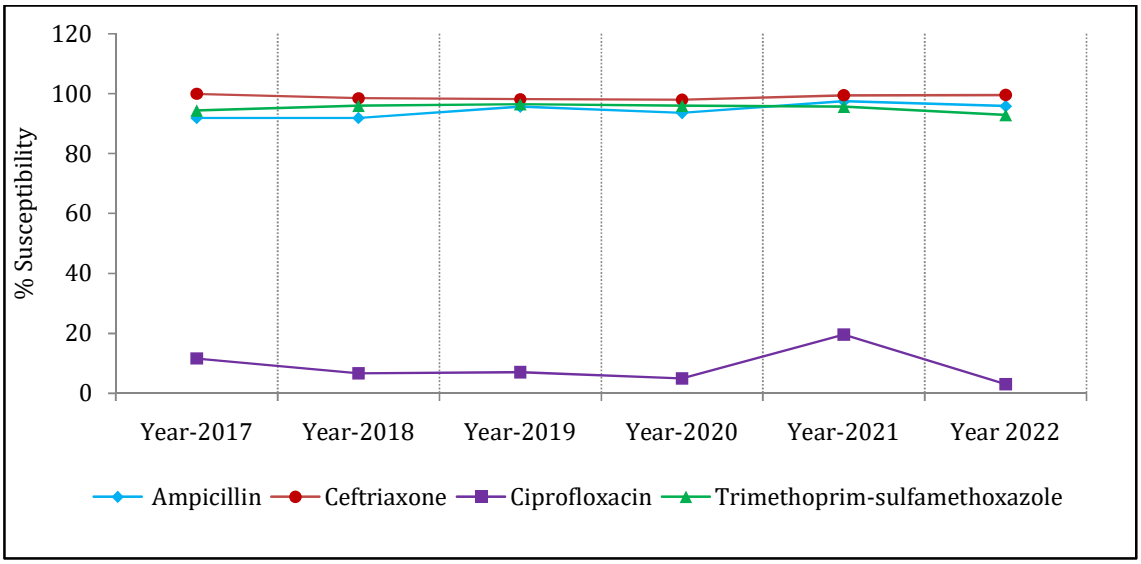
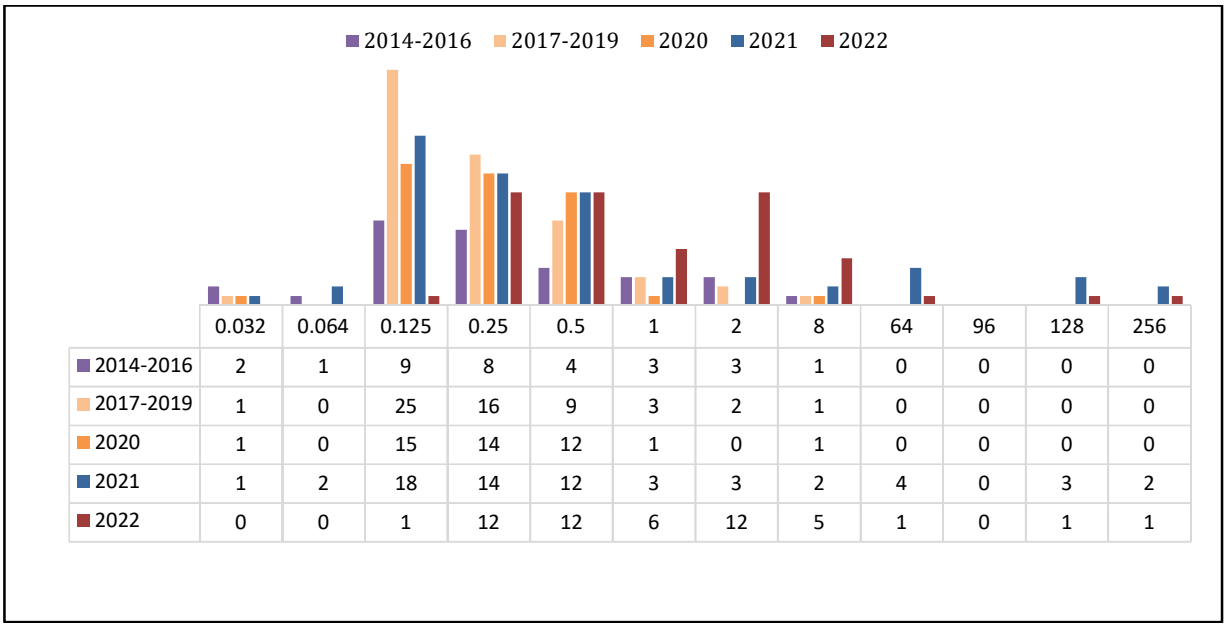


Figure 4.5: Yearly susceptibility trends of S. Paratyphi A from Blood

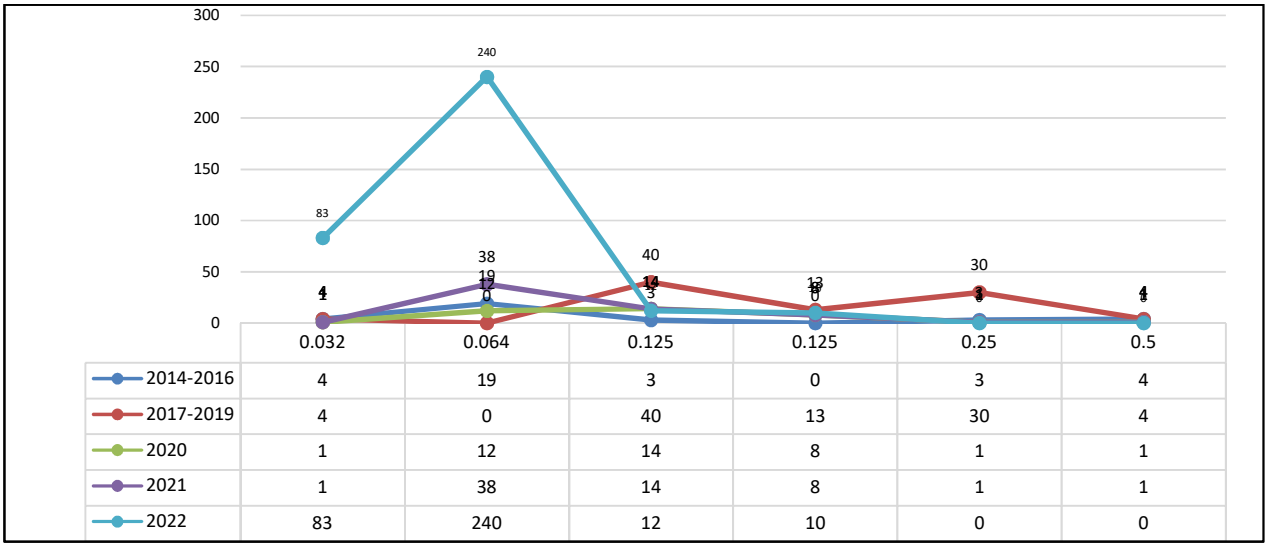
Among Salmonella Paratyphi A, the majority of isolates exhibited an intermediate MIC range (0.125-0.5 µg/ml) for ciprofloxacin. However, a significant shift occurred in 2021 and 2022, with the emergence of isolates showing higher MIC ranges of 128 µg/ml to 256 µg/ml. In 2022, 50% of the isolates exhibited intermediate susceptibility, while the remaining 50% showed complete non-susceptibility to fluoroquinolones (Figure 4.6).

In S. Paratyphi A, both MIC50 and MIC90 values for ciprofloxacin have increased over time. In 2014, the MIC50 was observed to be 0.38 µg/ml, which gradually increased to 0.5 µg/ml by 2019. Since 2020, the MIC50 has remained stable at 0.75 µg/ml, while the MIC90 has continued to rise, reaching 6 µg/ml in 2022. It is noteworthy that fluoroquinolone resistance is higher in S. Paratyphi A compared to S. Typhi. During the period of 2014-2016, the majority of isolates fell within the MIC range of 0.064 µg/ml. However, there was a noticeable shift towards higher MIC values during 2017-2019, with the maximum number of isolates falling within the range of 0.125-0.25 µg/ml. In the years 2020 and 2021, the MIC range for the maximum number of isolates was observed to be 0.064-0.125 µg/ml. In 2022, there was a shift towards lower MIC values, specifically within the range of 0.032-0.064 µg/ml. It is important to note that some isolates with creeping MIC values were identified. None of the isolates, however, exhibited resistance to ceftriaxone (Figure 4.7). It is important to acknowledge the presence of isolates with creeping MIC values, indicating a potential for future resistance development. However, none of the isolates exhibited resistance to ceftriaxone during the study period.



	0.032	0.064	0.125	0.25	0.5	1	2	8	64	96	128	256
2014-2016	2	1	9	8	4	3	3	1	0	0	0	0
2017-2019	1	0	25	16	9	3	2	1	0	0	0	0
2020	1	0	15	14	12	1	0	1	0	0	0	0
2021	1	2	18	14	12	3	3	2	4	0	3	2
2022	0	0	1	12	12	6	12	5	1	0	1	1

Figure 4.6: Ciprofloxacin MIC trends in Salmonella Paratyphi A from Pan India over a period of nine years



	0.032	0.064	0.125	0.125	0.25	0.5
2014-2016	4	19	3	0	3	4
2017-2019	4	0	40	13	30	4
2020	1	12	14	8	1	1
2021	1	38	14	8	1	1
2022	83	240	12	10	0	0

Figure 4.7: Ceftriaxone creeping MIC in S. Paratyphi A from pan India over a period of nine years

Clinical relevance and treatment guidance

Considering the increasing resistance to antibiotics, the analysis of antimicrobial susceptibility results highlights the importance of accurate diagnosis and appropriate antibiotic treatment for typhoid fever.

The isolation trends revealed a dynamic pattern of S. Typhi prevalence and geographical distribution in India over a five-year period from 2017 to 2022. It is also important to

highlight that the number of strains exhibiting higher MIC values has increased in both 2021 and 2022, indicating a potential shift towards reduced susceptibility to ciprofloxacin in recent years.

The historical development of antibiotic resistance demonstrates the gradual acquisition of resistance, leading to the designation of fluoroquinolones as the first-line drugs due to the emergence of multidrug-resistant strains.

Currently, third-generation cephalosporins and azithromycin are the available treatment options for multidrug-resistant and fluoroquinolone-resistant typhoid fever. However, the emergence of extensively drug-resistant (XDR) strains in Asian countries has severely limited treatment choices. Continuous surveillance and focused attention are necessary to prevent the spread of these XDR strains, considering the elimination of geographical boundaries due to travel and the dissemination of drug-resistant isolates.

In a small percentage of strains, susceptibility was observed despite the presence of resistance genes, particularly for chloramphenicol and cotrimoxazole. Notably, no resistance to ceftriaxone or the presence of the CTXM-15 gene was detected in any typhoidal strain, while OXA-232 and TEM-1 were detected in three Salmonella species. Furthermore, none of the studied isolates exhibited resistance genes associated with azithromycin, indicating susceptibility to this antibiotic. Due to the small numbers of isolates from each regional center, no significant regional variations were observed in the distribution of resistance genes. However, when comparing different regions of India (East, West, North, and South), the presence of gyrase mutations other than S83F was observed primarily in strains from North and West India. On a national scale, the distribution of fluoroquinolone resistance mechanisms and genes exhibited variability.

Predominantly, 96% (74/77) mutation were present in gyrase and 38% (29/77) were reported in topoisomerase IV. In gyrase, mutation at S83F was the most common and accounted for 80% (60/77) of all mutations while S83Y mutations were reported in 21% (16/77) isolates followed by 27% (21/77) mutations at D87N. Distribution of mutation in topoisomerase IV accounted for 32% (25/77) in parC gene at S80I and 1% (1/77) in parE gene at L416F.

Strains with intermediate ciprofloxacin susceptibility had single mutation at gyrA S83F or double mutation at gyrA S83F and parC S80I of the QRDR. While strains with higher ciprofloxacin MIC had triple mutation at gyrA at S83F, D87N and parC S80I or parE D420N. Mutation in parE gene at L416F, was also found in one isolate each with ciprofloxacin intermediate MIC.

Therefore, not all strains showed an association of genetic mutations and phenotypic resistance and supporting the fact that mere presence of gene may not be sufficient to impart clinical resistance and many factors may come into play including expression of gene and antibiotic selection pressure while the patient is on treatment. Region-wise there was no significant difference in the distribution of mutation and antibiotic susceptibility pattern. However, the presence of resistance mutation in susceptible strains is a cause of concern because it can lead to their expression on exposure to fluoroquinolones and subsequent emergence of ciprofloxacin resistance. Therefore, the

genotypic studies and continuous surveillance of antimicrobial resistance is necessary to understand the mechanism and epidemiology of resistance.

The antimicrobial susceptibility analysis provides variable sensitivity patterns of S. Typhi and S. Paratyphi A to various antibiotics. While S. Typhi shows higher sensitivity rates to some antibiotics, such as ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole, its sensitivity to ciprofloxacin has decreased over the years. The susceptibility patterns of S. Paratyphi A also exhibit variations across different antibiotics. These findings accentuate the importance of continued surveillance and the need for alternative treatment strategies to combat the rising levels of antibiotic resistance in typhoid fever.

Characterisation of resistance mechanism

The relationships between resistance gene content identified from WGS was deciphered with the drug resistance profile for each corresponding clinical isolate (phenotype). 25% of all representative samples from all centers were selected. The following observations were made on the basis of WGS analysis. Total 105 isolates were selected for WGS which includes 65 Salmonella Typhi, 26 *Salmonella* Paratyphi A and 14 *Salmonella* Species. In Salmonella Typhi, the ampicillin resistance is associated with the presence of beta-lactam genes which were observed in 4.6% strains (3/65) by WGS. In all the strains, blaTEM-1D beta-lactam resistance gene was observed. The resistance genes encode for the predominant plasmid-mediated β-lactamases of Enterobacterales. An earlier report for amoxicillin resistance in Salmonella from pan-India was 2%. In case of Salmonella Paratyphi A, all strains were sensitive. Other gene responsible for resistance rsmA, sdi A and marA were present. Chloramphenicol resistance determinants were observed in 6% (4/65) Salmonella Typhi strains by WGS. All non-susceptible strains harboured catA1 gene which encodes chloramphenicol acetyltransferase enzyme causing chloramphenicol resistance by chemical modification of the drug molecule, whereas ten isolates harboured the catI genes. Our findings are consistent with other studies reporting chloramphenicol susceptibility in *S. enterica.*

Trimethoprim-sulfamethoxazole were considered in combination for treatment as the first-line drug, co-trimoxazole. Out of 65 strains, trimethoprim resistance determining genes were found in 6% (4/65). Likewise, gene sul1 and sul2, encoding dihydropteroate synthases known to disseminate sulfamethoxazole resistance, were also detected in 6% (4/65).

Molecular determinants of resistance to fluoroquinolone including ciprofloxacin and pefloxacin antibiotics encoded by gyrA and parC, genes were detected in 72.3% strains (47/65) by WGS. Mutations in gyrA and parC, was observed in 44.6% (21/47) followed by only gyrA mutation in 48.9% (23/47) isolates. The identified genes were associated with mutations in Quinolone Resistance Determining Region of DNA gyrase enzyme, the binding site for fluoroquinolone. Antimicrobial resistance to fluoroquinolones was 72.3% by both disc diffusion and E-test method. MIC distribution ranged between 2–

256 mg/L and peaked at 12 mg/L. DNA Gyrase A mutations at position 83 (Ser-83→Phe, Ser-83→Tyr and Asp 87→ Phe) are the most prevalent resistance mechanisms for Fluoroquinolone in India, followed by Ser-80→Ile substitution in parC gene. Highly non-susceptible strains (with ciprofloxacin MIC > 8 mg/L) were found to be double or triple mutants with mutations in gyrA83, gyrA87 and parC80. Strains with moderate resistance to ciprofloxacin possessed single mutations in DNA gyrA gene at Ser83 position.

In case of Salmonella Paratyphi A, phenotypically 80.7% (21/26) strains were intermediate and 15.3% (4/26) were resistant to fluoroquinolone. Mutations in gyrA gene were detected in 100% of the strains. Double mutation in gyrAS83F and D87N was observed in one strain followed by triple mutation in only one strain. Other fluoroquinolone resistance mechanism CRP, acrR, marR, soxR, acrB, emrA, emrB, mdtk and rsmA were also present.

Although all the strains were cephalosporin sensitive, mutations in PBP3 gene at D350N, S357N, *Escherichia coli* ampC1 beta-lactamase, and *Escherichia coli* ampH beta-lactamase gene was present in all tested isolates. This clearly raises an alarm towards the judicial use of these antibiotics. All isolates were azithromycin susceptible. Other genes responsible for macrolide resistance nalD, KpnE, CRP were also observed by WGS. *S.* Typhi can demonstrate resistance to multiple antibiotics by acquiring new resistance genes through horizontal genes transfer (HGT). The acquired antimicrobial resistance genes including aac(6')-Iaa, AAC(6')-Iy, aadA1, aph(3")-Ib, aph(6)-Id, strA, and strB that provided resistance to aminoglycosides were observed in 100% (89/89) isolates. In addition, S. Typhi isolates harboured the genes baeR, emrb, H-NS, marA, mdfA, mdtK, msbA, acrA, emrR, kpnE, kpnF, marR, sdiA, crp, soxR, and soxS that could confer multidrug resistance and were detected in all 133 strains. The mds ABC complex, a multidrug transporter of Salmonella, comprising mdsA, mdsB, and mdsC units was also observed in all isolate. The mdsABC complex is recognized to contribute resistance against a diverse set of drugs and toxins. The identified multi-efflux pump mdtK gene, conferring resistance against the drugs, acriflavin, doxorubicin and norfloxacin, was observed in 100% of the isolates. The gene, sdiA, a multi-drug resistance pump regulator for AcraB, was also present in 100% of the isolates.

The pathogenicity and resistance profile of the various Salmonella isolates can be attributed to the presence of identified genes.

Multi-locus sequence typing (MLST) profile disclosed low genetic variation in housekeeping genes (aroC, dnaN, hemD, hisD, purE, sucA, and thrA) among Salmonella Typhi, Salmonella Paratyphi A and other *Salmonella* isolates. Two different sequence types (STs) including ST1 and ST2 were observed in Salmonella Typhi while Salmonella Paratyphi A was divided in ST 85 and ST129 respectively. ST1 was the predominant type, accounting for 70% of examined strains, whereas ST2 was observed in 29% of the strains (Table 4.5). In case of *S.* Paratyphi A, ST85 was observed in 3 and ST129 was observed in 10 isolates. S*.* Typhimurium was grouped in to ST19, ST313, ST36 followed by *S.* enteritidis grouped as ST11. *Salmonella* Alachua was grouped as ST2061 and S.

Bovismorbificans was grouped as ST2345. Presence of different type of plasmids (IncFIB(S)/IncFII(S), IncFI (pN55391), IncX1) was also observed in Salmonellae species. In summary, our findings demonstrate a consistent correlation between the presence of resistance-associated genes or mutations and the observed antimicrobial susceptibility patterns.

MLST:

Multi-locus sequence typing (MLST) profile disclosed low genetic variation in housekeeping genes (aroC, dnaN, hemD, hisD, purE, sucA, and thrA) among Salmonella Typhi, Salmonella Paratyphi A and other *Salmonella isolates*. Two different sequence types (STs) including ST1 and ST2 were observed in Salmonella Typhi while Salmonella Paratyphi A was divided in ST 85 and ST129 respectively. ST1 was the predominant type, accounting for 70% of examined strains, whereas ST2 was observed in 29% of the strains (Table 4.5). In case of *S.*Para A, ST85 was observed in 3 and ST129 was observed in 10 isolates. *S.* Typhimurium was grouped in to ST19, ST313, ST36 followed by S. enteritidis grouped as ST11. *Salmonella* Alachua was grouped as ST2061 and S. Bovismorbificans was grouped as ST2345. Presence of different type of plasmids (IncFIB(S)/IncFII(S), IncFI (pN55391), IncX1) was also observed in Salmonella species.

Table 4.5.a: MLST grouping of all Salmonella

Organism	Sequence Type	Total Sequence Type/organism
S. Typhi	ST1, ST2	ST1- 46 ST2- 19
S. Paratyphi A	ST85, ST129	ST85- 3 ST129 - 10
S.Enteritidis	ST11	ST11- 12
S. Typhimurium	ST19, ST313, ST36	ST19- 5 ST313- 2 ST36- 1
S. Alachua	ST2061	ST2061- 1
S. Kentucky	ST198	ST198- 1
S. Bovismorbificans	ST2345	ST2345- 1
S. Infantis	ST32	ST32- 1

Table 4.5.b:- Mutations imparting resistance to ciprofloxacin in *S.* Typhi

S. Typhi Ciprofloxacin resistance													
			gyrA			gyrB	ParC		ParE		CIP* MIC	CIP Disk Diffusion zone (mm)	
S.No.	Lab ID / Centre Name	Mutation	S83F	S83Y	D87N	S464F	S80I	D420N/E84G	L416F	D420N	µg/ml		
1	323336/ST/JP	T*	P	P*	Np	Np	P	NP	Np	Np	96	6	R
2	330738/ST/JP	T*	P	P*	Np	Np	P	NP	Np	Np	64	11	R*
3	331040/ST/JP	S	P	Np	NP	Np	NP	Np	Np	Np	0.19	27	I
4	337759/ST/JP	S	P	Np	NP	Np	NP	Np	Np	Np	0.19	28	I
5	337765/ST/JP	S	P	Np	NP	Np	NP	Np	Np	Np	0.19	27	I
6	378227/ST/JP	S	P	Np	NP	Np	NP	Np	Np	Np	0.25	26	I
7	368917/ST/RIMS	S	NP	P	NP	Np	NP	Np	Np	Np	0.19	26	I
8	386260/ST/RIMS	T	P	NP	P	Np	P	NP	p	Np	4	10	R
9	367825/ST/SKIMS	T	P	Np	P	Np	P	Np	Np	Np	64	6	R
10	372025/ST/SKIMS	S	NP	Np	P	Np	NP	Np	Np	Np	0.19	6	I
11	5641/ST/ND AIIMS	S	P	Np	Np	Np	Np	Np	Np	Np	0.19	28	I
12	9965/ST/ND AIIMS	S	NP	Np	NP	Np	P	Np	Np	Np	0.12	27	I
13	307886/ST/SGH	T	P	Np	P	Np	P	Np	Np	Np	64	6	R
14	307888/ST/SGH	S	P	Np	NP	Np	NP	Np	Np	Np	0.25	28	I
15	367170/ST/SGH	S	P	NP	NP	Np	NP	Np	Np	Np	0.19	28	I
16	367171/ST/SGH	S	P	Np	Np	NP	Np	Np	Np	Np	0.19	26	I
17	387858/ST/SGH	S	NP	P	Np	Np	NP	Np	Np	Np	0.125	28	I
18	387861/ST/SGH	D	P	Np	p	Np	NP	Np	Np	Np	0.19	27	I
19	387870/ST/SGH	D	P	Np	Np	Np	NP	Np	P	Np	0.19	26	I
20	429877/ST/LTMMC	T	P	Np	P	Np	P	Np	Np	Np	64	6	R
21	429940/ST/LTMMC	NP	NP	NP	NP	NP	NP	NP	NP	NP	0.064	31	S
22	429948/ST/LTMMC	S	NP	P	Np	Np	NP	Np	Np	Np	0.25	28	I

23	429962/ST/LTMMC	S	NP	P	Np	Np	NP	Np	Np	Np	0.25	28	I
24	395917/ST/PDH	S	NP	P	Np	Np	Np	Np	Np	Np	0.19	30	I
25	395931/ST/PDH	S	P	Np	NP	Np	NP	Np	Np	Np	0.38	27	I
26	395974/ST/PDH	S	NP	P	NP	Np	NP	Np	Np	Np	0.25	26	I
27	431174/ST/PDH	T	P	Np	P	Np	P	Np	Np	Np	256	6	R
28	431242/ST/PDH	S	NP	P	NP	Np	NP	Np	Np	Np	0.5	28	I
29	437615/ST/PDH	D	P	Np	NP	Np	NP	P	Np	Np	0.75	27	I
30	36749/ST/PDH	T	P	Np	P	Np	P	Np	Np	Np	48	10	R
31	343217/ST/PDH	S	P	Np	NP	Np	NP	Np	Np	Np	0.19	10	R
32	343220/ST/PDH	T	P	Np	P	Np	P	Np	Np	Np	48	10	R
33	368743/ST/PDH	S	NP	N	NP	Np	NP	Np	Np	Np	0.25	28	I
34	368746/ST/PDH	T	P	Np	P	Np	P	Np	Np	Np	48	12	R
35	368753/ST/PDH	S	P	Np	Np	Np	NP	Np	Np	Np	0.5	24	I
36	317967/ST/CMC	S	NP	P	NP	Np	NP	Np	Np	Np	0.19	28	I
37	317990/ST/CMC	D	P	Np	Np	Np	Np	P	Np	Np	0.5	28	I
38	323360/ST/CMC	D	P	Np	NP	Np	P	Np	Np	Np	0.19	26	I
39	344272/ST/CMC	D	P	Np	NP	Np	P	Np	Np	Np	0.25	28	I
40	353959/ST/CMC	T	P	Np	P	Np	P	Np	Np	Np	96	14	R
41	96454/ST/TMC	S	p	Np	NP	Np	NP	Np	Np	Np	0.19	28	I
42	99226/ST/TMC	S	p	Np	Np	Np	NP	Np	Np	Np	0.19	28	I
43	109927/ST/TMC	T	p	Np	p	Np	P	Np	Np	Np	4	12	R
44	249860/ST/TMC	S	P	Np	Np	Np	NP	Np	Np	Np	0.125	28	I
45	43710/ST/PGI	S	NP	P	NP	Np	NP	Np	Np	Np	0.25	26	I
46	437113/ST/PGI	S	NP	P	NP	Np	NP	Np	Np	Np	0.25	26	I
47	437158/ST/PGI	S	NP	P	NP	Np	NP	Np	Np	Np	0.19	29	I
48	437165/ST/PGI	S	P	Np	NP	Np	NP	Np	Np	Np	0.38	30	I
49	437171/ST/PGI	S	P	Np	Np	Np	Np	NP	Np	Np	0.25	28	I
50	1805/ST/PGI	T	P	Np	P	Np	P	Np	Np	Np	256	17	R

51	2701/ST/PGI	S	P	Np	NP	Np	NP	Np	Np	Np	0.25	26	I
52	11460/ST/PGI	S	P	Np	NP	Np	NP	Np	Np	Np	0.25	26	I
53	257569/ST/JDH_AIIMS	D	NP	P	P	Np	P	P	Np	Np	0.38	9	R
54	257570/ST/JDH_AIIMS	T	P	Np	P	Np	P	Np	Np	Np	24	14	R
55	257572/ST/JDH_AIIMS	S	P	Np	Np	Np	Np	NP	Np	Np	0.5	28	I
56	270820/ST/JDH_AIIMS	T	P	Np	P	Np	P	Np	Np	Np	8	17	R
57	270825/ST/JDH_AIIMS	S	P	Np	NP	Np	NP	Np	Np	Np	0.25	27	I
58	270827/ST/JDH_AIIMS	T	P	Np	P	Np	P	Np	Np	Np	4	14	R
59	271299/ST/JDH_AIIMS	S	NP	P	Np	Np	Np	NP	Np	Np	0.25	28	I
60	270834/ST/JDH_AIIMS	S	P	Np	NP	Np	NP	Np	Np	Np	0.3	26	I
61	271303/ST/JDH_AIIMS	T	P	Np	P	Np	P	Np	Np	Np	16	14	R
62	271308/ST/JDH_AIIMS	S	P	Np	Np	Np	Np	NP	Np	Np	0.5	28	I
63	452804/ST/NIMS	T	P	Np	P	Np	P	Np	Np	Np	128	17	R

Table 4.5.c:- Mutations imparting resistance to ciprofloxacin in *S.* Paratyphi A

			gyrA			gyrB	ParC		ParE		CIP* MIC	CIP Disk Diffusion zone (mm)	
S.No.	Lab ID / Centre Name	Mutation	S83F	S83Y	D87N	S464F	S80I	D420N/E84G	L416F	D420N	µg/ml		
1	372023/SPA/SKIMS	S	P	Np	NP	Np	NP	Np	Np	Np	0.19	6	I
2	385554/SP/SKIMS	S	P	Np	Np	Np	Np	Np	Np	Np	0.75	26	I
3	307885/SPA/SGH	S	P	Np	Np	Np	Np	Np	Np	Np	0.5	28	I
4	307887/SPA/SGH	S	P	Np	Np	Np	Np	Np	Np	Np	0.75	28	I
5	307889/SPA/SGH	T	P	Np	P	Np	P	Np	Np	Np	1.5	16	R
6	367167/SPA/SGH	S	P	Np	Np	Np	NP	Np	Np	Np	0.25	28	I
7	367173/SPA/SGH	S	P	Np	Np	Np	NP	Np	Np	Np	0.25	26	I
8	387868/SPA/SGH	S	P	Np	Np	Np	NP	Np	Np	Np	0.19	27	I
9	317981/SPA/CMC	S	Np	P	Np	Np	Np	Np	Np	Np	0.75	25	I
10	184945/SPA/TMC	S	P	Np	Np	Np	P	Np	Np	Np	0.38	30	I
11	2353/SPA/PGI	S	P	Np	NP	Np	NP	Np	Np	Np	0.38	28	I
12	4322/SPA/PGI	T	P	Np	P	Np	P	Np	Np	Np	1	17	R
13	257567/SPA/JDH_AIIMS	S	P	Np	NP	Np	NP	Np	Np	Np	0.5	28	I
14	270822/SPA/JDH_AIIMS	S	P	Np	NP	Np	NP	Np	Np	Np	0.38	27	I

Table 4.5.d:- Mutations imparting resistance to ciprofloxacin in Salmonella Spp.

Ciprofloxacin resistance in Salmonella Species													
			gyrA			gyrB	ParC		ParE		CIP* MIC	CIP Disk Diffusion zone (mm)	
S.No.	Lab ID / Centre Name	Mutation	S83F	S83Y	D87N	S464F	S80I	D420N/E84G	L416F	D420N	µg/ml		
1	378228/S. Enteritidis/JP	NP	NP	NP	NP	NP	NP	NP	NP	NP	0.032	31	S
2	337767/S. Enteritidis/JP	S	P	Np	Np	Np	Np	Np	Np	Np	0.047	31	S
3	337768/S. typhimurium/JP	S*	P	Np	Np	Np	Np	Np	Np	Np	0.19	28	I
4	345555/S.Alachua/JP	NP	NP	Np	Np	Np	Np	Np	Np	Np	0.047	31	S
5	378223/S.Enteritidis/JP	NP	NP	Np	Np	Np	Np	Np	Np	Np	0.047	31	S
6	378224/S.Enteritidis/JP	NP	NP	NP	NP	NP	NP	NP	NP	NP	0.047	31	S
7	316428/S.Enteritidis/JP	NP	NP	NP	NP	NP	NP	NP	NP	NP	0.047	31	S
8	329868/S.Enteritidis/JP	NP	NP	NP	NP	NP	NP	NP	NP	NP	0.047	31	S
9	264203/S. Typhimurium/RIMS	S	P	Np	Np	Np	Np	Np	Np	Np	0.25	27	I
10	432179/S. Kentucky/LTMMC	T	P	Np	P	Np	P	Np	Np	Np	48	6	R
11	343215/S. Bovismorbificans/PDH	NP	NP	NP	NP	NP	NP	NP	NP	NP	0.064	31	S
12	347798/S.Enteritidis/PDH	NP	NP	NP	NP	NP	NP	NP	NP	NP	0.064	31	S
13	347800/S. Infantis/PDH	S	P	Np	Np	Np	Np	Np	Np	Np	0.19	27	I
14	358142/S.Enteritidis/PDH	S	P	Np	Np	Np	Np	Np	Np	Np	0.25	27	I
15	395794/S. typhimurium/PDH	S	P	Np	Np	Np	Np	Np	Np	Np	0.19	28	I
16	431143/S.Enteritidis/PDH	NP	NP	NP	NP	NP	NP	NP	NP	NP	0.047	27	I
17	316086/S. Saintpaul/CMC	NP	NP	NP	NP	NP	NP	NP	NP	NP	0.032	17	R
18	345791/S. Enteritidis/CMC	T	P	Np	P	Np	P	Np	Np	Np	8	12	R
19	353958/S. Typhimurium/CMC	NP	NP	NP	NP	NP	NP	NP	NP	NP	0.047	31	S
20	353960/S. Enteritidis/CMC	NP	NP	NP	NP	NP	NP	NP	NP	NP	0.032	31	S

21	53802/S.Enteritidis/TMC	NP	NP	Np	Np	Np	Np	Np	Np	Np	0.064	26	I
22	79972/S.Typhimurium/TMC	T	P	Np	P	Np	P	Np	Np	Np	4	10	R
23	86592/S.Typhimurium/TMC	T	P	Np	P	Np	P	Np	Np	Np	3	12	R
24	103657/S.Typhimurium/TMC	NP	NP	Np	Np	Np	Np	Np	Np	Np	0.032	31	S
25	248713/S.Typhimurium/TMC	NP	NP	Np	NP	Np	NP	Np	Np	Np	0.064	31	S

Table 4.5 e: Distribution of FQ resistance imparting mutations in DNA gyrases and topoisomerase IVof studied strains and coorelation with MIC

MIC (µg/ml)	Single Mutation	Double mutation	Triple mutation
0.064 (n=1)	***gyrA*** S83F (n= 1)	----------	----------
0.125 (n=3)	***gyrA*** S83F (n= 1) ***parC*** S80 I (n= 1) ***gyrA*** S83Y (n= 1)	----------	----------
0.75 (n=4)	***gyrA*** S83F (n= 2) ***gyrA*** S83Y (n= 1)	***gyrA*** S83F, ***parC*** S80 I (n= 1)	
0.25 (n=16)	***gyrA*** S83F (n= 8) ***gyrA*** S83Y (n= 7)	-***gyrA*** S83F, ***parC*** S80 I (n= 1)	----------
0.19 (n=19) Single-16 Double -2	***gyrA*** S83F (n= 11) ***gyrA*** S83Y (n= 4) ***gyrA*** D87N (n=1)	***gyrA*** S83F, ***gyrA*** D87N(n= 1) ***gyrA*** S83F, ***parE*** L416F n= 1) ***gyrA*** S83F, ***parC*** S80 I (n= 1)	----------
0.5 (n=7)	***gyrA*** S83F (n= 5) ***gyrA*** S83Y (n= 1)	***gyrA*** S83F, ***parC*** S80 I (n= 1)	----------
0.38 (n=7)	***gyrA*** S83F (n= 6)	----------	***gyr A*** S83F, D87N ***parC*** S80I (n=1)
1-256 (n=20)			***gyr A*** S83F, D87N ***parC*** S80I (n=18) ***gyr A*** S83F, S83Y, ***par C*** S80I (n=2)

Table 4.6.a: Gnotyping analysis of antibiotic resistance by whole genome sequencing and comparison with phenotypic antibiotic sensitivity from JIPMER

	Fluoroquinolone			Cephalosporin		Macrolide		Ampicillin	diaminopyrimidine		phenicol	Sulfonamide		
	parC	gyrA	**Phenotypic Sensitivity**	**CTX-M-15**	**Phenotypic Sensitivity**	**ErmC**	**Phenotypic Sensitivity**	**TEM-1**	**dfrA15**	**dfrA7**	**catI**	**Sul 1**	**Sul 2**	**Phenotypic Sensitivity**
323336/ST	parC_S80I	gyrA_S83F/D87N	R	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
330738/ST	parC_S80I	gyrA_S83F/D87N	R	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
331040/ST	Np	gyrA_S83F	I	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
337759/ST	Np	gyrA_S83F	I	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
337765/ST	Np	gyrA_S83F	I	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
378227/ST	Np	gyrA_S83F	I	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
378228/S. Enteritidis	NP	NP	S	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
337767/S. Enteritidis	NP	gyrA_S83F	I	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
337768/S. typhimurium	NP	gyrA_S83F	I	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
345555S/Alachua	NP	NP	S	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
378223/S.Enteritidis	NP	NP	S	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
378224/S.Enteritidis	NP	NP	S	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
316428/S.Enteritidis	NP	NP	S	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
329868/S.Enteritidis	NP	NP	S	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR

P*- Present; **NP*-** Not present; **I*-** Intermediate; **R*-** Resistant; **S**-** Sensitive;
CRP, acrA,acrR,marR, soxR,acrB,emrA,emrB,emrR,marA,mdtK,mdtM,rsmA,sdiA - Present in all isolates for FQ resistance
acrA, acrR, ampC1, ampH, marR, soxR, soxS, PBP3, KpnE, acrB, marA, sdiA- Present in all isolates for Cephalosporin resistance
CRP, KpnE, kpnF- Present in all isolates for Macrolide resistance

Table 4.6.b: Genotyping analysis of antibiotic resistance by whole genome sequencing and comparison with phenotypic antibiotic sensitivity from RIMS, Imphal

	Fluoroquinolone			Cephalosporin		Macrolide		Ampicillin	diaminopyrimidine antibiotic		phenicol	Sulfonamide		
	parC	gyrA	Phenotypic Sensitivity	CTX-M-15	Phenotypic Sensitivity	ErmC	Phenotypic Sensitivity	TEM-1	dfrA15	dfrA7	catI	Sul1	Sul 2	Phenotypic Sensitivity
368917/ST	NP	gyrA_S83Y	I	Np	S	Np	S	Np	Np	Np	Np	Np	Np	S
386260ST	parC_S80I	gyrA_S83F /D87N	R	Np	S	Np	S	Np	Np	Np	Np	Np	Np	S
264203/S. Typhimurium	NP	gyrA_S83F	I	Np	S	Np	S	Np	Np	Np	Np	Np	Np	S

Table 4.6 c: Genotyping analysis of antibiotic resistance by whole genome sequencing and comparison with phenotypic antibiotic sensitivity from SKIMS, Srinagar

	Fluoroquinolone			Cephalosporin		Macrolide		Ampicillin	diaminopyrimidine antibiotic		phenicol antibiotic	Sulfonamide		
	parC	gyrA	Phenotypic Sensitivity	CTX-M-15	Phenotypic Sensitivity	ErmC	Phenotypic Sensitivity	TEM-1	dfrA15	dfrA7	catI	Sul1	Sul2	Phenotypic Sensitivity
367825/ ST	parC_S80I	gyrA_S83F/D87N	R	Np	S	Np	S	NP	Np	Np	Np	Np	Np	Non-MDR
372025/ ST	Np	gyrA_S83Y	I	Np	S	Np	S	Present	Np	Np	present	Np	Present	MDR
372023/ SP	Np	NP	I	Np	S	Np	S	NP	Np	Np	Np	Np	Np	Non-MDR
385554/ SP	Np	Np	i	Np	S	Np	S	NP	Np	Np	Np	Np	Np	Non-MDR

Table 4.6.d: Genotyping analysis of antibiotic resistance by whole genome sequencing and comparison with phenotypic antibiotic sensitivity from AIIMS, New Delhi

	Fluoroquinolone			Cephalosporin		Macrolide		Ampicillin	diaminopyrimidine		phenicol	Sulfonamide		
	parC	gyrA	Phenotypic Sensitivity	CTX-M-15	Phenotypic Sensitivity	ErmC	Phenotypic Sensitivity	TEM-1	dfrA15	dfrA7	catI	Sul1	Sul2	Phenotypic Sensitivity
5641/ST	NP	gyrA_S83F	S	Np	S	Np	S	NP	Np	Np	Np	Np	Np	Non-MDR
9965/ST	Np	gyrB_S464F	I	Np	S	Np	S	P	Np	P	P	P	Np	MDR

Table 4.6. e: Genotyping analysis of antibiotic resistance by whole genome sequencing and comparison with phenotypic antibiotic sensitivity fromLTMMC, Mumbai

	Fluoroquinolone			Cephalosporin		Macrolide		Ampicillin	diaminopyrimidine		phenicol	Sulfonamide		
	parC	gyrA	Phenotypic Sensitivity	CTX-M-15	Phenotypic Sensitivity	ErmC	Phenotypic Sensitivity	TEM-1	dfrA15	dfrA7	catI	Sul1	Sul2	Phenotypic Sensitivity
429877/ST	parC_S80I	gyrA_S83F/D87N	R	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
429940/ST	NP	NP	S	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
429948/ST	NP	gyrA_S83Y	I	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
429962/ST	NP	gyrA_S83Y	I	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
432179/S. Kentucky	parC_S80I	gyrA_S83F/D87N	R	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR

Table 4.6. f: Genotyping analysis of antibiotic resistance by whole genome sequencing and comparison with phenotypic antibiotic from Sir Gangaram, New Delhi

	Fluoroquinolone			Cephalosporin		Macrolide		Ampicillin	diaminopyrimidine		phenicol	Sulfonamide		
	parC	gyrA	Phenotypic Sensitivity	CTX-M-15	Phenotypic Sensitivity	ErmC	Phenotypic Sensitivity	TEM-1	dfrA15	dfrA7	catI	Sul1	Sul2	Phenotypic Sensitivity
307886/ST	parC_S80I	gyrA_S83F/D87N	R	Np	S	Np	Sensitive	Np	Np	Np	Np	Np	Np	non-MDR
307888/ST	Np	gyrA_S83F	I	Np	S	Np	Sensitive	Np	Np	Np	Np	Np	Np	non-MDR
367170/ST	Np	gyrA_S83F	I	Np	S	Np	Sensitive	Np	Np	Np	Np	Np	Np	non-MDR
367171/ST	Np	gyrA_S83F	I	Np	S	Np	Sensitive	Np	Np	Np	Np	Np	Np	non-MDR
387858/ST	Np	gyrA_S83Y	I	Np	S	Np	Sensitive	Np	Np	Np	Np	Np	Np	non-MDR
387861/ST	Np	gyrA_S83F/D87N	I	Np	S	Np	Sensitive	Np	Np	Np	Np	Np	Np	non-MDR
387870/ST	parE_L416F	gyrA_S83F,	I	Np	S	Np	Sensitive	Np	Np	Np	Np	Np	Np	non-MDR
	Np	Np	I	Np	S	Np	Sensitive	Np	Np	Np	Np	Np	Np	non-MDR
307885/SPA	NP	gyrA_S83F	I	Np	S	Np	Sensitive	Np	Np	Np	Np	Np	Np	non-MDR
307887/SPA	Np	gyrA_S83F	I	Np	S	Np	Sensitive	Np	Np	Np	Np	Np	Np	non-MDR
307889/SPA	parC_S80I	gyrA_S83F/D87N	R	Np	S	Np	Sensitive	Np	Np	Np	Np	Np	Np	non-MDR
367167/SPA	NP	gyrA_S83F	I	Np	S	Np	Sensitive	Np	Np	Np	Np	Np	Np	non-MDR
367173/SPA	NP	gyrA_S83F	I	Np	S	Np	Sensitive	Np	Np	Np	Np	Np	Np	non-MDR
387868/SPA	Np	gyrA_S83F	I	Np	R	Np	Sensitive	Np	Np	Np	Np	Np	Np	non-MDR

Table 4.6. g: Genotyping analysis of antibiotic resistance by whole genome sequencing and comparison with phenotypic antibiotic sensitivity from PD Hinduja

	Fluoroquinolone			Cephalosporin		Macrolide		Ampicillin	diaminopyrimidine		phenicol	Sulfonamide		
	parC	gyrA	Phenotypic Sensitivity	CTX-M-15	Phenotypic Sensitivity	ErmC	Phenotypic Sensitivity	TEM-1	dfrA15	dfrA7	catI	Sul1	Sul2	Phenotypic Sensitivity
395917/ST	NP	gyrA_S83Y	I	Np	S	Np	S	NP	Np	NP	NP	NP	NP	Non-MDR
395931/ST	NP	gyrA_S83F	I	Np	S	Np	S	NP	Np	Np	Np	Np	Np	Non-MDR
395974/ST	NP	gyrA_S83Y	I	Np	S	Np	S	NP	Np	Np	Np	Np	Np	Non-MDR
395917ST	NP	gyrA_S83Y	I	Np	S	Np	S	NP	Np	Np	Np	Np	Np	Non-MDR
431174/ST	parC_S80I	gyrA_S83F/D87N	R	Np	S	Np	S	NP	Np	Np	Np	Np	Np	Non-MDR
431242/ST	NP	gyrA_S83Y	I	Np	S	Np	R	NP	Np	Np	Np	Np	Np	Non-MDR
437615/ST	parE_D420N	gyrA_S83F,	I	Np	S	Np	S	NP	Np	Np	Np	Np	Np	Non-MDR
36749/ST	parC_S80I	gyrA_S83F/D87N	R	Np	S	Np	S	NP	Np	Np	Np	Np	Np	Non-MDR
343217/ST	NP	gyrA_S83F	I	Np	S	Np	S	NP	Np	Np	Np	Np	Np	Non-MDR
343220/ST	parC_S80I	gyrA_S83F/D87N	R	Np	S	Np	S	NP	Np	Np	Np	Np	Np	Non-MDR
368743/ST	NP	gyrA_S83Y	I	Np	S	Np	S	NP	Np	Np	Np	Np	Np	Non-MDR
368746/ST	parC_S80I	gyrA_S83F/D87N	R	Np	S	Np	S	NP	Np	Np	Np	Np	Np	Non-MDR
368753/ST	Np	gyrA_S83F	I	Np	S	Np	S	NP	Np	Np	Np	Np	Np	Non-MDR
343215/S. Bovismorbificans	Np	NP	S	Np	S	Np	S		Np	Np	Np	Np	Np	Non-MDR
347798/S.Enteritidis	Np	NP	S	Np	S	Np	S		Np	dfrA7	catA1	Sul1	Np	MDR
347800/S. Infantis	Np	gyrA_S83F	I	Np	S	Np	S		Np	Np	Np	Np	Np	Non-MDR
358142/S.Enteritidis	Np	gyrA_S83F	I	Np	S	Np	S		Np	Np	Np	Np	Np	Non-MDR
395794/S. typhimurium	NP	gyrA_S83F	I	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
431143/S.Enteritidis	Np	NP	S	Np	S	Present	R	blaTEM-1D	Present	dfrA7	catA1	Sul1	Sul2	MDR

431143/S.Enteritidis-OXA-232 (P)

Table 4.6.h: Genotyping analysis of antibiotic resistance by whole genome sequencing and comparison with phenotypic antibiotic sensitivity from Vellore

	Fluoroquinolone			Cephalosporin		Macrolide		Ampicillin	diaminopyrimidine		phenicol	Sulfonamide		
	parC	gyrA	Phenotypic Sensitivity	CTX-M-15	Phenotypic Sensitivity	ErmC	Phenotypic Sensitivity	TEM-1	dfrA15	dfrA7	catI	Sul1	Sul2	Phenotypic Sensitivity
317967/ST	NP	gyrA_S83Y	I	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
317990/ST	parC_E84G	gyrA_S83F,	R	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
323360/ST	parC_S80I	gyrA_S83Y	R	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
344272/ST	parC_S80I	gyrA_S83Y	R	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
353959/ST	parC_S80I	gyrA_S83F/D87N	R	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
316086/S. Saintpaul	NP	NP	S	Np	S	Present	R		Present	Present	Present	Np	Np	Non-MDR
317981/SPA	NP	gyrA_S83Y	I	Np	S	Np	S		Np	Np	Np	Np	Np	Non-MDR
345791/S. Enteritidis	parC_S80I	gyrA_S83F/D87N	R	Np	S	Np	S		Np	Np	Np	Np	Np	Non-MDR
353958/S. Typhimurium	NP	NP	S	Np	S	Np	S		Np	Np	Np	Np	Np	Non-MDR
353960/S. Enteritidis	NP	NP	S	Np	S	Np	S		Np	Np	Np	Np	Np	Non-MDR

316086/S. Saintpaul-OXA-232 (P)

Table 4.6. i: Genotyping analysis of antibiotic resistance by whole genome sequencing and comparison with phenotypic antibiotic sensitivity from TMC

	Fluoroquinolone			Cephalosporin		Macrolide		Ampicillin	diaminopyrimidine		phenicol	Sulfonamide		
	parC	gyrA	Phenotypic Sensitivity	CTX-M-15	Phenotypic Sensitivity	ErmC	Phenotypic Sensitivity	TEM-1	dfrA15	dfrA7	catI	Sul 1	Sul 2	Phenotypic Sensitivity
96454/ST	NP	gyrA_S83F	I	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
99226/ST	NP	gyrA_S83F	I	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
109927/ST	parC_S80I	gyrA_S83F/D87N	R	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
249860/ST	NP	gyrA_S83F	I	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
53802/S.Enteritidis	NP	NP	S	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
79972/S.Typhurium	parC_S80I	gyrA_S83F/D87N	R	Np	S	Present	R	Np	Np	Np	Np	Np	Np	Non-MDR
86592/S.Typhurium	parC_S80I	gyrA_S83F/D87N	R	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
103657/S.Typhurium	NP	NP	S	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
184945/SPA	NP	gyrA_S83F	I	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR
248713/S.Typhimurium	NP	NP	S	Np	S	Np	S	Np	Np	Np	Np	Np	Np	Non-MDR

79972/S.Typhurium-OXA-232 (P), TEM-1 (P), 96454/ST-TEM-1- P

Table 4.6. j: Genotyping analysis of antibiotic resistance by whole genome sequencing and comparison with phenotypic antibiotic sensitivity from PGI

	Fluoroquinolone			Cephalosporin		Macrolide		Ampicillin	diaminopyrimidine		phenicol	Sulfonamide		
	parC	gyrA	Phenotypic Sensitivity	CTX-M-15	Phenotypic Sensitivity	ErmC	Phenotypic Sensitivity	TEM-1	dfrA15	dfrA7	catI	Sul1	Sul2	Phenotypic Sensitivity
43710/ST	Np	gyrA_S83Y	I	NP	S	NP	S	Np	NP	NP	NP	Np	Np	Non-MDR
437113/ST	Np	gyrA_S83Y	I	NP	S	NP	S	Np	NP	NP	NP	Np	Np	Non-MDR
437158/ST	Np	gyrA_S83Y	I	NP	S	NP	R	Np	NP	NP	NP	Np	Np	Non-MDR
437165/ST	Np	gyrA_S83F	I	NP	S	Np	S	Np	NP	NP	NP	Np	Np	Non-MDR
437171/ST	Np	gyrA_S83F	I	NP	S	Np	S	Np	NP	NP	NP	Np	Np	Non-MDR
1805/ST	parC_S80I	gyrA_S83F/D87N	R	NP	S	Np	S	Np	NP	NP	NP	Np	Np	Non-MDR
2701/ST	Np	gyrA_S83F	I	NP	S	Np	S	Np	NP	NP	NP	Np	Np	Non-MDR
11460/ST	Np	gyrA_S83F	I	NP	S	Np	S	Np	NP	NP	NP	Np	Np	Non-MDR
2353/SPA	Np	gyrA_S83F	I	NP	S	Np	S	Np	NP	NP	NP	Np	Np	Non-MDR
4322/SPA	Np	gyrA_S83F/D87N	R	NP	S	Np	S	Np	NP	NP	NP	Np	Np	Non-MDR

Table 4.6.k : Gnotyping analysis of antibiotic resistance by whole genome sequencing and comparison with phenotypic antibiotic sensitivity from JDH_AIIMS

	Fluoroquinolone			Cephalosporin		Macrolide		Ampiicillin	diaminopyrimidine		phenicol	Sulfonamide		
	parC	gyrA	Phenotypic Sensitivity	CTX-M-15	Phenotypic Sensitivity	ErmC	Phenotypic Sensitivity	TEM-1	dfrA15	dfrA7	catI	Sul1	Sul2	Phenotypic Sensitivity
257569/ST	parE_D420N	gyrA_S83Y,	I	NP	S	Present	R	Present	Present	Present	Present	Present	Present	MDR
257570/ST	parC_S80I	gyrA_S83F/D87N;	R	NP	S	NP	S	Np	NP	NP	NP	Np	Np	Non-MDR
257572/ST	NP	gyrA_S83F	I	NP	S	NP	R	NP	NP	NP	NP	NP	NP	Non-MDR
270820/ST	parC_S80I	gyrA_S83F/D87N	R	NP	S	Np	S	Np	NP	NP	NP	Np	Np	Non-MDR
270825/ST	NP	gyrA_S83F	I	NP	S	Np	S	Np	NP	NP	NP	Np	Np	Non-MDR
270827/ST	parC_S80I	gyrA_S83F/D87N	R	NP	S	Np	S	Np	NP	NP	NP	Np	Np	Non-MDR
271299/ST	NP	gyrA_S83Y	I	NP	S	Np	S	Np	NP	NP	NP	Np	Np	Non-MDR
270827/ST	parC_S80I	gyrA_S83F/D87N	R	NP	S	Np	S	Np	NP	NP	NP	Np	Np	Non-MDR
270834/ST	Np	gyrA_S83F	I	NP	S	Np	S	Np	NP	NP	NP	Np	Np	Non-MDR
271303/ST	parC_S80I	gyrA_S83F/D87N	R	NP	S	Np	S	Np	NP	NP	NP	Np	Np	Non-MDR
271308/ST	NP	gyrA_S83F	I	NP	S	NP	S	Np	NP	NP	NP	Np	Np	Non-MDR
452804/ST	parC_S80I	gyrA_S83F/D87N	R	NP	S	NP	S	Np	NP	NP	NP	Np	Np	Non-MDR
25767/SPA	NP	gyrA_S83F	R	NP	S	NP	S	Np	NP	NP	NP	Np	Np	Non-MDR
270822/SPA	NP	gyrA_S83F	R	NP	S	NP	S	Np	NP	NP	NP	Np	Np	Non-MDR

Chapter 5. Non fermenting Gram-negative Bacteria (NFGNB)

Among non-fermenting Gram-negative bacilli, *Pseudomonas aeruginosa* (50%) was more common followed by *Acinetobacter baumannii* (46%), *Stenotrophomonas maltophilia* (3%) and *Burkholderia cepacia* (0.4%). *A. baumannii* and *P. aeruginosa* causes serious healthcare associated infections such as pneumonia, bloodstream infections and postoperative wound infections. While, *S. maltophilia* and *B. cepacia* are the opportunistic pathogens in causing invasive infections, a significant increase in the trend of the isolation of *Pseudomonas aeruginosa* (9.5% in 2017 vs 22% in 2022), *A. baumannii* (7% in 2017 vs 25% in 2022) and *S. maltophilia* (6% in 2017 vs 30% in 2022) were seen. However, no significant difference in the trend of isolation of these pathogens was noticed in the last two years, except for *S. maltophilia.*

Pseudomonas aeruginosa

Infections with *P. aeruginosa* have become a real concern in hospital-acquired infections, especially in critically ill and immunocompromised patients. The major problem leading to high mortality lies in the appearance of drug-resistant strains. The rate of isolation of *P. aeruginosa* is higher in wards compared to OPD followed by ICU (Table 5.1). *P. aeruginosa* isolated from ward/ICU were found to multi-drug resistant than those that were isolated from OPD, which represent the increasing prevalence of multi-drug resistance in *P. aeruginosa* in hospital settings (Table 5.1). The percentage of susceptibility to anti-pseudomonal cephalosporin such as ceftazidime (56.4% vs 47.1%) and cefepime (60.3% vs 49.8%) was higher in those *P. aeruginosa* that were isolated from wards, compared to ICU. Overall, 36% of *P. aeruginosa* isolates were resistant to carbapenems and was higher in ICU population (49%) compared to wards (63%). More than 50% of susceptibility to various aminoglycosides such as amikacin, gentamicin and tobramycin was noticed. Fluroquinolones (levofloxacin and ciprofloxacin) showed limited activity with the susceptibility of 40 – 57% (Table 5.1).

P. aeruginosa isolates from UTI and CSF showed higher rate of resistance to ceftazidime (41.2% & 43.6%), cefepime (46.1% & 48.1%), piperacillin-tazobactam (57.2% & 56.4%), imipenem (51.1% & 40.5%), meropenem (54.1% & 47.9%), amikacin (51.4% & 60.4%), gentamicin (48.2% & 44.4%), tobramycin (50.1% & 65.8%), ciprofloxacin (35.9% & 38.5%) and levofloxacin (33.3% & 42.6%), except colistin. No significant change in the susceptibility was noticed in *P. aeruginosa* isolated from BSI, LRTI, superficial infection and deep infections (Table 5.2). In *P. aeruginosa*, there was no change in the trend of susceptibility to piperacillin/tazobactam, anti-pesudomonal cephalosporins such as ceftazidime and cefepime and aminoglycosides (Table 5.3 and Figure 5.1). A gradual increase in the resistance to carbapenems was noticed in *P. aeruginosa*, however it is not statistically significant. All the tested *P. aeruginosa* isolates were highly susceptible to colistin and there was no change in the trend of susceptibility to colistin for the five years.

Table 5.1: Location-wise susceptible percentage of *Pseudomonas aeruginosa* isolated from all samples (except faeces) across OPD, Ward and ICU

AMA	Total n=13227	OPD n=4155	Ward n=6646	ICU n=2426
Piperacillin-tazobactam	9016/13074 (69)	3238/4116 (78.7)	4405/6553 (67.2)	1373/2405 (57.1)
Cefepime	7886/12619 (62.5)	2893/3934 (73.5)	3845/6381 (60.3)	1148/2304 (49.8)
Ceftazidime	7527/12759 (59)	2807/4004 (70.1)	3613/6407 (56.4)	1107/2348 (47.1)
Imipenem	8182/12733 (64.3)	2961/3944 (75.1)	4068/6451 (63.1)	1153/2338 (49.3)
Meropenem	8523/12843 (66.4)	3148/3985 (79)	4155/6479 (64.1)	1220/2379 (51.3)
Colistin*	6675/6885 (96.9)	2029/2097 (96.7)	3278/3380 (97.2)	1368/1408 (97.1)
Amikacin	9000/13116 (68.6)	3216/4129 (77.9)	4354/6577 (66.2)	1430/2410 (59.3)
Gentamicin	6321/9871 (64)	2216/3060 (72.4)	3109/4995 (62.2)	996/1816 (54.8)
Tobramycin	4364/6378 (68.4)	1687/2165 (77.9)	1981/2981 (66.5)	696/1232 (56.5)
Ciprofloxacin	6039/12685 (47.6)	2133/3976 (53.6)	2983/6429 (46.4)	923/2280 (40.5)
Levofloxacin	5635/11044 (51)	2076/3583 (57.9)	2706/5419 (49.9)	853/2042 (41.8)

*Colistin represents percentage Intermediate susceptibility

Table 5.2: Sample-wise susceptible percentage of *Pseudomonas aeruginosa*

AMA	Blood	LRT	Superficial Infection	Deep Infection	CSF	Urine
	n=1479	n=3693	n=3299	n=1224	n=117	n=1594
Piperacillin-tazobactam	974/1465 (66.5)	2685/3679 (73)	2371/3253 (72.9)	778/1211 (64.2)	66/117 (56.4)	902/1578 (57.2)
Cefepime	887/1442 (61.5)	2365/3544 (66.7)	2090/3179 (65.7)	697/1135 (61.4)	50/104 (48.1)	678/1470 (46.1)
Ceftazidime	858/1440 (59.6)	2292/3651 (62.8)	1999/3130 (63.9)	633/1132 (55.9)	51/117 (43.6)	648/1574 (41.2)
Imipenem	876/1441 (60.8)	2349/3541 (66.3)	2223/3167 (70.2)	725/1162 (62.4)	47/116 (40.5)	802/1571 (51.1)
Meropenem	891/1447 (61.6)	2513/3648 (68.9)	2323/3163 (73.4)	739/1159 (63.8)	56/117 (47.9)	850/1572 (54.1)
Colistin*	810/824 (98.3)	1899/1929 (98.4)	1476/1534 (96.2)	770/808 (95.3)	93/94 (98.9)	982/1024 (95.9)
Amikacin	976/1476 (66.1)	2770/3682 (75.2)	2326/3270 (71.1)	815/1218 (66.9)	64/106 (60.4)	818/1590 (51.4)
Gentamicin	692 / 1104 (62.7)	1747 / 2484 (70.3)	1595 / 2392 (66.7)	707 / 1124 (62.9)	28 / 63 (44.4)	640 / 1327 (48.2)
Tobramycin	414 / 660 (62.7)	1739 / 2304 (75.5)	1191 / 1759 (67.7)	157 / 262 (59.9)	48 / 73 (65.8)	287 / 573 (50.1)
Ciprofloxacin	645 / 1407 (45.8)	1903 / 3370 (56.5)	1691 / 3270 (51.7)	447 / 1229 (36.4)	40 / 104 (38.5)	568 / 1584 (35.9)
Levofloxacin	645/1196 (53.9)	1977/3352 (59)	1485/2730 (54.4)	351/937 (37.5)	43/101 (42.6)	435/1308 (33.3)

*Colistin represents percentage Intermediate susceptibility

Table 5.3: Yearly susceptible trend of *Pseudomonas aeruginosa* isolated from all samples

AMA	Year-2017	Year-2018	Year-2019	Year-2020	Year-2021	Year-2022
	Total n=5687	Total n=8880	Total n=12634	Total n=7839	Total n=11622	Total n=13228
Piperacillin-tazobactam	3757/5450 (68.9)	6034/8499 (71)	8416/11430 (73.6)	5012/7418 (67.6)	7548/10835 (69.7)	9017/113156 (68.5)
Cefepime	3074/5003 (61.4)	5259/8284 (63.5)	7660/12038 (63.6)	4497/7355 (61.1)	7263/11233 (64.7)	7887/12625 (62.4)
Ceftazidime	3602/5504 (65.4)	5663/8598 (65.9)	7545/11977 (63)	4647/7635 (60.9)	6914/11028 (62.7)	7528 / 12767 (58.9)
Imipenem	4059/5514 (73.6)	5627/8377 (67.2)	6425/10230 (62.8)	4411/7036 (62.7)	6749/10389 (65)	8183 / 12795 (63.9)
Meropenem	3490/5083 (68.7)	5736/8292 (69.2)	8255/12242 (67.4)	4955/7661 (64.7)	7581/11280 (67.2)	8524 / 12898 (66.1)
Colistin*	1727/1738 (99.4)	983/1075 (91.4)	1767/1899 (93)	1291/1355 (95.3)	2226/2298 (96.9)	6675/6885 (96.9)
Amikacin	3864/5609 (68.9)	6019/8747 (68.8)	8340/12329 (67.6)	5276/7723 (68.3)	7990/11480 (69.6)	9000 / 13133 (68.5)
Gentamicin	2526/4249 (59.4)	4077/6462 (63.1)	5820/9383 (62)	3241/5341 (60.7)	5277/8311 (63.5)	6321/9896 (63.8)
Tobramycin	2954/4365 (67.7)	3809/5603 (68)	4627/6783 (68.2)	2907/4331 (67.1)	4148/6015 (69)	4364/6379 (68.4)
Ciprofloxacin	2930/5069 (57.8)	4814/8026 (60)	6281/10945 (57.4)	3768/6541 (57.6)	6126/10159 (60.3)	6039/12719 (47.4)
Levofloxacin	3236/5351 (60.5)	4794/8217 (58.3)	6148/10922 (56.3)	3771/6743 (55.9)	5863/10123 (57.9)	5635/11048 (51.0)

*Colistin represents percentage Intermediate susceptibility

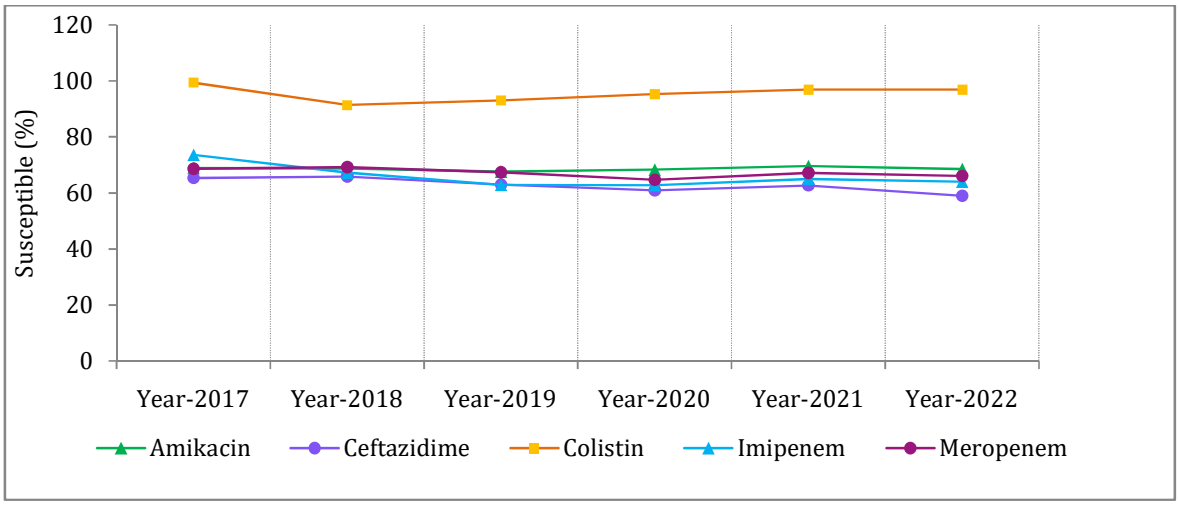


Figure 5.1. Yearly susceptible trend of *Pseudomonas aeruginosa* isolated from all samples.

Acinetobacter baumannii

Isolation rate of *A. baumannii* was found to be higher in wards and ICUs, compared to OPD (Table 5.4), indicates the adaption of pathogen to hospital settings with increased resistance to various antibiotics. All the tested antibiotics showed limited activity against *A. baumannii* isolates and the pattern of susceptibility was similar, irrespective of the location and clinical source of the isolation (Table 5.4 and Table 5.5). Nearly, 88% of the isolates were resistant to carbapenems (Table 5.4) and left with limited treatment options. Against *A. baumannii*, piperacillin/tazobactam, cefepime, ceftazidime, amikacin and levofloxacin showed limited activity (Table 5.4). No change in the trend of susceptibility was observed between 2017 and 2022 (Table 5.6 and Figure 5.2). Nearly 55% of the tested isolates were found to be susceptible to minocycline and 8% drop in the susceptibility to minocycline was noticed (67% in 2017 vs 59% in 2022) and there was no significant change in the susceptibility to minocycline was noticed for the last two years. All the tested *A. baumannii* isolates were highly susceptible to colistin.

Table 5.4: Location-wise susceptible percentage of *A. baumannii* isolated from all samples except faeces across OPD, Ward and ICU

AMA	Total n=12142 (S%)	OPD n=1520 (S%)	Ward n=5997 (S%)	ICU n=4625 (S%)
Piperacillin-tazobactam	1578/12114 (13.0)	419 / 1516 (27.6)	812 / 5988 (13.6)	347 / 4620 (7.5)
Cefepime	1280/11899 (10.8)	364 / 1497 (24.3)	656 / 5887 (11.1)	260 / 4516 (5.8)
Ceftazidime	1023/11193 (9.1)	309 / 1328 (23.3)	492 / 5485 (9)	222 / 4384 (5.1)
Imipenem	1456/11915 (12.2)	405 / 1459 (27.8)	765 / 5881 (13)	286 / 4578 (6.2)
Meropenem	1690/11902 (14.2)	447 / 1456 (30.7)	892 / 5875 (15.2)	351 / 4579 (7.7)
Colistin*	7362/7700 (95.6)	959/1028 (93.2)	3769/3953 (95.3)	2634/2719 (96.8)
Amikacin	2053/11829 (17.4)	460 / 1494 (30.8)	1103 / 5872 (18.8)	490 / 4526 (10.8)
Minocycline	6207/10514 (59)	911 / 1326 (68.7)	3086 / 5196 (59.4)	2210 / 4020 (55)
Levofloxacin	1755/10003 (17.5)	416 / 1297 (32.1)	959 / 4903 (19.6)	380 / 3813 (10)

*Colistin represents percentage Intermediate susceptibility of *Acinetobacter* spp.

Table 5.5: Sample-wise susceptible percentage of *A. baumannii*

AMA	Blood	LRT	Superficial infection	Deep infection	CSF	Urine
	n=2412	n=5216	n=1978	n=611	n=425	n=312
Piperacillin-tazobactam	434 / 2413 (18)	511 / 5211 (9.8)	209 / 1974 (10.6)	79 / 608 (13)	74 / 423 (17.5)	105 / 312 (33.7)
Cefepime	385 / 2373 (16.2)	373 / 5107 (7.3)	169 / 1950 (8.7)	63 / 603 (10.4)	62 / 412 (15)	78 / 303 (25.7)
Ceftazidime	322 / 2314 (13.9)	315 / 5010 (6.3)	132 / 1776 (7.4)	35 / 403 (8.7)	51 / 388 (13.1)	60 / 296 (20.3)
Imipenem	409 / 2403 (17)	440 / 5198 (8.5)	200 / 1877 (10.7)	88 / 582 (15.1)	63 / 418 (15.1)	97 / 310 (31.3)
Meropenem	456 / 2397 (19)	509 / 5200 (9.8)	243 / 1875 (13)	101 / 584 (17.3)	71 / 422 (16.8)	111 / 308 (36.0)
Colistin*	1618/1666 (97.1)	3248/3312 (98.1)	1003/1117 (89.8)	335/363 (92.3)	322/327 (98.5)	189/193 (97.9)
Amikacin	518 / 2361 (21.9)	668 / 5144 (13)	281 / 1953 (14.4)	123 / 606 (20.3)	89 / 386 (23.1)	119 / 295 (40.3)
Minocycline	1354 / 2125 (63.7)	2480 / 4627 (53.6)	1106 / 1759 (62.9)	309 / 467 (66.2)	257 / 381 (67.5)	153 / 223 (68.6)
Levofloxacin	448 / 1891 (23.7)	489 / 4596 (10.6)	270 / 1615 (16.7)	171 / 472 (36.2)	89 / 356 (25.0	75 / 245 (30.6)

*Colistin represents percentage Intermediate susceptibility of *Acinetobacter* spp.

Table 5.6: Yearly susceptible trend of *A. baumannii* isolated from all samples except faeces

AMA	Year -2017 Total=3359	Year -2018 Total=4549	Year -2019 Total=8531	Year -2020 Total=6849	Year -2021 Total=12393	Year -2022 Total=12142
	(S%)	(S%)	(S%)	(S%)	(S%)	(S%)
Piperacillin-tazobactam	484/3187 (15.2)	760/4494 (16.9)	1245/8010 (15.5)	770/6724 (11.5)	1327/12052 (11)	1578 / 12124 (13.0)
Cefepime	368/3300 (11.2)	587/4457 (13.2)	1040/8271 (12.6)	587/6571 (8.9)	1086/11986 (9.1)	1280/11900 (10.7)
Ceftazidime	355/3202 (11.1)	575/4164 (13.8)	905/7453 (12.1)	546/6441 (8.5)	890/10395 (8.6)	1023 / 11197 (9.1)
Imipenem	501/3346 (15)	818/4517 (18.1)	1098/7272 (15.1)	744/6702 (11.1)	1445/11934 (12.1)	1456 / 11918 (12.2)
Meropenem	615/3287 (18.7)	953/4178 (22.8)	1742/8399 (20.7)	779/6747 (11.5)	1516/12083 (12.5)	1690 / 11910 (14.2)
Colistin*	28/31 (90.3)	36/38 (94.7)	103/108 (95.4)	91/94 (96.8)	4553/4758 (95.7)	7362/7700 (95.6)
Amikacin	638/3312 (19.3)	877/3795 (23.1)	1429/7016 (20.4)	1014/5863 (17.3)	1925/10734 (17.9)	2053 / 11892 (17.2)
Minocycline	926/1380 (67.1)	2393/3725 (64.2)	3893/6431 (60.5)	2794/5139 (54.4)	5547/10185 (54.5)	6207/10542 (58.5)
Levofloxacin	886/3040 (29.1)	959/4047 (23.7)	1500/7841 (19.1)	825/6181 (13.3)	1382/9919 (13.9)	1755/10013 (17.5)

*Colistin represents percentage Intermediate susceptibility of *Acinetobacter* spp.

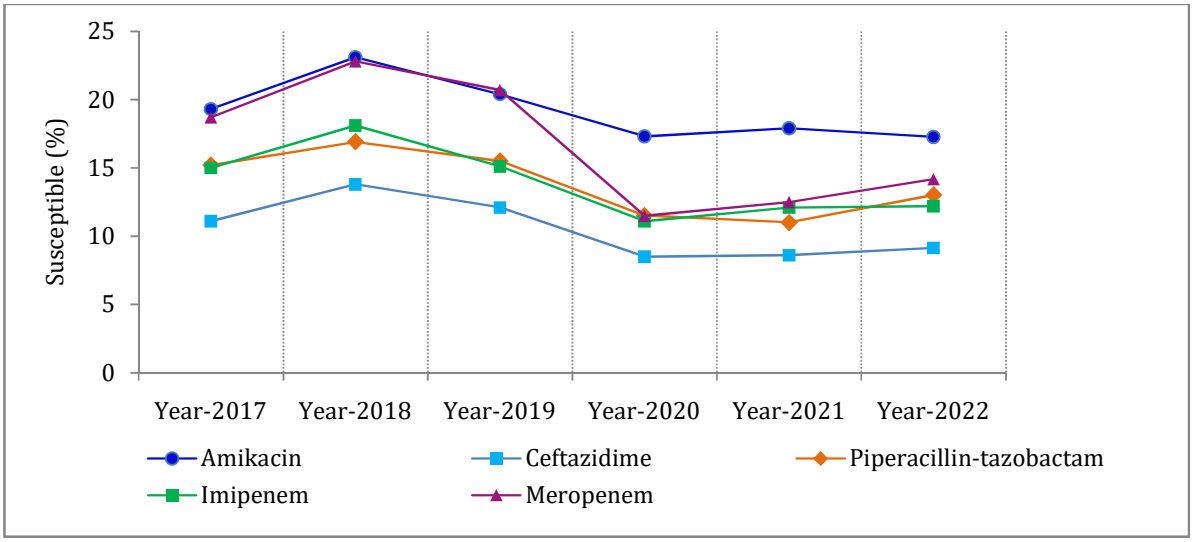


Figure 5.2: Yearly susceptible trend of *A. baumannii* isolated from all samples except faeces

Stenotrophomonas maltophilia

S. maltophilia was frequently isolated from wards and ICU compared to OPD (Table 5.7). No significant change in the susceptibility pattern was seen, irrespective of the location and sample of isolation (Table 5.7 and Table 5.8). Overall, *S. maltophilia* were highly susceptible to minocycline (96.6%), levofloxacin (90.3 %) and trimethoprim-sulfamethoxazole (86.1%) and ceftazidime (75.3%) (Table 5.8). There is no significant change in the trend of susceptibility was noticed between 2017 and 2022 (Table 5.9 and Figure 5.3).

Table 5.7. Location-wise susceptible percentage of *Stenotrophomonas maltophilia* isolated from all samples across OPD, Ward and ICU

AMA	Total n=827	OPD n=136	Ward n=462	ICU n=229
Ticarcillin-clavulanic acid	*11 / 12	*1 / 1	*4 / 4	*6 / 7
Ceftazidime	159 / 211 (75.3)	41 / 48 (85.4)	86 / 111 (77.4)	32 / 52 (61.5)
Minocycline	776/803 (96.6)	130/134 (97.0)	439/452 (97.1)	207/217 (95.3)
Levofloxacin	741 / 820 (90.3)	126 / 136 (92.6)	422 / 459 (91.9)	193 / 225 (85.7)
Trimethoprim-sulfamethoxazole	704 / 817 (86.1)	120/135 (88.8)	397/456 (87.0)	187/226 (82.7)
Chloramphenicol	*4 / 5	*1 / 1	*0/ 0	*3 /4

Table 5.8: Sample-wise susceptible percentage of *Stenotrophomonas maltophilia*

AMA	All Specimens (except faeces)	Blood	LRT	Superficial Infection	Deep Infection
	n=827	n=366	n=238	n=76	n=22
Ticarcillin-clavulanic acid	*11/12 (-)	*5/6 (-)	*6/6 (-)	*0/0 (-)	*0/0 (-)
Ceftazidime	159/211 (75.4)	97/116 (83.6)	35/53 (66)	*13/16 (-)	*4/5 (-)
Minocycline	776/801 (96.9)	348/353 (98.6)	222/233 (95.3)	72/74 (97.3)	*20/20
Levofloxacin	741/817 (90.7)	328/356 (92.1)	217/238 (91.2)	68/76 (89.5)	21/22 (95.5)
Trimethoprim-sulfamethoxazole	704/816 (86.3)	320/362 (88.4)	203/234 (86.8)	68/76 (89.5)	20/22 (90.9)
Chloramphenicol	*4/5 (-)	*3/4 (-)	*0/0 (-)	*0/0 (-)	*0/0 (-)

Table 5.9: Yearly susceptible trend of *Stenotrophomonas maltophilia* isolated from all samples

AMA	Year-2017	Year-2018	Year-2019	Year-2020	Year 2021	Year 2022
	Total n=157	Total n=310	Total n=374	Total n=360	Total n=766	Total n=827
Ticarcillin-clavulanic acid	19/26 (73.1)	45/60 (75)	59/68 (86.8)	28/33 (84.8)	34/39 (87.2)	11 / 12 (91.7)
Ceftazidime	15/27 (55.6)	42/63 (66.7)	46/73 (63)	41/73 (56.2)	42/84 (50)	159 / 211 (75.3)
Minocycline	143/151 (94.7)	272/299 (91)	331/350 (94.6)	332/346 (96)	717/739 (97)	776/803 (96.6)
Levofloxacin	126/152 (82.9)	225/257 (87.5)	225/261 (86.2)	324/358 (90.5)	694/764 (90.8)	741 / 820 (90.3)
Trimethoprim-sulfamethoxazole	132/150 (88)	255/308 (82.8)	333/372 (89.5)	318/359 (88.6)	674/765 (88.1)	704/817 (86.1)
Chloramphenicol	*0/0	*1/2	*3/3	*8/9	*2/2	*4/5

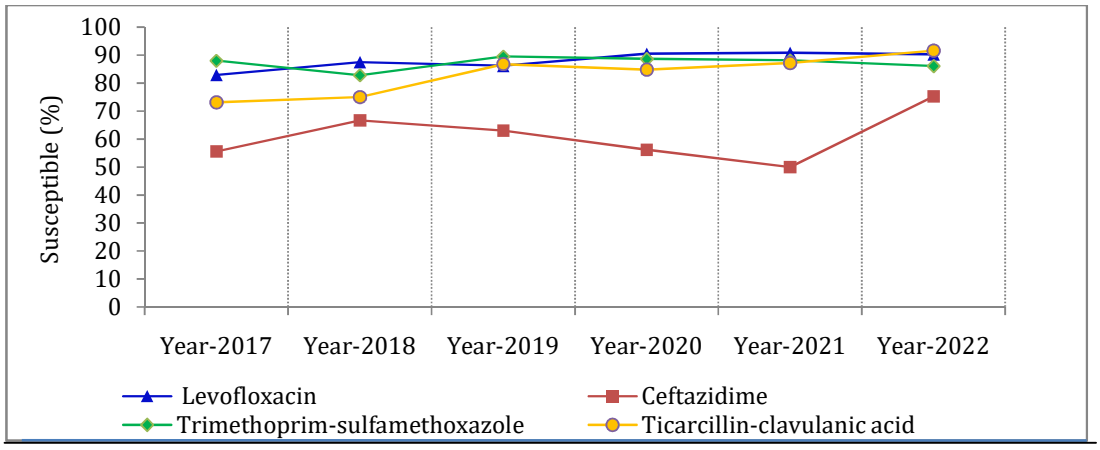


Figure 5.3: Yearly susceptible trend of *Stenotrophomonas maltophilia* isolated from all samples

Burkholderia cepacia

Burkholderia cepacia is an important opportunistic pathogen and intrinsically resistant to multiple classes of antibiotics, including aminoglycosides and polymyxins. Among the tested antibiotics, higher rate susceptibility to ceftazidime (90%), meropenem (72.4%), minocycline (76.9%) and trimethoprim-sulfamethoxazole (85.2%) were seen. There is no significant difference in the susceptibility profile of *B. cepacia* in location-wise (Table 5.10) and the clinical source of isolation (Table 5.11). There is no notable change in the trend of susceptibility in *B. cepacia* during the surveillance period from 2017 to 2022 (Table 5.12 and Figure 5.4). Trimethoprim-sulfamethoxazole (TMP-SMX) and ceftazidime are considered first-line options for *B. cepacia* infections, however, in-vitro resistance to trimethoprim-sulfamethoxazole and ceftazidime seen in this surveillance, clearly demonstrates limited treatment options. Carbapenems and minocycline can be used as an alternative.

Table 5.10: Location-wise susceptible percentage of *Burkholderia cepacia* isolated from all samples across OPD, Ward and ICU

AMA	Total n=114	OPD n=16	Ward n=38	ICU n=60
Ceftazidime	102 / 113 (90.1)	*13 / 16	35/ 37 (94.4)	54 / 60 (90.0)
Meropenem	84 / 116 (72.4)	*10 / 16	30/ 41 (73.1)	44/ 59 (74.5)
Minocycline	90 / 117 (76.9)	*13 / 18	31 / 39 (79.4)	46 / 60 (76.6)
Levofloxacin	27 / 68 (39.7)	*5 / 11	*7 / 19	15 / 38 (39.4)
Trimethoprim-sulfamethoxazole	98 / 115 (85.2)	*10 / 17	32 / 39 (82.0)	56 / 59 (94.9)
Chloramphenicol	*1 / 1	*0 / 0	*1 / 1	*0 / 0

Table 5.11: Sample-wise susceptible percentage of *Burkholderia cepacia*

AMA	All Specimens (except faeces)	Blood	LRT	Superficial Infection	Deep Infection	Urine
	n=247	n=147	n=61	n=*8	n=*5	n=*9
Ticarcillin-clavulanic acid	*1 / 1	*1 / 1	*0 / 0	*0 / 0	*0 / 0	*0 / 0
Ceftazidime	101 / 112 (90.2)	54 / 58 (93.1)	30 / 34 (88.2)	4 / 4 (100)	2 / 2 (100)	7 / 8 (87.5)
Meropenem	84 / 116 (72.4)	44 / 60 (73.3)	25 / 34 (73.5)	*4 / 4	*1 / 1	*6 / 8
Minocycline	90 / 117 (76.9)	52 / 63 (82.5)	24 / 33 (72.7)	*3 / 4	*2 / 2	*5 / 8
Levofloxacin	27 / 68 (39.7)	18 / 42 (42.9)	3 / 14 (21.4)	*1 / 1	*0 / 0	*4 / 7
Trimethoprim-sulfamethoxazole	98 / 115 (85.2)	50 / 59 (84.7)	33 / 34 (97.1)	*4 / 4	*2 / 2	*5 / 8
Chloramphenicol	*1 / 1	*0 / 0	*0 / 0	*0 / 0	*0 / 0	*0 / 0

Table 5.12: Yearly susceptible trend of *Burkholderia cepacia* isolated from all samples

AMA	Year-2017	Year-2018	Year-2019	Year-2020	Year 2021	Year 2022
	Total n=112	Total n=197	Total n=181	Total n=200	Total n=247	Total n=114
Ticarcillin-clavulanic acid	*0/9	4/51 (7.8)	36/103 (35)	36/80 (45)	13/58 (22.4)	*1/1
Ceftazidime	73/101 (72.3)	137/192 (71.4)	156/178 (87.6)	172/198 (86.9)	180/237 (75.9)	102 / 113 (90.1)
Meropenem	83/111 (74.8)	140/171 (81.9)	161/181 (89)	166/198 (83.8)	199/241 (82.6)	84/116 (72.4)
Minocycline	89/104 (85.6)	146/185 (78.9)	133/174 (76.4)	163/191 (85.3)	191/225 (84.9)	90 / 117 (76.9)
Levofloxacin	*4/13	34/66 (51.5)	70/124 (56.5)	81/125 (64.8)	49/90 (54.4)	27 / 68 (39.7)
Trimethoprim-sulfamethoxazole	84/109 (77.1)	179/192 (93.2)	164/177 (92.7)	174/200 (87)	193/234 (82.5)	98 / 115 (85.2)
Chloramphenicol	*0/0	*1/1	*3/3	*4/4	*3/3	*1/1

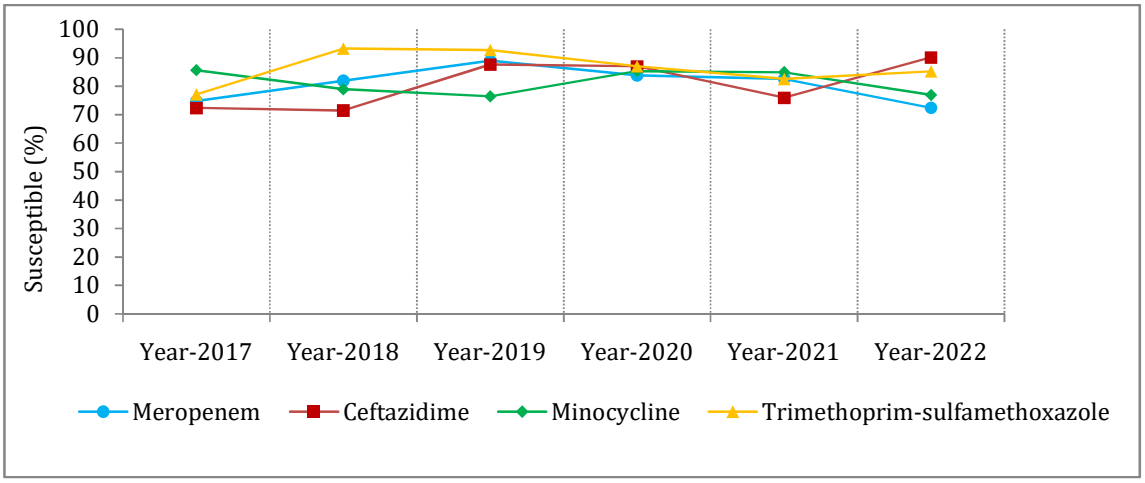


Figure 5.4: Yearly susceptible trend of *Burkholderia cepacia* isolated from all samples

Clinical relevance and treatment guidance

Pseudomonas aeruginosa:

NDM-expressing *P. aeruginosa* and *A. baumannii* are difficult to treat and there are no defined treatment options. Deficiency of OprD and overproduction of active efflux pumps, ampC β-lactamase, extended-spectrum β-lactamases, and carbapenemases, especially metallo-β-lactamase (MBL) production, have been reported as the main contributors to multi-drug resistant phenotypes of *P. aeruginosa* isolates. Resistance to piperacillin-tazobactam, ceftazidime, cefepime, aztreonam, meropenem, imipenem-cilastatin, ciprofloxacin, and levofloxacin but with preserved susceptibility to the novel BL-BLI combinations and colistin was proposed and denominated difficult-to-Treat (DTR) Resistant *P. aeruginosa.* Colistin or fosfomycin based combination strategy would be the best alternative for the treatment of DTR *P. aeruginosa* infection.

Acinetobacter baumannii

Infection with carbapenem *A. baummannii* results in 40% mortality, irrespective of therapy. High-dose ampicillin-sulbactam, in combination with either colistin, polymyxin B, or tigecycline are the recommended front-line treatment of invasive carbapenem resistant *A. baumannii* infections. The preferred treatment options are ampicillin-sulbactam with tigecycline for pneumonia and complicated intra-abdominal infection, ampicillin-sulbactam with polymyxin B for bloodstream infection, ampicillin-sulbactam with colistin for urinary tract infections. It is suggested to reserve the addition of a third agent for patients with delayed clinical responses or recurrent infections. As with any treatment regimen selected, timely source control and close monitoring for clinical response and toxicity are required.

Stenotrophomonas maltophilia

S. maltophilia has emerged as a difficult-to-treat opportunistic nosocomial pathogen. The clinical challenges posed by this microorganism extend beyond its intrinsic multidrug resistance. *S. maltophilia* is intrinsically resistant to β-lactams is mediated by the expression of two inducible β-lactamases, L1, a class B3 metallo-β-lactamase (MBL), and L2, a class A clavulanic acid susceptible cephalosporinase. L1 MBLs inactivate carbapenems and other β-lactams quite readily and are not inhibited by currently available β-lactamase inhibitors. However, an important exception is aztreonam, a monobactam, which is not inactivated by L1 MBLs. L2 β-lactamases are inducible cephalosporinases that confer resistance to extended-spectrum cephalosporins and aztreonam but are susceptible to inhibition by commercially available serine-β-lactamase inhibitors such as clavulanic acid and avibactam. Therefore, the combination of ceftazidime/avibactam with azteronam would be the better alternative for minocycline in the treatment of *S. maltophilia* infections.

Burkholderia cepacia

Infections due to *B. cepacia* can be challenging to treat, as it is intrinsically resistant to a number of commonly used antibiotics. *B. cepacia* often is susceptible to trimethoprim-sulfamethoxazole, meropenem, minocycline, and tigecycline. Ceftazidime-avibactam has shown activity against multidrug-resistant *B. cepacia* complex strains and was found to be useful in persistent bacteraemia.

Characterisation of resistance mechanism

P. aeruginosa

A total of 884 *P. aeruginosa* isolates recovered from various clinical specimens were received at the reference laboratory. Of them 753 isolates were retrieved and available for further molecular testing (Table 5.13). Of the 753 isolates, 324 were identified as carbapenem resistant and were screened for the presence of beta lactamases by molecular methods (ESBLs and carbapenemases). Among ESBLs, blaVEB was identified as the most common ESBL followed by blaTEM gene. None of the isolates had blaSHV and blaPER like seen in the previous year of 2021. Among the carbapenemases, blaNDM was found as the most common metallo beta lactamase, followed by blaVIM and blaIMP genes (Table 5.13). In *P. aeruginosa*, co- producers of ESBLs and carbapenemases were common. Among the co- producers, blaNDM co-carried with ESBLs such as blaTEM, blaVEB and blaGES genes were predominantly seen (n = 22, 73%). Trend analysis over the last two years highlights that there is a significant shift from blaVIM to blaNDM producers across different geographical location.

Table 5.13: Molecular characterization of carbapenem resistant *P. aeruginosa* collected across India during the year 2022

CENTER	Total (Revived tested)	CR	CS	ESBL				Class A Carbapenemase		Class B carbapenemase (MβLs)				Co-producers (n)	PCR Negative
				SHV	TEM	VEB	PER	KPC	GES	SPM	IMP	VIM	NDM		
CMC	56(56)	56	-	-	-	-	-		-	1	-	-	37	-	18
AIIMS	157 (142)	80	62	-	-	6	-	-	1	-	2	10	25	VEB+NDM (4) TEM+NDM (2) VIM+NDM (1) GES+TEM (1) TEM,IMP+NDM (1)	91
JIPMER	60 (55)	24	31	-	-	-	-	-	2	-	-	2	7	TEM+VIM (1) TEM+NDM (1) VEB+VIM (1)	41
PGIMER	50(38)	17	21	-	-	2	-	-	-	-	-	2	8	TEM+VIM (1) VEB+NDM (1)	24
TATA MEDICAL CENTRE	8(7)	4	3	-	1	-	-	-	-	-	-	-	1	-	5
SIR GANGARAM	30(29)	17	12	-	2	1	-	-	-	-	-	3	4	TEM&NDM (1)	18
MGIMS	55(40)	9	31	-	-	-	-	-	-	-	1	2	-	TEM+NDM (1) VIM+NDM (1)	35
APOLLO	36(16)	6	10	-	-	-	4	-	-	-	-	-	-	-	12
P.D.HINDUJA	52(49)	9	40	-	-	1	-	-	-	-	-	-	3	VEB+NDM (3)	42
NIIMS	47(47)	8	39	-	-	1	-	-	-	-	-	-	2	-	44
SKIMS	30(27)	4	23	-	1	-	-	-	-	-	-	1	-	-	25

KMC	27(27)	7	20	-	-	-	-	-	1	-	-	1	3	GES, VEB &NDM (1)	21
AMC	45(41)	6	35	-	-	-	-	-	-	-	-	-	2	VEB&NDM (1)	38
AFMC	22(14)	4	10	-	-	1	-	-	-	-	-	-	-	-	13
RIIMS	43(40)	20	20	-	3	2	-	-	1	-	-	2	2	GES&NDM (1) GES&VIM (1) VEB&NDM (1)	27
KGMU	19(19)	12	7	-	1	-	-	-	-	-	-	1	2	TEM&NDM (1)	14
LTMMC	72(40)	9	31	-	-	1	-	-	1	-	-	2	2	VIM+NDM (1) VEB&NDM (1) TEM&NDM (1)	31
IPGIMER	75(66)	32	34	-	1	2	-	-	1	-	-	1	8	TEM&NDM (1)	52
Total	884(753)	324	429	-	9	17	4	-	7	1	3	27	106	30	551

A. baumannii

A total of 738 isolates received from various regional centers were subjected to PCR for characterization of antimicrobial resistance genes (Table 5.14). All the isolates harboured the blaOXA-51 like gene, which is intrinsic to *Acinetobacter baumannii*. Molecular gene profile of all the of the tested *A. baumannii* isolates is given in Table 3.14. As expected, blaOXA-23 like only was the predominant carbapenemase across all the centers contributing to 76% of the carbapenem resistance. Co- producers of OXA-23 with ESBLs and/or NDM was observed across all the centers. Of which, the majority of the isolates 56% (n=357) had dual carbapenemases of blaOXA-23 like with blaNDM like. The combination of blaOXA-23 with blaPER in 13% (n=88) and blaOXA-23 with blaTEM in 5% (n=30) was noted. The antimicrobial resistance gene profile was found to be consistent across all the centers with blaOXA-23 like being the predominant carbapenemase and sporadic presence of blaOXA-58 like were observed. There was no significant change in the trend dual carbapenemase co- producers (blaOXA-23 like with blaNDM like) from 57% in 2020 to 56% in 2022.

Table 5.14: Molecular characterization of carbapenem resistant *A. baumannii* collected across India during the year 2022

Centres		CR	CS	ESBL				Class A		Class B carbapenemase (MβLs)				Class D carbapenemase			Co-producers	PCR Neg
				SHV	TEM	VEB	PER	KPC	GES	IMP	VIM	NDM	SIM	OXA-23	OXA-24	OXA-58		
CMC	67(60)	53	7	-	5	-	5	-	-	-	-	45	-	48	-	-	OXA23&NDM=38 OXA23,NDM&PER=4 NDM=3 OXA23&TEM=5 OXA23&PER=1 OXA51 Carbapenem Susceptible=3	-
SKIMS	44(33)	29	4	-	2	-	8	-	-	-	-	6	-	15	-	-	OXA23&NDM=5 OXA23&PER=7 OXA23&TEM=2 OXA23,NDM&PER=1 OXA51 Carbapenem Susceptible=3	-
RIMS	50(40)	31	9	-	-	-	5	-	-	-	-	23	-	34	-	-	OXA32=6 OXA23&NDM=23 OXA23&PER=5 OXA51 Carbapenem Susceptible=6	-
Armed Forces	1(0)	0	1	-	-	-	-	-	-	-	-	0	-	-	-	-	-	-
APOLLO	35(11)	7	4	-	1	-	-	-	-	-	-	3	-	4	-	-	OXA23&NDM=3 OXA23,&PER=1 OXA51 Carbapenem	-

																Susceptible=3	
AIIMS	185(149)	145	4	-	18	-	40	-	-	-	-	72	-	107	-	-	OXA23&NDM=49 OXA23&PER=25 OXA23,NDM,,PER=15 OXA23&TEM=10 OXA 23,NDM,TEM=8 OXA51 Carbapenem Susceptible=1	-
IPGIMER	73(64)	62	2	-	5	-	12	-	-	-	-	32	-	44	-	-	OXA23&NDM=27 OXA 23,NDM,TEM=3 OXA 23,TEM=2 OXA23&PER=10 OXA23,NDM,,PER=2 OXA51 Carbapenem Susceptible=1	-
LTMMC	72(47)	44	3	-	12	-	14	-	-	-	-	16	-	37	-	1	OXA23&NDM=11 OXA23&PER=11 OXA 23,TEM=8 OXA23,OXA58,TEM=2 OXA23,NDM,,PER=3 OXA 23,NDM,TEM=2 OXA51 Carbapenem Susceptible=3	-
MGIMS	55(39)	30	9	-	-	-	3	-	-	-	-	20	-	21	-	-	OXA23&NDM=18 OXA23&PER=1 OXA23,NDM,,PER=2 OXA51 Carbapenem Susceptible=2	-
KMC	50(46)	40	6	-	-	-	7	-	-	-	-	27	-	32	-	-	OXA23&NDM=25 OXA23&PER=5 OXA23,NDM,,PER=2 OXA51 Carbapenem Susceptible=5	-

NIMS	52(44)	27	17	-	-	-	-	-	-	-	-	26	-	26	-	-	OXA23&NDM=26 OXA51 Carbapenem Susceptible=16	4
KGMU	39(35)	35	-	-	1	-	8	-	-	-	-	10	-	17	1	-	OXA23&PER=6 OXA23&NDM=8 OXA 23,TEM=1 OXA23,NDM,,PER=2	-
JIPMER	60(56)	28	28	-	2	-	2	-	-	-	-	19	-	23	-	-	OXA23&NDM=19 OXA 23,TEM=2 OXA23&PER=2 OXA51 Carbapenem Susceptible=23	-
SIR GANGARAM	45(44)	44	-	-	2	-	12	-	-	-	-	27	-	31	-	-	OXA23&NDM=17 OXA23,NDM,,TEM=2 OXA23,NDM,,PER=8 OXA23&PER=4	-
PGIMER	33(25)	25	-	-	-	-	5	-	-	-	-	9	-	14	-	-	OXA23,NDM,,PER=5 OXA23,NDM=4 OXA23,PER=5	-
PD HINDUJA	7(7)	5	2	-	-	-	1	-	-	-	-	5	-	5	-	-	OXA23&NDM=4 OXA23,NDM,,PER=1 OXA51 Carbapenem Susceptible=2	
ASSAM MEDICAL	45(33)	23	10	-	-	-	5	-	-	-	-	17	-	22	-	-	OXA23&NDM=15 OXA58&NDM=2 OXA23&PER=5 OXA51 Carbapenem Susceptible=9	-
TATA MEDICAL	7(5)	5	-	-	-	-	-	-	-	-	-	3	-	3	-	2	OXA23&NDM=3	
TOTAL	920(738)	633	105	0	48	0	127	0	0	0	0	360	0	483	1	3	-	4

Chapter 6. Staphylococci and Enterococci

A total of 9415 *Staphylococcus aureus*, 6333 CoNS and 6965 enterococci isolates collected across India were analysed in the year 2022. The total number of isolates available for analysis in 2022 was higher than in 2021.

Staphylococcus aureus

A total of 9415 isolates of *S. aureus* was reported from different centres across India. Identification of MRSA was done by testing susceptibility to cefoxitin (8387) and/or oxacillin (3036). The overall proportion of MRSA was 44.5% and 43.7% based on the 2 methods respectively.The proportion of MRSA in 2022 was slightly higher than the rate reported in 2021 (42.6%) (Table 6.1). There was a discrepancy in the MRSA rates detected by oxacillin MIC and cefoxitin DD/MIC (43.7% vs 44.5%). This discrepancy could be because of the smaller number of isolates tested against oxacillin than against cefoxitin. Moreover the same isolates may not have been tested by both the methods. As per CLSI guidelines, an isolate of *S.aureus* may be identified as MRSA using cefoxitin and /or oxacillin. On some occasions, only one of the two methods may be positive for eg: *mec*C isolates may sometimes be cefoxitin sensitive but oxacillin resistant. This could explain the few isolates of MRSA in table 6.1 which demonstrated susceptibility to cefoxitin or oxacillin.

Susceptibility to tetracycline, clindamycin co-trimoxazole, erythromycin and ciprofloxacin, was more evident in MSSA when compared to MRSA. The anti MRSA antibiotics such as vancomycin and tigecycline showed excellent in vitro activity (100% against MRSA isolates). Linezolid resistance was encountered in MRSA, MSSA as well as CoNS isolates (2.1%, 0.6% and 0.9% respectively). These rates were slightly higher than those encountered in 2021.

Table 6.2 shows the susceptibility pattern of *S. aureus* and CoNS across different hospital locations. As expected, the overall MRSA rates among *S.aureus* were lowest in the OPD isolates (40.1%) while it was moderate among ward isolates (47.3%) and higher among in the ICU isolates (50.1%). The susceptibility to most antibiotics was least among ICU isolates and highest among OPD isolates of *S. aureus* including MRSA and CoNS. However, among *S. aureus*, susceptibility to ciprofloxacin was slightly higher among ICU and OPD isolates than ward although the difference was not significant. Linezolid resistance among MRSA, CoNS and MSSA isolates showed rates of 2.1 %, 0.9%, and 0.6% respectively. Teicoplanin resistance was slightly higher among CoNS and MSSA than the MRSA isolates and showed rates of 4 %, 0.6 percent, and 0.2 percent, respectively. There was not much difference observed across different locations.

Table 6.1: Percentage susceptibility of *S. aureus*, MSSA, MRSA and CoNS isolated from all samples

AMA	All specimens			
	S. aureus n=9415	MSSA n=5050	MRSA n=4266	CoNS n=6333
Cefoxitin	4657/8387 (55.5)	4525/4525 (100)	0/3862 (0)	883/4049 (21.8)
Oxacillin	1709/3036 (56.3)	1670/1670 (100)	0/1366 (0)	1281/2525 (50.7)
Vancomycin	7731/7731 (100)	4335/4335 (100)	3348/3348 (100)	5680/5680 (100)
Teicoplanin	3450/3466 (99.5)	1720/1724 (99.8)	1690/1700 (99.4)	1701/1771 (96)
Erythromycin	3586/9282 (38.6)	2557/4983 (51.3)	1009/4230 (23.9)	875/6267 (14)
Tetracycline	6963/8144 (85.5)	3889/4291 (90.6)	3007/3782 (79.5)	2739/4329 (63.3)
Tigecycline	2452/2452 (100)	1136/1136 (100)	1281/1281 (100)	358/358 (100)
Ciprofloxacin	1948/9050 (21.5)	1412/4879 (28.9)	524/4096 (12.8)	1980/6015 (32.9)
Clindamycin	6815/9154 (74.4)	4081/4913 (83.1)	2671/4181 (63.9)	2273/6019 (37.8)
Trimethoprim-sulfamethoxazole	6374/8620 (73.9)	3555/4547 (78.2)	2771/4013 (69.1)	2347/4356 (53.9)
Linezolid	8934/9055 (98.7)	4761/4789 (99.4)	4084/4173 (97.9)	5502/5550 (99.1)

Table 6.2: Location-wise susceptibility of *S. aureus*, MSSA, MRSA and CoNS from all samples

AMA	*Staphylococcus aureus*				*MSSA*				*MRSA*				*CoNS*			
	Total n=9415	OPD n=3940	Ward n=4571	ICU n=904	Total n=5050	OPD n=2297	Ward n=2348	ICU n=405	Total n=4266	OPD n=1610	Ward n=2170	ICU n=486	Total n=6333	OPD n=1544	Ward n=3541	ICU n=1248
Cefoxitin	4657/8387 (55.5)	2126 / 3548 (59.9)	2133 / 4044 (52.7)	398 / 798 (49.9)	4525 / 4525 (100.0)	2080 / 2080 (100)	2076 / 2076 (100)	369 / 369 (100)	0 / 3862 (0)	0 / 1466 (0)	0 / 1967 (0)	0 / 429 (0)	883 / 4049 (21.8)	309 / 1041 (29.7)	439 / 2246 (19.5)	135 / 762 (17.7)
Oxacillin	1709/3036 (56.3)	735 / 1233 (59.6)	823 / 1455 (56.6)	151 / 348 (43.4)	1670 / 1670 (100.0)	723 / 723 (100.0)	803 / 803 (100.0)	144 / 144 (100.0)	0 / 1366 (0)	0 / 510 (0)	0 / 652 (0)	0 / 204 (0)	1281 / 2525 (50.7)	216 / 552 (39.1)	901 / 1445 (62.4)	164 / 528 (31.1)
Vancomycin*	7371/7731 (100)	3359 / 3359 (100)	3726 / 3726 (100)	646 / 646 (100)	4335 / 4335 (100)	2077 / 2077 (100)	1983 / 1983 (100)	275 / 275 (100)	3348 / 3348 (100)	1270 / 1270 (100)	1715 / 1715 (100)	363 / 363 (100)	5680 / 5680 (100)	1431 / 1431 (100)	3171 / 3171 (100)	1078 / 1078 (100)
Teicoplanin	3450/3466 (99.5)	1429 / 1435 (99.6)	1622 / 1628 (99.6)	399 / 403 (99)	1720 / 1724 (99.8)	765 / 768 (99.6)	803 / 804 (99.9)	152 / 152 (100.0)	1690 / 1700 (99.4)	653 / 656 (99.5)	796 / 801 (99.4)	241 / 243 (99.2)	1701/ 1771 (96)	349 / 359 (97.2)	918 / 955 (96.1)	434 / 457 (95)
Erythromycin	3586/9282 (38.6)	1569 / 3890 (40.3)	1685 / 4517 (37.3)	332 / 888 (37.4)	2557 / 4982 (51.3)	1197 / 2266 (52.8)	1147 / 2316 (49.5)	213 / 400 (53.3)	1009 / 4230 (23.9)	369 / 1598 (23.1)	524 / 2154 (24.3)	116 / 478 (24.3)	875 / 6267 (14)	277 / 1529 (18.1)	475 / 3507 (13.5)	123 / 1231 (10)
Tetracycline	6963/8144 (85.5)	2978 / 3411 (87.3)	3391 / 4023 (84.3)	594 / 729 (81.5)	3889 / 4287 (90.7)	1815 / 1972 (92.0)	1784 / 1998 (89.3)	290 / 317 (91.5)	3007 / 3782 (79.5)	1143 / 1411 (81.0)	1566 / 1968 (79.6)	298 / 403 (73.9)	2739 / 2739 (100)	752 / 752 (100)	1453 / 1453 (100)	534 / 534 (100)
Tigecycline	2452/2452 (100)	1006 / 1006 (100)	1180 / 1180 (100)	266 / 266 (100)	1136 / 1136 (100)	506 / 506 (100)	539 / 539 (100)	91 / 91 (100)	1281 / 1281 (100)	489 / 489 (100)	622 / 622 (100)	170 / 170 (100)	358 / 358 (100)	75/ 75 (100)	166 / 166 (100)	117 / 117 (100)
Ciprofloxacin	1948/9050 (21.5)	879 / 3832 (22.9)	872 / 4408 (19.8)	197 / 856 (23)	1412 / 4871 (29.0)	685 / 2237 (30.6)	593 / 2254 (26.3)	134 / 380 (35.3)	524 / 4096 (12.8)	190 / 1550 (12.3)	274 / 2086 (13.1)	60 / 460 (13.0)	6015 / 6015 (100)	1493 / 1493 (100)	3347 / 3347 (100)	1175 / 1175 (100)

AMA	*Staphylococcus aureus*				*MSSA*				*MRSA*				*CoNS*			
	Total n=9415	**OPD n=3940**	**Ward n=4571**	**ICU n=904**	**Total n=5050**	**OPD n=2297**	**Ward n=2348**	**ICU n=405**	**Total n=4266**	**OPD n=1610**	**Ward n=2170**	**ICU n=486**	**Total n=6333**	**OPD n=1544**	**Ward n=3541**	**ICU n=1248**
Clindamycin	6815/9154 (74.4)	2958 / 3881 (76.2)	3295 / 4509 (73.1)	562 / 868 (64.7)	4081 / 4890 (83.5)	1880 / 2239 (84.0)	1886 / 2269 (83.1)	315 / 382 (82.5)	2671 / 4181 (63.9)	1059 / 1574 (67.3)	1372 / 2143 (64.0)	240 / 464 (51.7)	2273 / 6019 (37.8)	660 / 1455 (45.4)	1256 / 3357 (37.4)	357 / 1207 (29.6)
Trimethoprim-sulfamethoxazole	6374/8620 (73.9)	2619 / 3582 (73.1)	3150 / 4213 (74.8)	605 / 855 (70.8)	3555 / 4537 (78.4)	1584 / 2059 (76.9)	1669 / 2099 (79.5)	302 / 379 (79.7)	2771 / 4013 (69.1)	1017 / 1491 (68.2)	1457 / 2060 (70.7)	297 / 462 (64.3)	2347 / 4356 (53.9)	652 / 1106 (59)	1252 / 2372 (52.8)	443 / 878 (50.5)
Linezolid	8934/9055 (98.7)	3773 / 3821 (98.7)	4312 / 4375 (98.6)	849 / 870 (97.6)	4761 / 4788 (99.4)	2192 / 2204 (99.5)	2181 / 2193 (99.5)	388 / 391 (99.2)	4084 / 4173 (97.9)	1550 / 1581 (98.0)	2082 / 2124 (98.0)	452 / 468 (96.6)	5502 / 5550 (99.1)	1360 / 1367 (99.5)	3127 / 3155 (99.1)	1015 / 1028 (98.7)

**Although all isolates were found susceptible to vancomycin by MIC, a few of the isolates were found to be hVISA by PAP-AUC analysis.*

Centerwise analysis

The significant differences in MRSA rates observed between the various regional centres, the highest rate in the isolates from RC18 and RC20 (86.3% and 85.3%) (Table 6.3). The lowest MRSA rates were observed from the RC08 (27.7%) and RC04 (23.8%) based on cefoxitin test results. However, it should be noted that in RC02 and RC11 oxacillin resistance was used to identify MRSA rather than cefoxitin (592vs 1 and 203 vs 33, respectively). This variation in MRSA rates across centres may be indicative of the differences in the antibiotic prescription practices and usage in the different regions. It could also reflect different methodologies adopted across centres to identify MRSA. Ciprofloxacin susceptibility was extremely low across all the centres. The susceptibility rate of other antibiotics varied widely between the centres for many of the antibiotics like erythromycin (15.5 % in RC 13 to 59.3% in RC 04), tetracycline (67.2 % in RC19 to 94.4% in RC08), clindamycin (49.3% in RC13 to 97.9 % in RC14), co-trimoxazole (35.1% in RC12 to 94.8 % in RC03). Linezolid resistance ranged from 0.2% in RC 01 to 35.2% in RC 12.

Most of the *S. aureus* isolates were obtained from superficial infections followed by blood stream and deep infections. MRSA rates differed based on the source of isolation, with isolates from deep infection demonstrating highest rates (51.5%) while those from superficial infections showed the lowest rates (41.5%).

Although *S. aureus*, overall, showed increasing trends of resistance to most antibiotics over the years, no such prominent trend could be observed with MSSA isolates. There was only a marginal decrease in the susceptibility rates to erythromycin. Overall susceptibility rates to erythromycin, clindamycin, ciprofloxacin, co-trimoxazole was more evident in MSSA when compared to MRSA.

The comparison of the susceptibility rates of *S.aureus* in 2022 with the rates seen between 2017-21 was depicted (**Table 6.4 and Figure 6.1).** Overall MRSA rates have increased each year from 2017 to 2022 (32.9% to 45.5%). Susceptibility to most antibiotics showed almost similar rates as in the previous years. Resistance to tigecycline was not seen in 2016 but it appeared in a small number of isolates in 2017 and 2018 (0.5%), 2019 (0.4%), 2021 (0.8%). No tigecycline resistance was observed among 2022 isolates. Cefoxitin resistance, the surrogate marker for MRSA, was observed nearly twice as frequently among CoNS compared to *S. aureus* (78.2% vs 45.5%).

Table 6.3: Antimicrobial Susceptibility (AMS) Percentage RC wise of *Staphylococcus aureus* from all samples except faeces and urine

RC/ Antibiotics	Cefoxitin (n=8169)	Oxacillin (n=2987)	Vancomycin* (n=7537)	Teicoplanin (n=3396)	Erythromycin (n=9077)	Tetracycline (n=7961)	Tigecycline (n=2411)	Ciprofloxacin (n=8858)	Clindamycin (n=9033)	Trimethoprim-sulfamethoxazole (n=8411)	Linezolid (n=8828)
	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
RC1	343 / 589 (58.2)	-	502 / 502 (100.0)	-	238 / 589 (40.4)	450 / 589 (76.4)	-	252 / 589 (42.8)	434 / 589 (73.7)	446 / 589 (75.7)	588 / 589 (99.8)
RC2	*0 / 1	397 / 592 (67.1)	577 / 577 (100)	356 / 364 (97.8)	224 / 583 (38.4)	*1 / 1	*1 / 1	43 / 572 (7.5)	275 / 513 (53.6)	*1 / 1	306 / 306 (100.0)
RC3	165 / 282 (58.5)	-	41 / 41 (100.0)	-	118 / 250 (47.2)	138 / 158 (87.3)	-	36 / 41 (87.8)	115 / 170 (67.6)	235 / 248 (94.8)	277 / 279 (99.3)
RC4	1421 / 1866 (76.2)	*1 / 4	1862 / 1862 (100.0)	421 / 421 (100.0)	1113 / 1878 (59.3)	1714 / 1874 (91.5)	299 / 299 (100)	574 / 1900 (30.2)	1663 / 1960 (84.8)	1302 / 1885 (69.1)	1862 / 1867 (99.7)
RC5	161 / 246 (65.4)	167 / 255 (65.5)	156 / 156 (100.0)	139 / 139 (100.0)	97 / 255 (38.0)	202 / 244 (82.8)	*17 / 17	17 / 245 (6.9)	233 / 245 (95.1)	170 / 251 (67.7)	257 / 257 (100.0)
RC6	193 / 400 (48.3)	190 / 392 (48.5)	402 / 402 (100)	403 / 403 (100.0)	118 / 400 (29.5)	319 / 371 (86.0)	356 / 356 (100)	14 / 403 (3.5)	272 / 403 (67.5)	194 / 403 (48.1)	393 / 401 (98.0)
RC7	22 / 51 (43.1)	33 / 102 (32.4)	121 / 121 (100)	116 / 118 (98.3)	47 / 131 (35.9)	103 / 117 (88.0)	101 / 101 (100)	13 / 115 (11.3)	105 / 132 (79.5)	91 / 124 (73.4)	132 / 134 (98.5)
RC8	172 / 238 (72.3)	174 / 237 (73.4)	238 / 238 (100.0)	237 / 237 (100.0)	88 / 238 (37.0)	218 / 231 (94.4)	238 / 238 (100)	45 / 238 (18.9)	231 / 237 (97.5)	81 / 145 (55.9)	238 / 238 (100.0)
RC9	178 / 337 (52.8)	-	-	-	101 / 337 (30.0)	295 / 336 (87.8)	-	135 / 337 (40.1)	283 / 336 (84.2)	277 / 337 (82.2)	335 / 337 (99.4)
RC10	153 / 259 (59.1)	-	258 / 258 (100.0)	258 / 258 (100.0)	95 / 249 (38.2)	-	-	48 / 258 (18.6)	193 / 260 (74.2)	208 / 253 (82.2)	250 / 250 (100.0)
RC11	14 / 33 (42.4)	80 / 203 (39.4)	212 / 212 (100)	211 / 211 (100.0)	69 / 222 (31.1)	210 / 244 (86.1)	200 / 200 (100)	12 / 246 (4.9)	201 / 241 (83.4)	131 / 227 (57.7)	225 / 238 (94.5)
RC12	116 / 192 (60.4)	77 / 216 (35.6)	217 / 217 (100)	210 / 210 (100.0)	76 / 227 (33.5)	179 / 211 (84.8)	210 / 210 (100)	8 / 228 (3.5)	155 / 226 (68.6)	79 / 225 (35.1)	149 / 230 (64.8)

RC/ Antibiotics	Cefoxitin (n=8169)	Oxacillin (n=2987)	Vancomycin* (n=7537)	Teicoplanin (n=3396)	Erythromycin (n=9077)	Tetracycline (n=7961)	Tigecycline (n=2411)	Ciprofloxacin (n=8858)	Clindamycin (n=9033)	Trimethoprim-sulfamethoxazole (n=8411)	Linezolid (n=8828)
	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)
RC13	218 / 506 (43.1)	*4 / 27	196 / 196 (100)	41/ 44 (93.2)	83 / 536 (15.5)	382 / 466 (82.0)	*22 / 22	81 / 506 (16.0)	263 / 533 (49.3)	420 / 539 (77.9)	535 / 540 (99.1)
RC14	418 / 668 (62.6)	420 / 668 (62.9)	667 / 667 (100.0)	668 / 668 (100.0)	303 / 669 (45.3)	655 / 669 (97.9)	668 / 668 (100)	150 / 669 (22.4)	655 / 669 (97.9)	589 / 669 (88.0)	667 / 667 (100.0)
RC15	456 / 888 (51.4)	-	861 / 861 (100.0)	-	279 / 889 (31.4)	681 / 835 (81.6)	-	70 / 884 (7.9)	552 / 889 (62.1)	777 / 888 (87.5)	866 / 866 (100.0)
RC16	128 / 383 (33.4)	*2 / 4	387 / 387 (100.0)	*4 / 4	65 / 386 (16.8)	275 / 385 (71.4)	*4 / 4	86 / 387 (22.2)	263 / 386 (68.1)	220 / 387 (56.8)	386 / 387 (99.7)
RC17	100 / 215 (46.5)	112 / 223 (50.2)	222 / 222 (100.0)	222 / 223 (99.6)	130 / 223 (58.3)	197 / 224 (87.9)	221 / 221 (100)	36 / 224 (16.1)	171 / 225 (76.0)	145 / 224 (64.7)	222 / 223 (99.6)
RC18	35 / 256 (13.7)	-	103 / 103 (100)	-	106 / 256 (41.4)	222 / 256 (86.7)	-	99 / 256 (38.7)	194 / 256 (75.8)	235 / 256 (91.8)	255 / 256 (99.6)
RC19	155 / 417 (37.2)	-	413 / 413 (100.0)	-	96 / 416 (23.1)	279 / 415 (67.2)	*1 / 1	100 / 416 (24.0)	213 / 416 (51.2)	365 / 416 (87.7)	416 / 416 (100.0)
RC20	38 / 258 (14.7)	*1 / 1	*18 / 18	*18 / 18	79 / 262 (30.2)	223 / 252 (88.5)	-	47 / 260 (18.1)	175 / 263 (66.5)	168 / 262 (64.1)	257 / 263 (97.7)
RC21	77 / 84 (91.7)	28 / 63 (44.4)	84 / 84 (100)	76 / 78 (97.4)	8 / 81 (9.9)	74 / 83 (89.2)	73 / 73 (100)	10 / 84 (11.9)	32 / 84 (38.1)	60 / 82 (73.2)	82 / 84 (97.6)
Total	4564 / 8169 (55.9)	1686 / 2987 (56.4)	7537 / 7537 (100)	3380 / 3396 (99.5)	3533 / 9077 (38.9)	6817 / 7961 (85.6)	2411 / 2411 (100)	1876 / 8858 (21.2)	6678 / 9033 (73.9)	6194 / 8411 (73.6)	8698 / 8828 (98.5)

**Although all isolates were found susceptible to vancomycin by MIC, a few of the isolates were found to be hVISA by PAP-AUC analysis.*

Table 6.4: Year wise susceptibility trends of *Staphylococcus aureus* from all samples

AMA	Year-2017	Year-2018	Year-2019	Year-2020	Year-2021	Year-2022
	Total n=5708	Total n=8644	Total n=12320	Total n=6281	Total n=8827	Total n=9415
Cefoxitin	3805/5668 (67.1)	4863/7919 (61.4)	6272/10835 (57.9)	3394/5787 (58.6)	3869/6740 (57.4)	4657/8387 (55.5)
Oxacillin	314/438 (71.7)	1218/2196 (55.5)	2280/3773 (60.4)	1140/1869 (61)	2440/3685 (66.2)	1709/3036 (56.3)
Vancomycin	2602/2602 (100)	4640/4640 (100)	6996/6996 (100)	3846/3846 (100)	6203/6204 (100)	7731/7731 (100)
Teicoplanin	5233/5257 (99.5)	6544/6697 (97.7)	6194/6269 (98.8)	2043/2050 (99.7)	3351/3356 (99.9)	3450/3466 (99.5)
Erythromycin	2755/5570 (49.5)	3593/8102 (44.3)	4803/11975 (40.1)	2594/6096 (42.6)	3617/8355 (43.3)	3586/9282 (38.6)
Tetracycline	3492/3860 (90.5)	6255/7050 (88.7)	9269/10329 (89.7)	4734/5284 (89.6)	5686/6400 (88.8)	6963/8144 (85.5)
Tigecycline	433/435 (99.5)	1529/1536 (99.5)	2902/2914 (99.6)	1559/1559 (100)	2113/2131 (99.2)	2452/2452 (100)
Ciprofloxacin	1224/5260 (23.3)	1497/8094 (18.5)	1990/11200 (17.8)	1101/5845 (18.8)	1455/8341 (17.4)	1948/9050 (21.5)
Clindamycin	4235/5475 (77.4)	6460/8456 (76.4)	9153/11984 (76.4)	4645/6084 (76.3)	6334/8579 (73.8)	6815/9154 (74.4)
Trimethoprim-sulfamethoxazole	3064/4306 (71.2)	4764/7565 (63)	7927/11401 (69.5)	3926/5821 (67.4)	4718/6954 (67.8)	6374/8620 (73.9)
Linezolid	5424/5445 (99.6)	8054/8148 (98.8)	11461/11547 (99.3)	5846/5877 (99.5)	8233/8236 (100)	8934/9055 (98.7)

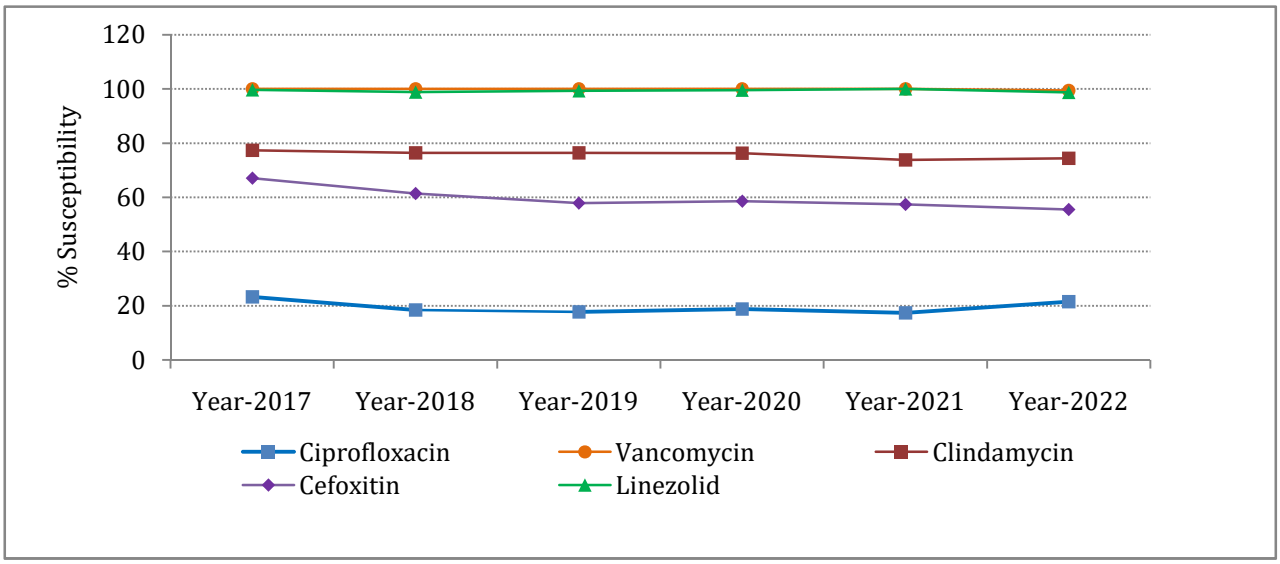


Figure 6.1: Year wise susceptibility trends of *S. aureus* from all samples

Table 6.5 depicts the susceptibility rates of staphylococci from blood. MRSA rate was slightly higher among blood isolates when compared to the overall rate (47% vs 45.5%). CoNS were more commonly isolated from blood than *S. aureus* from the different centres across India. Cefoxitin resistance was observed more commonly among CoNS than the *S.aureus* (80% vs 47%). When compared to MRSA, MSSA was more susceptible to tetracycline, co-trimoxazole, clindamycin, erythromycin and ciprofloxacin. The anti MRSA antibiotics such as linezolid, tigecycline and vancomycin showed excellent in vitro activity.

As seen from Table 6.6, around 45% of the total *S. aureus* and 5.9% of CoNS isolates were from superficial infections, MRSA rate was 41.5%. When compared to MRSA, MSSA was more susceptible to tetracycline, co-trimoxazole, clindamycin, erythromycin and ciprofloxacin. The anti MRSA antibiotics such as teicoplanin, linezolid, tigecycline and vancomycin showed excellent in vitro activity Teicoplanin and linezolid resistance was found in CoNS isolates (6.2% and 2.3%). The proportion of MRSA from deep seated infections is higher than the overall rate (51.5% vs 44.5%) (Table 6.7). The anti MRSA antibiotics such as tigecycline and vancomycin showed excellent in vitro activity. Teicoplanin and linezolid resistance was found in CoNS isolates (1.6% and 1.1%).

Table 6.8 and figure 6.2 depict trends in antimicrobial susceptibility among MSSA isolates across the 6 years of study (2017-22). Although *S.aureus*, overall, showed increasing trends of resistance to most antibiotics over the years, no such prominent trend could be observed with MSSA isolates. There was only a marginal increase in the susceptibility rates to clindamycin and co-trimoxazole. The unusual occurrence of linezolid resistance rates was slightly increased in MSSA isolates (0.1 to 0.6 %). Table 6.9 and figure 6.3 depict trends in antimicrobial resistance in MRSA isolates across the 6 years (2017-22). Susceptibility rates across the years were similar to most antibiotics except co-trimaxazole which showed a slight increase in the susceptibility among 2021 isolates which continued into 2022. The teicoplanin resistance rates were increased in 2022 when compared to 2021 rates (0.1% and 0.6 %). Linezolid resistance was slightly increased 0.1% to 2.1% respectively.

Table 6.5: Susceptibility percentages of staphylococci isolated from blood

	S. aureus n=1783	MSSA n=962	MRSA n=821	CoNS n=5287
Cefoxitin	742/1400 (53)	702/702 (100)	0/698 (0)	653/3258 (20)
Oxacillin	450/738 (61)	437/437 (100)	0/301 (0)	1200/2213 (54.2)
Vancomycin	1381/1381 (100)	766/766 (100)	615/615 (100)	4805/4805 (100)
Teicoplanin	785/789 (99.5)	445/446 (99.8)	340/343 (99.1)	1351/1401 (96.4)
Erythromycin	686/1768 (38.8)	487/953 (51.1)	199/815 (24.4)	677/5249 (12.9)
Tetracycline	1111/1328 (83.7)	601/667 (90.1)	510/661 (77.2)	2133/3431 (62.2)
Tigecycline	402/402 (100)	191/191 (100)	211/211 (100)	224/224 (100)
Ciprofloxacin	383/1632 (23.5)	275/886 (31)	108/746 (14.5)	1580/5020 (31.5)
Clindamycin	1163/1713 (67.9)	728/911 (79.9)	435/802 (54.2)	1793/5005 (35.8)
Trimethoprim-sulfamethoxazole	1039/1421 (73.1)	566/707 (80.1)	473/714 (66.2)	1815/3403 (53.3)
Linezolid	1488/1510 (98.5)	753/758 (99.3)	735/752 (97.7)	4491/4522 (99.3)

Table 6.6: Susceptible percentages of staphylococci isolated from Superficial Infections

	S. aureus n=4245	MSSA n=2421	MRSA n=1824	CoNS n=354
Cefoxitin	2310/3947 (58.5)	2247/2247 (100)	0/1700 (0)	109/313 (34.8)
Oxacillin	722/1297 (55.7)	705/705 (100)	0/592 (0)	14/61 (23)
Vancomycin	3698/3698 (100)	2152/2152 (100)	1546/1546 (100)	298/298 (100)
Teicoplanin	1481/1489 (99.5)	719/722 (99.6)	762/767 (99.3)	75/80 (93.8)
Erythromycin	1685/4216 (40)	1247/2401 (51.9)	438/1815 (24.1)	79/353 (22.4)
Tetracycline	3449/3964 (87)	2075/2247 (92.3)	1374/1717 (80)	229/335 (68.4)
Tigecycline	1230/1230 (100)	570/570 (100)	660/660 (100)	30/30 (100)
Ciprofloxacin	1004/4199 (23.9)	772/2397 (32.2)	232/1802 (12.9)	154/338 (45.6)
Clindamycin	3320/4211 (78.8)	2059/2402 (85.7)	1261/1809 (69.7)	190/353 (53.8)
Trimethoprim-sulfamethoxazole	3050/4074 (74.9)	1817/2308 (78.7)	1233/1766 (69.8)	176/353 (49.9)
Linezolid	4146/4213 (98.4)	2383/2401 (99.3)	1763/1812 (97.3)	342/350 (97.7)

Table 6.7 Susceptibility percentages of staphylococci isolated from Deep Infections

AMA	Deep Infection			
	S. aureus n=1112	MSSA n=535	MRSA n=577	CoNS n=99
Cefoxitin	445/918 (48.5)	433/433 (100)	0/485 (0)	24/81 (29.6)
Oxacillin	280/531 (52.7)	275/275 (100)	0/256 (0)	17/55 (30.9)
Vancomycin	810/810 (100)	429/429 (100)	381/381 (100)	83/83 (100)
Teicoplanin	630/632 (99.7)	328/329 (99.7)	302/303 (99.7)	62/63 (98.4)
Erythromycin	364/1094 (33.3)	232/521 (44.5)	132/573 (23)	21/97 (21.6)
Tetracycline	796/908 (87.7)	377/417 (90.4)	419/491 (85.3)	65/90 (72.2)
Tigecycline	462/462 (100)	237/237 (100)	225/225 (100)	31/32 (100)
Ciprofloxacin	147/1084 (13.6)	90/523 (17.2)	57/561 (10.2)	41/95 (43.2)
Clindamycin	800/1096 (73)	425/522 (81.4)	375/574 (65.3)	46/97 (47.4)
Trimethoprim-sulfamethoxazole	672/1020 (65.9)	322/472 (68.2)	350/548 (63.9)	69/97 (71.1)
Linezolid	1085/1095 (99.1)	519/521 (99.6)	566/574 (98.6)	94/95 (98.9)

Table 6.8: Year wise susceptibility trends of MSSA from all samples

AMA	Year-2017	Year-2018	Year-2019	Year-2020	Year-2021	Year-2022
	Total n=3819	Total n=5135	Total n=7029	Total n=3655	Total n=5273	Total n=5050
Cefoxitin	3801/3801 (100)	4857/4857 (100)	6255/6255 (100)	3388/3388 (100)	3845/3845 (100)	4525/4525 (100)
Oxacillin	306/306 (100)	1187/1187 (100)	2195/2195 (100)	1100/1100 (100)	2399/2399 (100)	1670/1670 (100)
Vancomycin	1935/1935 (100)	3041/3041 (100)	3986/3986 (100)	2153/2153 (100)	4010/4010 (100)	4335/4335 (100)
Teicoplanin	3509/3517 (99.8)	3642/3682 (98.9)	3391/3419 (99.2)	1074/1075 (99.9)	1945/1949 (99.8)	1720/1724 (99.8)
Erythromycin	2251/3739 (60.2)	2757/4841 (57)	3527/6895 (51.2)	1962/3570 (55)	2665/4975 (53.6)	2557/4983 (51.3)
Tetracycline	2508/2665 (94.1)	3809/4137 (92.1)	5383/5791 (93)	2838/3047 (93.1)	3297/3579 (92.1)	3889/4291 (90.6)
Tigecycline	300/302 (99.3)	902/902 (100)	1608/1613 (99.7)	861/861 (100)	1102/1112 (99.1)	1136/1136 (100)
Ciprofloxacin	1051/3524 (29.8)	1167/4816 (24.2)	1587/6452 (24.6)	888/3386 (26.2)	1112/4971 (22.4)	1412/4879 (28.9)
Clindamycin	3162/3666 (86.3)	4341/5021 (86.5)	5837/6839 (85.3)	3021/3548 (85.1)	4057/5137 (79)	4081/4913 (83.1)
Trimethoprim-sulfamethoxazole	2202/2959 (74.4)	3030/4499 (67.3)	4750/6475 (73.4)	2425/3344 (72.5)	2884/3927 (73.4)	3555/4547 (78.2)
Linezolid	3630/3636 (99.8)	4775/4800 (99.5)	6433/6448 (99.8)	3343/3349 (99.8)	4838/4839 (100)	4761/4789 (99.4)

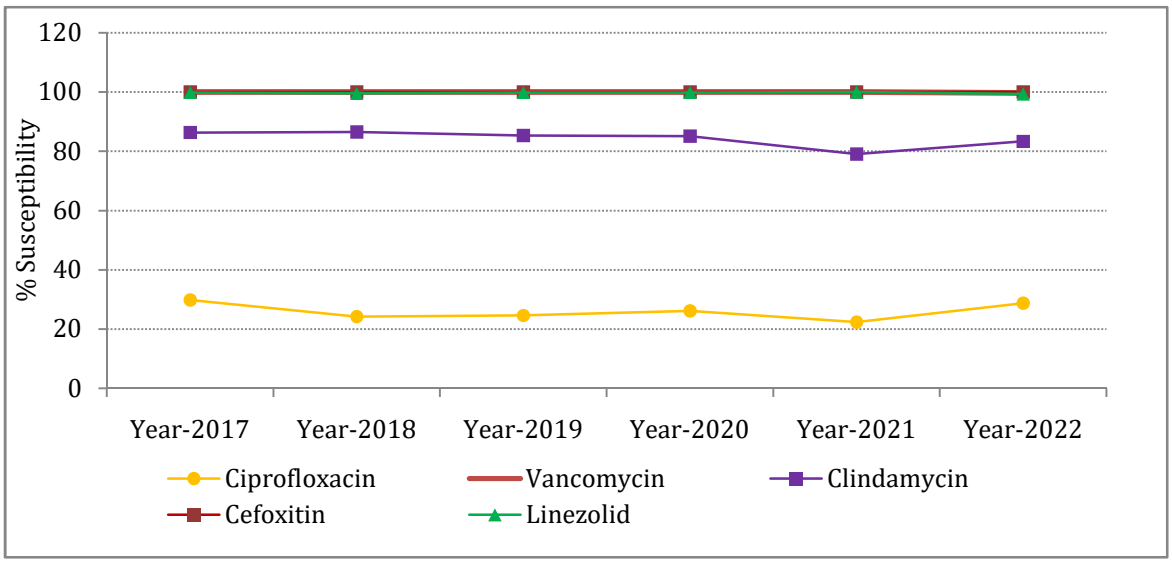


Figure 6.2: Year wise susceptibility trends of MSSA from all samples

Table 6.9: Year wise susceptibility trends of MRSA from all samples

AMA	Year-2017	Year-2018	Year-2019	Year-2020	Year-2021	Year-2022
	Total n=1870	Total n=3445	Total n=5185	Total n=2582	Total n=3423	Total n=4266
Cefoxitin	0/1867 (0)	0/3062 (0)	0/4578 (0)	0/2399 (0)	24/2895 (0.8)	0/3862 (0)
Oxacillin	8/132 (6.1)	31/1009 (3.1)	85/1578 (5.4)	40/769 (5.2)	41/1286 (3.2)	0/1366 (0)
Vancomycin	667/667 (100)	1581/1581 (100)	2960/2960 (100)	1676/1676 (100)	2153/2154 (100)	3348/3348 (100)
Teicoplanin	1719/1735 (99.1)	2848/2956 (96.3)	2729/2775 (98.3)	948/953 (99.5)	1369/1370 (99.9)	1690/1700 (99.4)
Erythromycin	494/1813 (27.2)	822/3228 (25.5)	1251/4988 (25.1)	621/2490 (24.9)	917/3274 (28)	1009/4230 (23.9)
Tetracycline	983/1193 (82.4)	2397/2859 (83.8)	3829/4473 (85.6)	1885/2223 (84.8)	2348/2772 (84.7)	3007/3782 (79.5)
Tigecycline	133/133 (100)	627/634 (98.9)	1280/1286 (99.5)	694/694 (100)	990/998 (99.2)	1281/1281 (100)
Ciprofloxacin	165/1718 (9.6)	323/3222 (10)	397/4654 (8.5)	204/2417 (8.4)	328/3257 (10.1)	524/4096 (12.8)
Clindamycin	1067/1802 (59.2)	2083/3373 (61.8)	3248/5044 (64.4)	1598/2497 (64)	2228/3362 (66.3)	2671/4181 (63.9)
Trimethoprim-sulfamethoxazole	851/1332 (63.9)	1701/3006 (56.6)	3127/4848 (64.5)	1484/2449 (60.6)	1796/2961 (60.7)	2771/4013 (69.1)
Linezolid	1779/1794 (99.2)	3228/3296 (97.9)	4936/5001 (98.7)	2476/2500 (99)	3317/3319 (99.9)	4084/4173 (97.9)

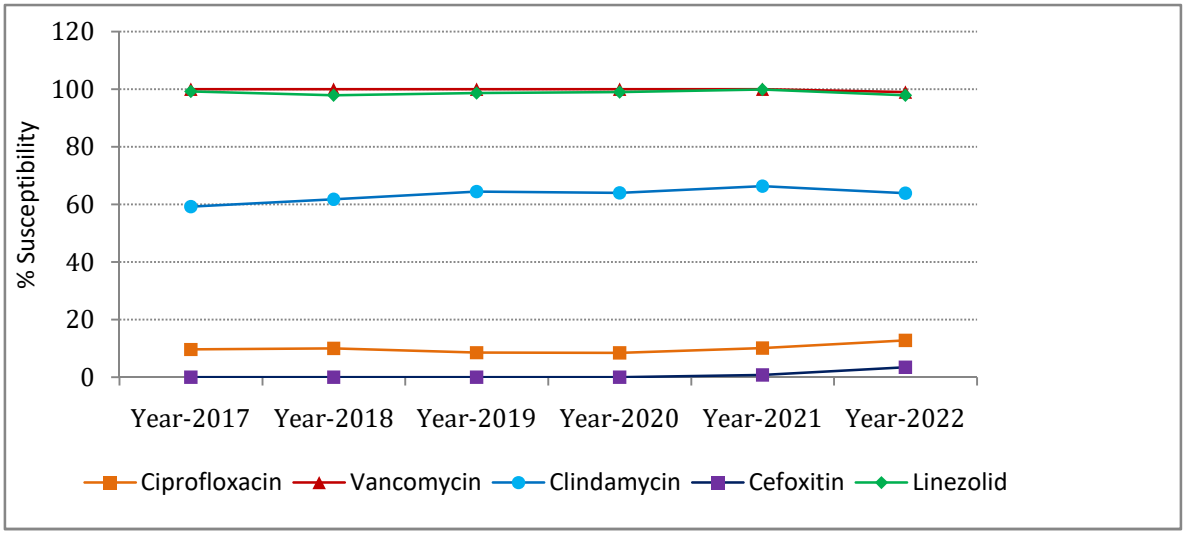


Figure 6.3: Year wise susceptibility trends of MRSA from all samples

Coagulase negative staphylococci

The common species were *S. haemolyticus, S. epidermidis, S. hominis, S. lugdunensis* and *S. saprophyticus*. Cefoxitin resistance was highest in *S. haemolyticus* (86.1 %) followed by *S. epidermidis* (75.1%) and *S. hominis* (74.6%). With the exception of teicoplanin, linezolid and tetracycline, *S. haemolyticus* exhibited much lower rates of susceptibility to all antibiotics when compared to the other species. Linezolid resistance rates remained unchanged in *S. haemolyticus* while it was slightly higher among *S. lugdunensis (*3.1%) and *S. saprophyticus* (2%) (Table 6.10). It can be clearly observed that there is a decrease in the susceptibility rates for most of the antibiotics except trimethoprim-sulfamethoxazole in 2021 and 2022.

Table 6.11 and figure 6.4 depict trends in antimicrobial susceptibility among CoNS isolates across the 6 years of study (2017-22). Although CoNS, overall, showed increasing trends of resistance to cefoxitin, erythromycin, tetracycline, ciprofloxacin and clindamycin over the years, there was only a marginal increase in the susceptibility rates to co-trimoxazole. Linezolid resistance rates were slightly increased in CoNS isolates (0.5 to 0.9 %) compared to 2021 but was lower than in 2018 and 2019.

Table 6.10: Susceptibility percentages of CoNS isolated from all specimens

	All specimens					
AMA	***S. haemolyticus* n=2372**	***S. epidermidis* n=1774**	***S. hominis* n=1472**	***S.* spp. n=560**	***S. lugdunensis* n=97**	***S. saprophyticus* n=49**
Cefoxitin	243/1742 (13.9)	220/884 (24.9)	254/1001 (25.4)	92/301 (30.6)	60/94 (63.8)	14/27 (51.9)
Vancomycin	2210/2210 (100)	1602/1602 (100)	1334/1334 (100)	459/459 (100)	27/27 (100)	45/45 (100)
Teicoplanin	549/572 (96)	647/669 (96.7)	285/294 (96.9)	169/184 (91.8)	*15/15 (-)	34/35 (97.1)
Erythromycin	188/2358 (8)	297/1745 (17)	225/1462 (15.4)	103/557 (18.5)	45/97 (46.4)	16/45 (35.6)
Tetracycline	1115/1862 (59.9)	640/960 (66.7)	634/1056 (60)	220/309 (71.2)	84/91 (92.3)	45/48 (93.8)
Ciprofloxacin	497/2287 (21.7)	663/1682 (39.4)	513/1408 (36.4)	191/489 (39.1)	72/96 (75)	44/50 (88)
Clindamycin	585/2322 (25.2)	701/1658 (42.3)	680/1396 (48.7)	206/496 (41.5)	74/97 (76.3)	26/47 (55.3)
Linezolid	2158/2187 (98.7)	1413/1418 (99.6)	1300/1304 (99.7)	486/491 (99)	94/97 (96.9)	49/50 (98)
Trimethoprim-sulfamethoxazole	923/1859 (49.7)	527/971 (54.3)	589/1043 (56.5)	198/333 (59.5)	71/98 (72.4)	38/49 (77.6)

Table 6.11: Year wise susceptibility trends of CoNS from all samples

AMA	All specimens					
	Year-2017	Year-2018	Year-2019	Year-2020	Year-2021	Year-2022
	Total n=2830	Total n=4016	Total n=3571	Total n=2018	Total n=2655	Total n=6333
Cefoxitin	930/2810 (33.1)	982/3574 (27.5)	921/3298 (27.9)	487/1907 (25.5)	566/2444 (23.2)	883/4049 (21.8)
Vancomycin	718/718 (100)	1619/1679 (96.4)	1681/1691 (99.4)	890/890 (100)	1374/1377 (99.8)	5680/5680 (100)
Teicoplanin	2212/2236 (98.9)	2912/3083 (94.5)	1324/1379 (96)	229/238 (96.2)	497/518 (95.9)	1701/1771 (96)
Erythromycin	742/2679 (27.7)	755/3459 (21.8)	815/3514 (23.2)	396/1999 (19.8)	455/2608 (17.4)	875/6267 (14)
Tetracycline	1177/1358 (86.7)	2236/2811 (79.5)	2658/3269 (81.3)	1582/1916 (82.6)	1809/2537 (71.3)	248/358 (69.3)
Ciprofloxacin	986/2236 (44.1)	1145/3015 (38)	1178/2798 (42.1)	563/1597 (35.3)	778/2210 (35.2)	1980/6015 (32.9)
Clindamycin	1613/2782 (58)	2151/3952 (54.4)	2058/3509 (58.6)	1057/2005 (52.7)	1363/2626 (51.9)	2273/6019 (37.8)
Linezolid	2638/2680 (98.4)	3796/3900 (97.3)	3340/3429 (97.4)	1958/1978 (99)	2600/2614 (99.5)	5502/5550 (99.1)
Trimethoprim-sulfamethoxazole	923/1940 (47.6)	1579/3452 (45.7)	1687/3428 (49.2)	861/1935 (44.5)	1224/2610 (46.9)	2347/4356 (53.9)

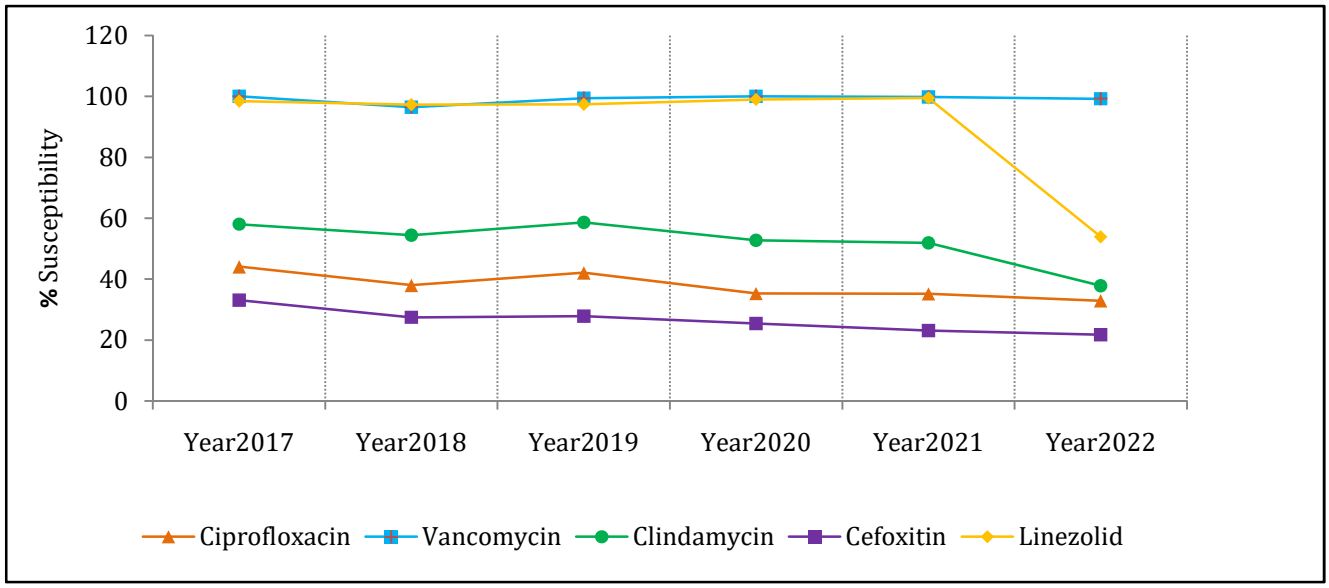


Figure 6.4: Year wise susceptibility trends of CoNS from all samples

Enterococci

E. faecalis is usually the commonest species followed by *E. faecium*. However in 2021, *E. faecium* was found to be the predominant species. This trend was again reversed in 2022 where *E. faecalis* was once more the predominant species. The susceptibility rate in *E. faecium* was significantly lower for ampicillin, high level gentamicin and vancomycin than in *E. faecalis*. Overall vancomycin resistance in enterococci was 16.7% (2022) slightly increased than the rate in 2021(14.9%). However, the rate was 5 times higher in *E. faecium* compared *to E. faecalis* (27% vs 5.3%). Isolates from blood (both the species) appear to be more resistant when compared to isolates from superficial and deep infections in *E. faecium* isolates. Although the numbers are too small for significance, vancomycin resistance among CSF isolates was much higher than the overall rate (Table 6.12).

The susceptibility to all the antibiotics was higher among *E. faecalis* isolates when compared to *E. faecium*. The difference was particularly marked for ampicillin, ciprofloxacin and nitrofurantoin. Fosfomycin resistance increased from 8.5% in 2021 to 21.2% in 2022 (Table 6.13). Resistance to this antibiotic was reported only from a few regional centres (RC09, RC07, RC12, RC13, RC16, RC18, RC19, RC20, RC01). As expected, most antibiotics showed lower susceptibility rates among ICU isolates when compared to ward or OPD isolates. This difference was noted in *E. faecalis* species (except for nitrofurantoin and linezolid) in both case susceptibility rate were slightly higher in ward isolates than the ICU (Table 6.14).

Enterococcus faecium

The trends in antibiotic susceptibility rates in *E. faecium* from 2017-2022 was depicted in Table 6.15 and figure 6.5. The susceptibility rates showed a slight increase for ampicillin, high-level gentamicin, nitrofurantoin in 2022 when compared to 2021 while there was a slight reduction in susceptibility to vancomycin, linezolid and teicoplanin. Compared to the index year of 2017, there was a significant reduction in susceptibility to nitrofurantoin while it showed improvement for HLG.

In *Enterococcus faecium* the susceptibility rates to vancomycin ranged from 54.2% to 95.5 % across regional centres (Table 6.16). Though the overall VRE rate is 27% slightly increased compared to 2021 (25.7%), there were significant differences observed between the various regional centres, the highest VRE rate in the isolates from RC06 and RC12 (45.1% and 45.8). The lowest VRE rates were observed from the RC17 (4.5%) and RC09 (9.7%). Susceptibility to linezolid was high (>90%) in most centres. However, one centre reported a very low susceptibility rate of 67.5%. Susceptibility to ampicillin was found to be lowest in the range of (2.6% to 41.9%), while susceptibility to high level gentamicin ranged between 29.7% to 67.6%.

Table 6.12: Susceptibility pattern of enterococci from all samples except urine

AMA	All Specimens (except urine)		Blood		Superficial Infection		Deep Infection		CSF	
	E. faecium n=2068	*E. faecalis* n=1879	*E. faecium* n=950	*E. faecalis* n=556	*E. faecium* n=405	*E. faecalis* n=689	*E. faecium* n=167	*E. faecalis* n=152	*E. faecium* n=65	*E. faecalis* n=38
Ampicillin	262/1764 (14.9)	1253/1650 (75.9)	113/810 (14)	319/489 (65.2)	65/378 (17.2)	488/602 (81.1)	13/129 (10.1)	119/137 (86.9)	11/53 (20.8)	15/25 (60)
Vancomycin	1497/2050 (73)	1755/1854 (94.7)	643/945 (68)	501/552 (90.8)	328/403 (81.4)	668/684 (97.7)	129/162 (79.6)	140/143 (97.9)	32/64 (50)	26/38 (68.4)
Teicoplanin	1516/2023 (74.9)	1759/1845 (95.3)	673/944 (71.3)	517/553 (93.5)	324/398 (81.4)	657/681 (96.5)	127/157 (80.9)	148/150 (98.7)	35/57 (61.4)	25/27 (92.6)
Gentamicin HL	688/1808 (38.1)	972/1674 (58.1)	280/829 (33.8)	286/504 (56.7)	168/376 (44.7)	370/639 (57.9)	53/117 (45.3)	70/115 (60.9)	16/48 (33.3)	13/35 (37.1)
Linezolid	1825/1975 (92.4)	805/1836 (98.3)	796/872 (91.3)	511/522 (97.9)	379/402 (94.3)	678/686 (98.8)	145/162 (89.5)	149/149 (100)	58/65 (89.2)	38/38 (100)

Table 6.13: Susceptibility pattern of enterococci from urine

AMA	Urine	
	Enterococcus faecalis n=1362	*Enterococcus faecium* n=938
Ampicillin	758/1182 (64.1)	138/815 (16.9)
Vancomycin	1288/1339 (96.2)	732/921 (79.5)
Teicoplanin	1236/1295 (95.4)	691/883 (78.3)
Gentamicin HL	607/1083 (56)	320/760 (42.1)
Ciprofloxacin	348/1305 (26.7)	119/884 (13.5)
Nitrofurantoin	1159/1317 (88)	438/888 (49.3)
Linezolid	1293/1333 (97)	845/918 (92)
Fosfomycin	722 / 916 (78.8)	-

Table 6.14: Susceptibility pattern of enterococci from all samples across OPD, Ward and ICU

AMA	*Enterococcus faecalis*				*Enterococcus faecium*			
	Total n=3240	OPD n=1061	Ward n=1736	ICU n=443	Total n=2998	OPD n=454	Ward n=1826	ICU n=726
Ampicillin	2011 / 2832 (71.0)	784/966 (81.2)	979/1480 (66.1)	248/386 (64.2)	400 / 2580 (15.5)	106/399 (26.6)	226/1570 (14.4)	68/611 (11.1)
Vancomycin	3043 / 3209 (94.8)	1010/1039 (97.2)	1636 / 1733 (94.4%)	397/437 (90.8)	2229 / 2984 (74.7)	361/452 (79.9)	1383/1814 (76.2)	485/718 (67.5)
Teicoplanin	2995 / 3141 (95.4)	999/1024 (97.6)	1591/1679 (94.8)	405/438 (92.5)	2207 / 2917 (75.7)	365/444 (82.2)	1352/1763 (76.7)	490/705 (69.5)
Gentamicin HL	1579 / 2764 (57.1)	541/860 (62.9)	834/1513 (55.1)	204/391 (52.2)	1008 / 2571 (39.2)	180/409 (44.0)	611/1590 (38.4)	217/572 (37.8)
Ciprofloxacin	385 / 1431 (26.9)	208/573 (36.3)	158/752 (21)	19/106 (17.9)	140 / 1141 (12.3)	47/213 (22.1)	79/726 (10.9)	14/202 (6.9)
Nitrofurantoin	1259 / 1425 (88.4)	587/624 (94.1)	590/703 (83.9)	82/98 (83.7)	449 / 918 (48.9)	121/196 (61.7)	289/578 (50)	39/144 (27.1)
Fosfomycin	722 / 916 (78.8)	300/352 (85.2)	370/492 (75.2)	52/72 (72.2)	-	-	-	-
Linezolid	3098 / 3169 (97.8)	1007/1028 (98)	1670/1712 (97.5)	421/429 (98.1)	2670 / 2909 (91.8)	400/429 (93.2)	1648/1774 (92.9)	622/706 (88.1)

Table 6.15: Year wise susceptibility trends of *Enterococcus faecium* from all samples

AMA	Year-2017	Year-2018	Year-2019	Year-2020	Year-2021	Year-2022
	Total n=937	Total n=1476	Total n=2700	Total n=1994	Total n=2422	Total n=2998
Ampicillin	172/860 (20)	214/1213 (17.6)	414/2290 (18.1)	200/1810 (11)	269/2154 (12.5)	400 / 2580 (15.5)
Vancomycin	697/914 (76.3)	1139/1465 (77.7)	2214/2683 (82.5)	1546/1966 (78.6)	1830/2372 (77.2)	2229 / 2984 (74.7)
Teicoplanin	740/926 (79.9)	1148/1461 (78.6)	2206/2638 (83.6)	1570/1947 (80.6)	1849/2342 (78.9)	2207 / 2917 (75.7)
Gentamicin HL	208/812 (25.6)	360/1247 (28.9)	836/2392 (34.9)	577/1696 (34)	612/1701 (36)	1008 / 2571 (39.2)
Ciprofloxacin	10/230 (4.3)	26/446 (5.8)	79/984 (8)	38/544 (7)	47/640 (7.3)	140 / 1141 (12.3)
Nitrofurantoin	181/251 (72.1)	259/509 (50.9)	559/1221 (45.8)	319/779 (40.9)	342/791 (43.2)	449 / 918 (48.9)
Linezolid	860/910 (94.5)	1352/1411 (95.8)	2562/2644 (96.9)	1813/1896 (95.6)	2216/2320 (95.5)	2670 / 2909 (91.8)

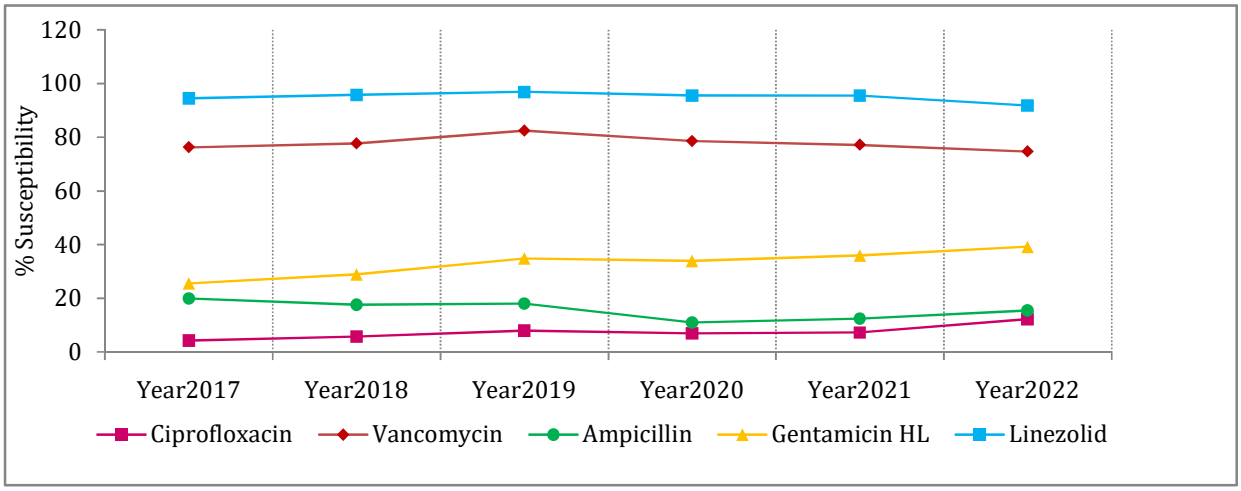


Figure 6.5: Year wise susceptibility trends of *Enterococcus faecium* from all samples

Table 6.16: Antimicrobial Susceptibilities (AMS) Percentage RC wise of *Enterococcus faecium* from Total (Except Faeces & Urine)

RC/ Antibiotics	Ampicillin (n=1765)	Vancomycin (n=2046)	Teicoplanin (n=2024)	Gentamicin_HL (n=1804)	Linezolid (n=1980)
	n(%)	n(%)	n(%)	n(%)	n(%)
RC1	17 / 170 (10.0)	109 / 170 (64.1)	112 / 170 (65.9)	58 / 170 (34.1)	169 / 170 (99.4)
RC2	20 / 89 (22.5)	95 / 138 (68.8)	108 / 140 (77.1)	35 / 118 (29.7)	68 / 69 (98.6)
RC3	24 / 134 (17.9)	100 / 134 (74.6)	101 / 133 (75.9)	55 / 126 (43.7)	123 / 133 (92.5)
RC4	45 / 394 (11.4)	315 / 394 (79.9)	321 / 397 (80.9)	173 / 397 (43.6)	386 / 395 (97.7)
RC5	*0 / 9	30 / 47 (63.8)	30 / 47 (63.8)	12 / 48 (25.0)	42 / 50 (84.0)
RC6	6 / 171 (3.5)	95 / 173 (54.9)	94 / 173 (54.3)	23 / 137 (16.8)	112 / 166 (67.5)
RC7	*1 / 4	23 / 32 (71.9)	26 / 34 (76.5)	*9 / 17	27 / 33 (81.8)
RC8	3 / 15 (20.0)	48 / 71 (67.6)	50 / 71 (70.4)	23 / 71 (32.4)	69 / 70 (98.6)
RC9	13 / 31 (41.9)	28 / 31 (90.3)	29 / 30 (96.7)	17 / 31 (54.8)	30 / 30 (100.0)
RC10	2 / 77 (2.6)	60 / 72 (83.3)	65 / 77 (84.4)	25 / 40 (62.5)	77 / 78 (98.7)
RC11	*5 / 28	47 / 72 (65.3)	50 / 75 (66.7)	*1 / 7	58 / 80 (72.5)
RC12	9 / 83 (10.8)	45 / 83 (54.2)	51 / 83 (61.4)	43 / 80 (53.8)	65 / 82 (79.3)
RC13	19 / 94 (20.2)	85 / 110 (77.3)	60 / 86 (69.8)	33 / 94 (35.1)	102 / 107 (95.3)
RC14	-	28 / 39 (71.8)	31 / 39 (79.5)	-	34 / 39 (87.2)
RC15	12 / 44 (27.3)	37 / 54 (68.5)	32 / 43 (74.4)	18 / 46 (39.1)	49 / 52 (94.2)
RC16	6 / 34 (17.6)	34 / 34 (100.0)	33 / 34 (97.1)	23 / 34 (67.6)	28 / 34 (82.4)
RC17	30 / 85 (35.3)	85 / 89 (95.5)	84 / 88 (95.5)	28 / 87 (32.2)	86 / 88 (97.7)
RC18	1 / 31 (3.2)	31 / 31 (100.0)	27 / 31 (87.1)	13 / 31 (41.9)	30 / 31 (96.8)
RC19	43 / 173 (24.9)	133 / 173 (76.9)	138 / 173 (79.8)	58 / 173 (33.5)	170 / 173 (98.3)
RC20	6 / 41 (14.6)	26 / 41 (63.4)	27 / 41 (65.9)	26 / 39 (66.7)	37 / 41 (90.2)
RC21	0 / 58 (0.0)	40 / 58 (69.0)	44 / 59 (74.6)	13 / 58 (22.4)	55 / 59 (93.2)
Total	262 / 1765 (14.8)	1494 / 2046 (73.0)	1513 / 2024 (74.8)	686 / 1804 (38.0)	1817 / 1980 (91.8)

Enterococcus faecalis

The trends in antibiotic susceptibility rates in *E. faecalis* from 2017-2022 was depicted in Table 6.17 and figure 6.6. Lower susceptibility trends were observed for all antibiotics in 2022 isolates when compared to 2021 except for ciprofloxacin (19.5 % to 26.9 %), high level gentamicin (55.6% to 57.1%), and nitrofurantoin (86.2% to 88.4%). In *E. faecalis* the susceptibility rates of vancomycin (56.9% to 100%) and teicoplanin ranged from (71.4% to 100 %) from most of the regional centres (**Table 6.18)**.

Though the overall VRE rate slightly increased 3.8% to 5.7%, there were significant differences observed between the various regional centres, the highest rate in the isolates from RC20 and RC15 (28.6% and 43.1%). The lowest VRE rates were observed from the RC04 (0.8%) and RC10 (1.2%). Susceptibility to linezolid was high in most of the centres in the range between 88.2% to 100%. Linezolid resistance was found to be the higher in the RC16 (11.8%) centre. The overall high level gentamicin susceptibility rate was at 57.8% which is the least recorded rate when compared to the other antibiotics. Susceptibility to ampicillin was found to be lowest in the range of (25.5% to 28.6%), while in the high level gentamicin moderate susceptibility was recorded in the range of (40% to 67.6%) across the centres.

Table 6.17: Year wise susceptibility trends of *Enterococcus faecalis* from all samples

AMA	Year-2017	Year-2018	Year-2019	Year-2020	Year-2021	Year-2022
	Total n=1034	Total n=2014	Total n=2895	Total n=2101	Total n=2373	Total n=3240
Ampicillin	633/987 (64.1)	1338/1813 (73.8)	1993/2467 (80.8)	1606/1942 (82.7)	1609/2127 (75.6)	2011 / 2832 (71.0)
Vancomycin	978/1016 (96.3)	1921/2000 (96.1)	2791/2860 (97.6)	2018/2073 (97.3)	2242/2335 (96)	3043 / 3209 (94.8)
Teicoplanin	992/1030 (96.3)	1889/1970 (95.9)	2582/2633 (98.1)	2001/2039 (98.1)	2235/2310 (96.8)	2995 / 3141 (95.4)
Gentamicin HL	512/993 (51.6)	982/1890 (52)	1411/2458 (57.4)	1059/1818 (58.3)	1015/1825 (55.6)	1579 / 2764 (57.1)
Ciprofloxacin	41/358 (11.5)	87/641 (13.6)	162/982 (16.5)	127/586 (21.7)	126/646 (19.5)	385 / 1431 (26.9)
Nitrofurantoin	352/375 (93.9)	710/763 (93.1)	1293/1421 (91)	812/895 (90.7)	757/878 (86.2)	1259 / 1425 (88.4)
Fosfomycin	209/222 (94.1)	469/536 (87.5)	669/706 (94.8)	483/498 (97)	478/524 (91.2)	722 / 916 (78.8)
Linezolid	998/1011 (98.7)	1832/1863 (98.3)	2727/2753 (99.1)	1874/1897 (98.8)	2207/2222 (99.3)	3098 / 3169 (97.8)

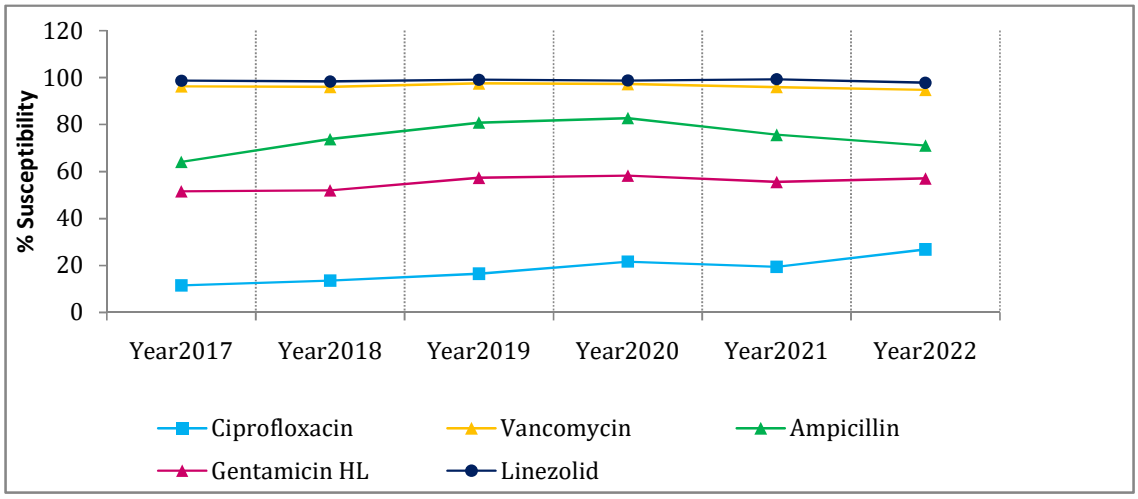


Figure 6.6: Year wise susceptibility trends of *Enterococcus faecalis* from all samples

Table 6.18 Antimicrobial Susceptibilities (AMS) Percentage RC wise of *Enterococcus faecalis* from all samples (Except Faeces & Urine)

RC/ Antibiotics	Ampicillin (n=1650)	Vancomycin (n=1861)	Teicoplanin (n=1845)	Gentamicin HL (n=1681)	Linezolid (n=1835)
	n(%)	n(%)	n(%)	n(%)	n(%)
RC1	17 / 64 (26.6)	61 / 64 (95.3)	61 / 63 (96.8)	42 / 64 (65.6)	64 / 64 (100.0)
RC2	33 / 39 (84.6)	56 / 60 (93.3)	58 / 58 (100.0)	38 / 54 (70.4)	27 / 27 (100.0)
RC3	56 / 61 (91.8)	57 / 61 (93.4)	59 / 61 (96.7)	34 / 53 (64.2)	56 / 61 (91.8)
RC4	603 / 665 (90.7)	660 / 665 (99.2)	660 / 666 (99.1)	382 / 672 (56.8)	665 / 665 (100.0)
RC5	*12 / 13	47 / 47 (100.0)	44 / 44 (100.0)	29 / 48 (60.4)	51 / 51 (100.0)
RC6	45 / 48 (93.8)	46 / 49 (93.9)	46 / 49 (93.9)	18 / 37 (48.6)	41 / 43 (95.3)
RC7	*4 / 6	70 / 72 (97.2)	65 / 71 (91.5)	21 / 37 (56.8)	68 / 71 (95.8)
RC8	*9 / 9	36 / 36 (100.0)	36 / 36 (100.0)	25 / 36 (69.4)	36 / 36 (100.0)
RC9	38 / 66 (57.6)	65 / 69 (94.2)	63 / 68 (92.6)	36 / 69 (52.2)	67 / 69 (97.1)
RC10	188 / 188 (100.0)	169 / 171 (98.8)	187 / 188 (99.5)	95 / 110 (86.4)	187 / 187 (100.0)
RC11	-	*4 / 6	*5 / 5	*0 / 2	*5 / 5
RC12	*14 / 21	*19 / 21	*20 / 21	*14 / 21	*19 / 21
RC13	28 / 32 (87.5)	28 / 33 (84.8)	*24 / 28	23 / 32 (71.9)	34 / 35 (97.1)
RC14	-	51 / 51 (100.0)	51 / 51 (100.0)	-	51 / 51 (100.0)
RC15	18 / 39 (46.2)	29 / 51 (56.9)	30 / 39 (76.9)	13 / 49 (26.5)	49 / 50 (98.0)
RC16	13 / 51 (25.5)	50 / 57 (87.7)	37 / 50 (74.0)	40 / 51 (78.4)	45 / 51 (88.2)
RC17	30 / 51 (58.8)	50 / 51 (98.0)	48 / 50 (96.0)	34 / 51 (66.7)	51 / 51 (100.0)
RC18	*14 / 22	*22 / 22	*20 / 22	*15 / 22	*21 / 22
RC19	118 / 215 (54.9)	189 / 215 (87.9)	199 / 215 (92.6)	86 / 215 (40.0)	211 / 215 (98.1)
RC20	12 / 42 (28.6)	30 / 42 (71.4)	30 / 42 (71.4)	24 / 40 (60.0)	39 / 42 (92.9)
RC21	*1 / 18	*15 / 18	*15 / 18	*3 / 18	*17 / 18
Total	1253 / 1650 (75.9)	1754 / 1861 (94.3)	1758 / 1845 (95.3)	972 / 1681 (57.8)	1804 / 1835 (98.3)

Clinical relevance and treatment guidance

The proportion of MRSA and VRE was found to be higher among blood isolates than from other specimens which are a cause for concern. Although vancomycin susceptibility remains very high among MRSA isolates, the occurrence of hVISA which is not usually detected in most clinical laboratories is worrisome as it may lead to therapeutic failure. Although vancomycin may continue to be used for serious MRSA infections, it is better to use alternate drugs if the MIC value is close to the breakpoint as such isolates are likely to be hVISA.

As susceptibility to daptomycin continues to be close to 100% among MRSA isolates, this antimicrobial may be considered as alternative agents besides vancomycin and linezolid for infections other than those of the respiratory tract. This may also remove some of the selection pressure on antimicrobial resistance genes exerted by these agents. The decision to start vancomycin empirically for serious *S. aureus* infections depends on the MRSA rates in that centre.

In centres where MRSA rates are high, vancomycin or linezolid may be used as empirical therapy with de-escalation if required. On the other hand, in centres where MRSA rates are low, Beta lactams may be used as empirical therapy with escalation to glycopeptides/ linezolid/ daptomycin as required. For skin and soft tissue infections, the possibility of using tetracyclines and or clindamycin may be considered as susceptibility rates to these two antibiotics continue to be high. Levonadifloxacin was tested on 771 isolates of MRSA, and all of them were shown to be susceptible. As per available literature, it appears to be highly efficient against acute bacterial skin and skin structure infections, as well as bacteraemia and diabetic foot infections.

While it is relatively easy to assign clinical significance to *S. aureus* and *Enterococcus* species, the same is not true for CoNS. They are often dismissed as colonizers though they are being increasingly recognized as opportunistic pathogens, particularly *S.haemolyticus*. Another feature of importance is that these isolates are often multi drug resistant; the genes are carried on mobile elements which make transfer of resistance a distinct possibility. In cases where there is a strong possibility of CoNS being pathogens, it may be prudent to use either vancomycin or linezolid as the rates of resistance to beta lactams are extremely high.

The numbers of *E. faecium* was almost equal to *E. faecalis* across most centres of India. This could signify a worrisome trend as this species is far more drug resistant when compared to *E. faecalis*. In serious infections, such as meningitis or bacteremia, linezolid may be tried as empirical therapy, with de-escalation if indicated. In centres which reported linezolid resistance in enterococci, daptomycin may be considered an alternative. The detection of *Enterococcus* species other than *faecalis* and *faecium* in high numbers is also significant as some of these species are intrinsically resistant to glycopeptides. Hence speciation of enterococci is of clinical significance and is not just an academic exercise.

Characterisation of resitance mechanism

PCR for resistance genes

The MRSA phenotype was conferred by *mecA* gene as determined by PCR of all randomly selected isolates from all centres. Since all were *mec*A positive, *mec*C gene PCR was not performed. Recently plasmid mediated *mec*B and *mec*D genes have been reported in *S.aureus* which may complicate detection methods even further (Becker K, 2018, Lakhundi and Zhang 2018). Unlike previous years, none of the randomly tested MSSA isolates (428) harboured *mec*A gene.

Among the non-beta lactam antibiotics, macrolide resistance was conferred either through *erm*A/*erm*C/*msr*A/B genes. In the present study, the overall prevalence of *erm*C genes was high (26.7%) followed by *msr*A/B (23.9%) and *erm*C and *msr*A/B together was (5.3%). None of the isolates harboured *erm*B genes. These genes are usually found among streptococci. Resistance to the high-level mupirocin (200µg) was conferred by *mupA* gene in all mupirocin resistant isolates (Table: 6.19A).

Full blown vancomycin resistance was not encountered in 2022. Although there were no VRSA or VISA identified among the 2022 isolates of MRSA, some of the isolates were found to be hVISA when tested by PAP/AUC analysis. Of the 73 MRSA isolates from JIPMER subjected to PAP-AUC, 7 were identified as hVISA (9.5%), while 36/456 were identified as hVISA (8%) from other centres. The overall rates of hVISA were 7.9% (43/529). Mupirocin resistance among MRSA isolates slightly increased from 5% to 7%. These rates have remained almost the same for last 3 years possibly suggesting that mupirocin resistance genes exert a large fitness cost on MRSA. Resistance to tigecycline was not seen in 2016 but it appeared in a small number of isolates in 2017 and 2018 (0.5%), 2019 (0.4%), 2021 (0.8%). In 2022, none of the isolates exhibited tigecycline resistance

MIC_{50} of different antibiotics against MRSA isolates

MIC creep for the anti MRSA antibiotics has been presented taking 2018 as the index year. There was a slight increase in MIC_{50} level of vancomycin in a few centers like RC09, RC07, RC20, RC02 isolates, (0.5 to0.75µg/ml), while in the RC04, RC03, RC01, RC06 centers, the increase was more significant, from 0.38 to 1µg/ml, (compared to the previous year). The median MIC for linezolid among RC04 and RC16, RC12 isolates increased slightly (0.75 to 1µg/ml), but it remained unchanged in isolates from other centers from the previous year for RC03, RC01, RC15, RC20, RC02. In the case of daptomycin, MIC level was slightly lower among RC06, RC07, RC16, RC09 isolates, but remained same for RC04, RC03, RC15, RC12. Tigecycline median MIC increased slightly in all the centres ranges between (0.032 to 0.25µg/ml), but remained the same in RC06 (0.064 µg/ml). Teicoplanin MIC slightly increased in all the centers (0.19 to 0.5µg/ml), (0.25 to 0.5µg/ml) and (0.5 to 0.75µg/ml). Vancomycin MIC in the majority of the hVISA isolates were in the ranges of 1µg/ml (24), 0.75 µg/ml (10) and 1.5 µg/ml (8).

Antibiotic resistance genes among phenotypically resistant and sensitive isolates

There were 593 isolates of vancomycin susceptible enterococci (269 *E. faecium* and 324 *E. faecalis*) which were screened for Vancomycin Variable *Enterococcus* (VVE) (by van A PCR). None of the isolates was identified as VVE. Antibiotic resistance genes among phenotypically resistant and sensitive isolates of *S.aureus*, CoNS and enterococci from nodal and regional centres are depicted in Table 6.19A and 6.19B respectively.

All MRSA isolates were mediated by mecA gene. No other mec gene was detected. Among the macrolide resistance genes, ermC was found more commonly among the isolates from regional centres when compared to JIPMER isolates (58% vs 24%) while ermA was seen in a larger number of JIPMER isolates compared to those from regional centres (12% vs 1%). The percentage of macrolide resistant *S. aureus* carrying msr genes were higher among JIPMER isolates when compared to 2021 (44% vs 28.6%). The percentage of isolates from regional centres carrying msr genes remained unchanged compared to the previous year. The genes coding for mupirocin resistance (mupA gene) and linezolid resistance (cfr gene) remained the same in the current year compared to the previous years.

All vancomycin resistant enterococci carried the vanA gene only. Among susceptible *S.aureus* isolates, the only resistance genes found were the msrA/B in 4 of the isolates while it was found only in one isolate in 2021. VVE was identified in 5 isolates in 2020 and 3 isolates in 2021. However there was no VVE detected in 2022.

Biocide resistance genes (*qac*A/B and *smr)* among MRSA and VRE isolates

480 isolates of MRSA and 185 VRE isolates were tested for the presence of *qac*A/B and *smr* genes. The overall prevalence of *qac*A/B and *smr* genes in MRSA isolates was 1.9% (9/480) and 1% (5/480) respectively. In *Enterococcus*, *qac*A/B was detected in 4.3 % (8/185) isolates while none had *smr* genes. Among MRSA isolates, *qac*A/B and *smr* genes slightly decreased from 2.4 % in 2021 to 1.9% in 2022 while in enterococci there was an 8 fold increase from 0.45 to 4.3%. Most disinfectant-resistance genes are plasmid borne and can spread between staphylococcal species.

Table- 6.19 A: Antibiotic resistance genes among phenotypically resistant isolates of *S. aureus*, CoNS and enterococci from nodal and regional centres

S.No	Phenotypic resistance	Genes detected	Nodal center (No.positive /no tested)	Regional centers (No.positive /no tested)
1	Methicillin resistant *S.aureus* (MRSA)	*mec*A	*mec*A : 73/73 (100%)	*mec*A :407/407 (100%)
2	Erythromycin resistant *S.aureus*	*erm* A, *erm* B and *erm* C	*erm*A :6/50 (12 %) *erm* B :0/50 *erm* C :12/50 (24 %) msrA/B : 22/50 (44 %) ermA and ermC :1/50 (2 %) ermC and msrA/B: 1/50 (2 %) ermA and msrA/B: 0/50 Negative for *erm*A,B,C and msr A/B genes: 0/50 (0 %)	*erm*A : 6/518 (1 %) *erm* B :0/518 *erm* C :303/518 (58 %) msrA/B : 211/518 (41 %) ermA and ermC :3/518 (1 %) ermC and msrA/B: 46/518 (9 %) ermA and msrA/B: 5/518 (1 %) ermA, ermC and msrB : 1/518 (0.19 %) Negative for *erm*A,B,C and msr A/B genes: 1 / 518 (0.19 %)
3	Mupirocin resistant *S.aureus*	*mup*A and *mup*B	*mup*A :11/11 (100 %) *mup* B : 0/11	*mup*A :11/11 (100 %) *mup* B : 0/11
4	Linezolid resistant MRSA	*cfr*	*cfr* : 5/5 (100%)	*cfr* : 3/3 (100%)
5	Vancomycin resistant Enterococci (VRE)	*van*A, *van*B, *van*C_1/C_2	*van*A :62/62 (100%) *van*B :0/62 *van*C_1/C_2 :0/62	*van*A :123/123 (100%) *van*B :0/123 *van*C_1/C_2 :0/123

Table- 6.19 B: Antibiotic resistance genes among phenotypically sensitive isolates of *S.aureus*, CoNS and enterococci from nodal and regional centres

S.No	Phenotypic resistance	Genes detected	Nodal center (No.positive /no tested)	Regional centers (No.positive /no tested)
1	Methicillin sensitive *S.aureus* (MSSA)	*mec*A	*mec*A : 0/54	*mec*A :0/374
2	Erythromycin sensitive *S.aureus*	*erm* A, *erm* B and *erm* C	*erm* A :0/23 *erm* B :0/23 *erm* C :0/23 msrA/B : 0/23 ermA and ermC :0/23 ermC and msrA/B: 0/23 ermA and msrA/B: 0/23 Negative for *erm*A,B,C and msr A/B genes: 0/23	*erm* A :0/263 *erm* B :0/263 *erm* C :0/263 msrA/B : 4/263 (1.5 %) ermA and ermC : 0/263 ermC and msrA/B: 0/263 ermA and msrA/B: 0/263 ermC and msrB : 0/263 Negative for *erm*A,B,C and msr A/B genes : 0/259
3	Vancomycin sensitive enterococci	*van*A, *van*B, *van*C_1/C_2	*van*A :0/61 *van*B :0/61 *van*C_1/C_2 :0/61	*van*A :0/563 *van*B : 0/563 *van*C_1/C_2 : 0/563

Fifty-four hVISA isolates collected during the period of 2020, 2021 and 2022 were subjected to whole genome sequencing. Denovo sequences were annotated using patric.brc.org software and obtained assembly files. SCC*mec* and sequence types were determined through Centre for Genomics Epidemiology (CGE) server (Center for Genomic Epidemiology) (Table 6.20 and Figure 6.7A).The antibiotic resistance gene profiles of 54 hVISA isolates against antibiotic classes such as aminoglycoside, methicillin, penicillin, macrolide, trimethoprim-sulfamethoxazole, fusidic acid, mupirocin, and tetracycline was studied. The most common genes were *mec*A (100%), *bla*Z (91%), *mph*C (57%), *msr*A (56%), *aac* (6')-*aph* (2'')_1 (56%), *aph*(3')-III_1 (56%), *erm*C (54%), and *dfr*G (43%) (Table 6.21A and Figure 6.7B). Fifty four isolates of hVISA were screened for virulence genes such as *pvl, tsst, hlg*, enterotoxins and intercellular adhesion (*ica*) based on WGS sequencing. The most common virulence gene detected was ica genes (87%), *hld* (87%), hla (87%), followed by *hlb* (83%), pvl (81%), TSST (18%) and the least one was selk (15%) (Table 6.21B).

Table 6.20: SCC *mec* types and Sequence types among hVISA isolates (n=54) based on WGS

S. No	Year	Zonal wise	Regional Centers	Sequence types	Clonal Complex	Scc *mec* types
1	2020	South	RC17	772	CC1	V
2	2020	South	RC17	22	CC22	IV
3	2021	South	RC04	239	CC8	III
4	2021	South	RC04	239	CC8	III
5	2021	South	RC04	1	CC1	V
6	2021	South	RC03	5	CC5	IV
7	2021	South	RC03	2990	CC1	II
8	2021	South	RC14	1	CC1	V
9	2021	South	RC14	772	CC1	V
10	2021	South	RC17	1	CC1	V
11	2021	South	RC04	772	CC1	V
12	2022	South	RC04	2668	CC97	VIII
13	2022	South	RC04	239	CC8	III
14	2022	South	RC04	672	SINGLETON	V
15	2022	South	RC04	2256	CC30	IV
16	2022	South	RC04	8	CC8	IV
17	2022	South	RC10	5	CC5	V
18	2022	South	RC10	5	CC5	V
19	2020	North	RC01	291	SINGLETON	IV
20	2020	North	RC06	772	CC1	V
21	2020	North	RC06	772	CC1	V
22	2020	North	RC06	772	CC1	V

S. No	Year	Zonal wise	Regional Centers	Sequence types	Clonal Complex	Scc *mec* types
23	2021	North	RC02	22	CC22	IV
24	2021	North	RC02	772	CC1	V
25	2021	North	RC02	789	CC8	IV
26	2021	North	RC06	772	CC1	V
27	2022	North	RC06	672	SINGLETON	V
28	2022	North	RC06	1482	SINGLETON	IV
29	2022	North	RC1	672	SINGLETON	IV
30	2020	East	RC21	8	CC8	IV
31	2021	East	RC08	6	CC15	V
32	2022	East	RC08	772	CC1	V
33	2022	East	RC08	772	CC1	V
34	2020	West	RC13	22	CC22	IV
35	2020	West	RC15	772	CC1	V
36	2020	West	RC15	772	CC1	V
37	2020	West	RC15	772	CC1	V
38	2021	West	RC15	88	SINGLETON	V
39	2021	West	RC15	789	CC8	V
40	2021	West	RC15	672	SINGLETON	V
41	2021	West	RC09	22	CC22	IV
42	2021	West	RC09	2233	SINGLETON	IV
43	2021	West	RC09	772	CC1	V
44	2021	West	RC05	8	CC8	V
45	2021	West	RC05	45	CC45	V
46	2021	West	RC05	8	CC8	IV
47	2021	West	RC15	22	CC22	IV
48	2021	West	RC09	772	CC1	V
49	2022	West	RC13	4133	CC30	IV
50	2022	West	RC13	30	CC30	V
51	2022	West	RC12	772	CC1	V
52	2022	West	RC12	8	CC8	IV
53	2022	West	RC5	6	CC15	V
54	2022	West	RC15	772	CC1	V

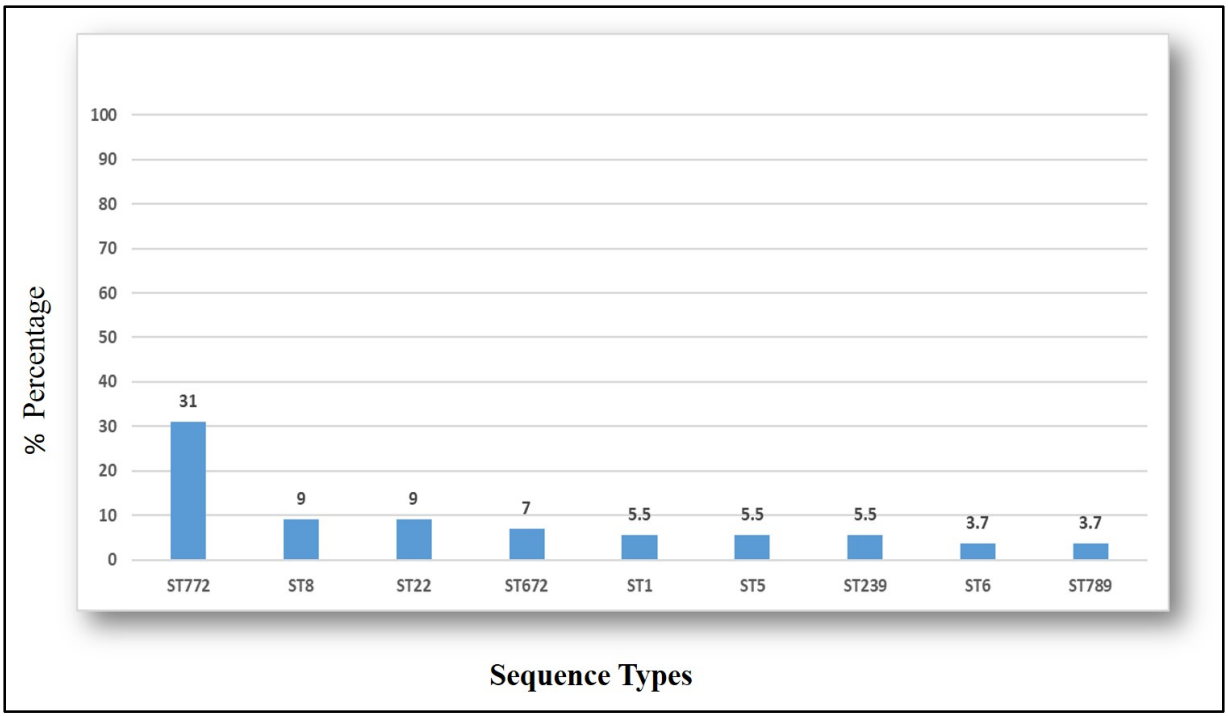


Figure 6.7A: Overall sequences types of hVISA isolates among (n=54) (2020, 2021, 2022)

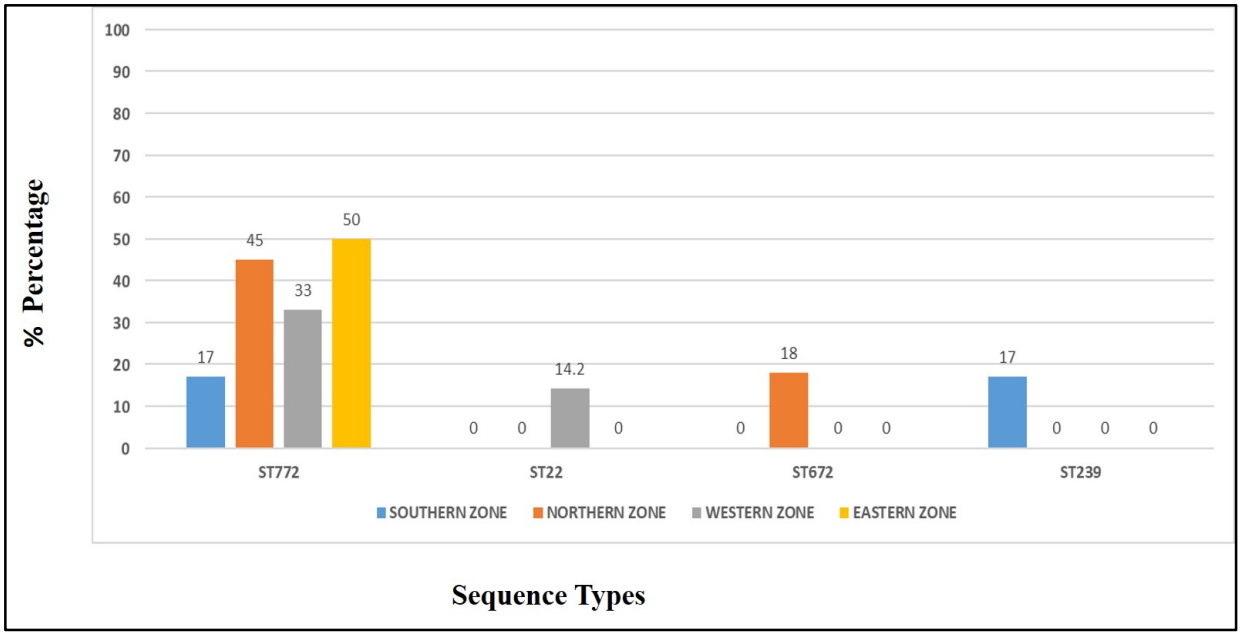


Figure 6.7B: Zone wise distribution of most common sequences types of hVISA isolates

Table 6.21A: Profile of antibiotic resistance genes among (n=54) hVISA isolates (Predicted by WGS sequence)

Antibiotics	Targetgene	Positive by WGS
Aminoglycoside	aac(6')-aph(2'')_1	30
	ant9	5
	ant(6)-Ia_1	23
	aph(3')-III_1	30
Methicillin	*mec*A	54
Penicillin	*blaZ*	49
Macrolide	*msr*A	30
	*mph*C	31
	*erm*A	4
	*erm*C	29
Lincosamide	*lsa*(B)	1
Clindamycin	lnu(A)_1	0
Linezolid	*cfr*	1
Streptogramin	vga(A)-LC	1
Trimethoprim–sulfamethoxazole	*dfr*G	24
Fusidic acid	FusC	7
Mupirocin	*mupA*	9
Tetracycline	*tet*K	10
	*tet*M	4

Table 6.21 B: Profile of virulence genes in hVISA isolates (n=54)

	Biofilm	*Capsular polysaccharide synthesis enzyme*		*tsst*	*pvl*	*Enterotoxins genes*						*α-toxin*	*B and δtoxins*
	*ica*A,B,C,D,R	*Cap8*A-8P	*Cap8*A-8G& *Cap8*L-8P	*tsst*	*pvl*	*sea*	*seb*	*seh*	*selk*	*sell*	*selq*	*hla*	*hlb*& *hld*
CMC31_2021	P	P	P	N	P	N	N	N	N	N	N	P	P
CMC75_2021	P	P	P	N	P	N	N	N	N	P	N	P	P
JIP30_2021	P	P	P	N	P	P	N	N	P	N	P	P	P
JIP80_2021	P	P	P	N	P	P	N	N	P	N	P	P	P
JIP93_2021	P	P	P	N	P	P	P	P	P	N	P	P	P
KMC09_2021	N	N	N	N	N	N	N	N	N	N	N	N	N
KMC32_2021	P	P	P	N	P	P	N	N	N	P	N	P	P
LT39_2021	P	P	P	N	P	N	P	N	P	N	P	P	P
LT66_2021	P	P	P	N	P	N	N	N	N	N	N	P	P
LT69_2021	P	P	P	N	P	N	N	N	N	N	N	P	P
LT72_2021	P	P	P	N	P	N	N	N	N	N	N	P	P
MGIMS18_2021	P	P	P	N	P	N	N	P	N	N	N	P	P
MGIMS25_2021	N	N	N	N	N	N	N	N	N	N	N	N	N
MGIMS_08	P	P	P	P	P	N	N	N	N	P	N	P	P
MGIMS39_2021	P	N	N	N	N	N	N	N	N	N	N	N	N
NIZAM64_2021	P	P	P	N	P	P	N	P	P	N	P	P	P
PD07_2021	P	P	P	N	P	P	P	P	P	N	P	P	P
PD24_2021	P	P	P	N	N	N	N	N	N	P	N	P	P
PD27_2021	P	P	P	P	P	N	P	N	N	N	N	P	P
PGI30_2021	P	P	P	P	P	N	N	N	N	P	N	P	P
PGI44_2021	P	P	P	N	P	P	N	N	N	P	N	P	P

	Biofilm	*Capsular polysaccharide synthesis enzyme*		*tsst*	*pvl*	*Enterotoxins genes*						*α-toxin*	*B and δtoxins*
	***ica*A,B,C,D,R**	***Cap8*A-8P**	***Cap8*A-8G& *Cap8*L-8P**	***tsst***	***pvl***	***sea***	***seb***	***seh***	***selk***	***sell***	***selq***	***hla***	***hlb*& *hld***
PGI57_2021	P	P	P	N	P	N	N	N	N	N	N	P	P
SGRH56_2021	P	P	P	N	P	P	N	N	N	P	N	P	P
TMC05_2021	P	P	P	N	P	P	N	N	N	N	N	P	P
AJ04_2022	P	P	P	N	P	N	N	N	N	N	N	P	P
AJ16_2022	P	P	P	N	P	N	N	N	N	N	N	P	P
Apollo_01_2022	P	P	P	N	P	N	P	N	N	N	N	P	P
J25_2022	N	P	N	N	N	N	N	N	N	N	N	N	N
J33_2022	P	P	P	N	P	P	N	N	P	N	P	P	P
J39_2022	P	P	P	N	P	N	N	N	N	N	N	P	P
J62_2022	P	P	P	N	P	N	N	N	N	N	N	P	P
J63_2022	P	P	P	N	P	N	N	N	N	N	N	P	P
SKIMS18_2022	P	P	P	N	P	N	N	N	N	N	N	P	P
TMC20_2022	N	N	N	N	N	N	N	N	N	N	N	P	N
AD09_2020	P	P	P	N	P	N	N	N	N	N	N	P	P
AJ14_2020	P	P	P	P	P	N	N	N	N	P	N	P	P
IPG11_2020	P	P	P	N	P	P	P	N	N	N	P	P	P
LT57_2020	N	N	N	N	N	N	N	N	N	N	N	N	N
LT29_2020	P	P	P	N	P	P	N	N	N	P	N	P	P
LT39_2020	P	P	P	N	P	P	N	N	N	P	N	P	P
NIMS27_2020	P	P	P	N	P	P	N	N	P	N	P	P	P
NIMS29_2020	P	P	P	P	P	N	N	N	N	P	N	P	P
SGRH14_2020	P	P	P	N	P	P	N	N	N	P	N	P	P
SGRH36_2020	P	P	P	N	P	P	N	N	N	P	N	P	P

	Biofilm	*Capsular polysaccharide synthesis enzyme*		*tsst*	*pvl*	*Enterotoxins genes*						*α-toxin*	*B and δtoxins*
	***ica*A,B,C,D,R**	***Cap8*A-8P**	***Cap8*A-8G& *Cap8*L-8P**	***tsst***	***pvl***	***sea***	***seb***	***seh***	***selk***	***sell***	***selq***	***hla***	***hlb*& *hld***
SKIMS23_2020	P	P	P	N	P	P	N	N	N	P	N	P	P
J95_2021	P	N	N	N	N	N	N	N	N	P	N	N	N
TMC19_2022	P	P	P	N	P	N	N	N	N	N	N	P	P
SKIMS22_2022	P	P	P	N	P	N	N	N	N	N	N	P	P
AB20_2022	N	N	N	N	N	N	N	N	N	N	N	P	N
AB31_2022	P	P	P	N	P	N	N	N	N	N	N	P	P
Apollo02_2022	P	P	P	P	P	N	N	N	N	P	N	P	P
PDH14_2022	P	P	P	N	P	P	P	N	N	N	P	P	P
AD36_2022	N	N	N	N	N	N	N	N	N	N	N	N	N
LT36_2022	P	P	P	N	P	N	N	N	N	N	N	P	P

Note: P- Positive, N-Negative

Whole genome sequence analysis of hVISA isolates for the period of 2020, 2021 and 2022

Molecular typing of hVISA isolates by WGS

SCC*mec* and sequence types of (n=54) hVISA was determined using centre for genomics software. The most common SCC*mec* type was V (45%) followed by SCC*mec* IV (39%) and III (7.8%). Nineteen different STs (ST1, ST5, ST6, ST7, ST8, ST22, ST25, ST30, ST88, ST239, ST672, ST772, ST789, ST2233, ST2256, ST2990, ST1482 and ST4133) were identified. The majority belonged to ST772 (31%), ST8, ST22 (9%), ST672 (7%), followed by ST1, ST5, ST239 (5.5%) and ST6, ST789 (3.7%). These sequences typed belonged to eight distinct clonal complexes (CC1, CC5, CC8, CC15, CC22, CC30, CC45 and CC97). There were 8 singletons (ST8, ST2233, ST1482, ST291 and ST2672).

MLST analysis revealed that there is genetic diversity among hVISA isolates across the country. The most predominant clone was ST772, accounting for 31% of the isolates, followed by ST8, ST22, and ST672. However, in JIPMER 2021 and 2022 isolates, ST239, ST772, and ST672 were the most common. The clonal complexes of CC1 and CC8 were found in 57.4% of the isolates from various centers, with CC8 predominating in JIPMER, followed by CC1 and CC30. In the southern zone, ST772 and ST239 were more common, while in the northern zone, STT772 and ST672 were prevalent. In the western zone, ST772 followed by ST22 were common, and in the eastern zone, ST772 was the most predominant ST. These findings suggest that a few clones may be circulating across the country. Eight isolates were identified as singletons, with four from the north (ST291, ST672, ST1482), three from the west (ST88, ST672, ST2233), and one from the south (ST672).

ST772 hVISA isolates in the current study were more commonly associated with SCCmec V while ST22 was more commonly associated with SCCmec IV. These findings are consistent with a previous study conducted in India (Dhawan et al., 2015; D'souza et al., 2010;) which reported a similar association in MRSA isolates. Majority of ST772 isolates harboured PVL genes while ST22 isolates harboured TSST genes. ST672 isolates were associated with SCC*mec* IV and V. Similar finding were reported in Australia by Coombs et al 2011.

Whole genome sequencing of Linezolid Non Susceptible and Susceptible *E. faecium* isolates

Cfr genes were detected only in the linezolid resistant isolate showing high level resistance. The other resistant isolate with lower MIC possessed only *optr*A along with 23s RNA (G2576T). There was no linezolid resistance mechanism detected in the sensitive isolate. The VRE isolate alone showed the entire van operon while the VVE isolate lacked the regulatory gene, vanR. All three isolates had the *tet*L, *tet*(M), *erm*B and *erm*T genes, which code for tetracycline and macrolide resistance, respectively.

The msrC gene, which is chromosomally encoded and expressed in *Enterococcus faecium* and confers resistance to erythromycin and other macrolide streptogramin B antibiotics was present in the LR-VVE (315747) and LS-VRE (348961) (Table 6.22).

Table 6.22: Profile of antibiotic resistance genes among Linezolid Non Susceptible and Susceptible *E. faecium* isolates (2021) (Predicted by WGS sequence)

Antibiotics	315747 (LR-VVE) LNZ (24 ug/ml) VAN (0.38 ug/ml)	348961 (LS-VRE) LNZ (0.5 ug/ml) VAN (>256 ug/ml)	384442 (LR-VSE) LNZ (8 ug/ml) VAN (0.5 ug/ml)
Oxazolidinone, Lincosamide	CfrA, CfrD, poxtA	Not found	OptrA , 23srRNA G2576T
Macrolide	ermB, msrC, ermT	ermB, msrC, ermT	ermA, ermB, ermT
Tetracycline	tet(L), tet (M)	tet (L)	tet (M), tet (L), tet (S)
Vancomycin	VanA, VanX, VanS, VanH, VanZ	VanA, VanX, VanR, VanH, VanZ	Not found
Aminoglycosides	aac6, aph2	aac6, aph (3),	aac6, aph2

Chapter 7. Streptococcus pneumoniae

The *S. pneumoniae* isolates were studied from various hospitals within India. The invasive isolates include *S. pneumoniae* isolated from sterile specimens such as CSF, blood and body fluids in children less than 5 years of age. The non-invasive isolates include *S. pneumoniae* isolated from respiratory specimens (Sputum).

Serotype Distribution:

A total of 81 invasive (Child<5 years n=20, children >5 years and adult n=61) and 128 non-invasive (child n=5, adult n=123) *S. pneumoniae* isolates were included in the analysis. The majority of the invasive isolates were from blood (n=63), followed by CSF (n=12) and sterile fluids (n=6). The serotype distribution among the invasive and non-invasive isolates of *S. pneumoniae* is depicted in Table 7.1 and Figure 7.1. The predominant serotypes were 19F, 19A and 9V with >5 number of isolates among the invasive isolates. Whereas, among the non-invasive, serotypes 19F, 6A, 35B and 18C were predominant with >6 number isolates. The Pneumosil serotype percentage coverage was 44% and 42% for the invasive and non-invasive *S. pneumoniae,* respectively. The non-vaccine serotypes were more than 50% of the total isolates. Among the serotypes not included in the Pneumosil (PCV10Sii), serotypes3, 18C and 4, constitute 10% of the invasive isolates and serotype 18C alone holds 5-6% among both the invasive and the non-invasive isolates. The predominant first five non-vaccine serotypes were serotypes 35B, 15B, 13, 34 and 17F.

Table 7.1: The number of serotypes among the invasive and non-invasive isolates of *Streptococcus pneumoniae*

Serotypes	Invasive(n=81)	Non-invasive (n=128)
19F	12	25
19A	6	5
9V	5	2
23F	4	6
6A	3	10
6B	2	4
7F	2	0
14	2	2
3	4	1
18C	4	8
4	2	2
16F	4	0
35B	2	10
15B	2	6
13	2	6
34	2	4

17F	1	5
10A	2	3
11A	0	3
15A	2	3
23A	1	3
31	1	2
24F	2	2
22F	2	2
28F	0	2
33B	3	1
6C	1	1
18B	2	0
18F	1	0
23B	1	0
8	1	1
20	2	1
25F/38	1	0

One serotype each of 40, 44, 15F, 17A, 19B, 35A, 35F, and 9N was isolated from non-ivasive specimens

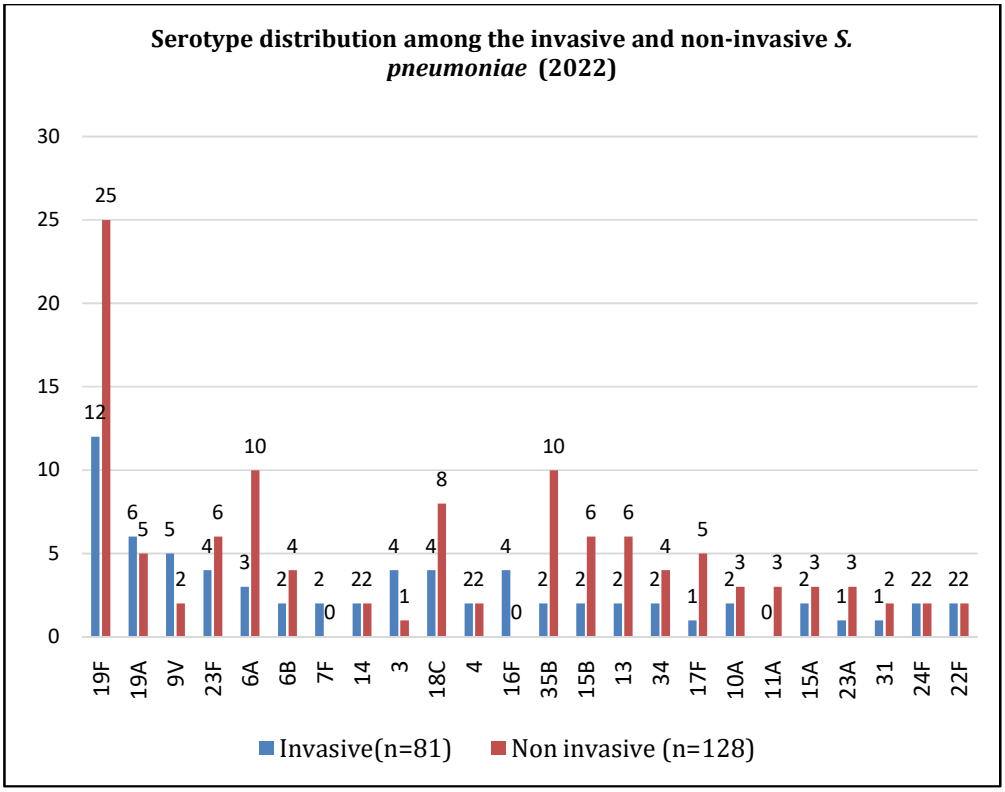


Figure 7.1: The serotype distribution of invasive (n=81) and non-invasive (n=128) isolates of *S. pneumoniae*

Antimicrobial Susceptibility Profile

The penicillin and cefotaxime antimicrobial susceptibility percentage of invasive *S. pneumoniae* isolates were calculated based on meningeal or non-meningeal criteria (Table 7.2 and Figure 7.2). This is due to the different breakpoints of penicillin and cefotaxime of meningeal and non-meningeal isolates. The penicillin and cefotaxime non susceptibility was high in meningeal isolates than the non-meningeal isolates. The antimicrobial susceptibility profile for antibiotics other than penicillin and cefotaxime is given in Table 7.3 and Figure 7.3. The antimicrobial susceptibility profile of non-invasive isolates is depicted in Table 7.4 and Figure 7.4.

Table 7.2: Number of *S. pneumoniae* invasive isolates susceptible to penicillin and cefotaxime

Antibiotics	Total no of invasive isolates (n=81)	
	No of susceptible Meningeal isolates n=22 (%)	**No of susceptible Non-meningeal isolates n=59 (%)**
Penicillin	7(32)	58(98)
Cefotaxime	18(82)	58(98)

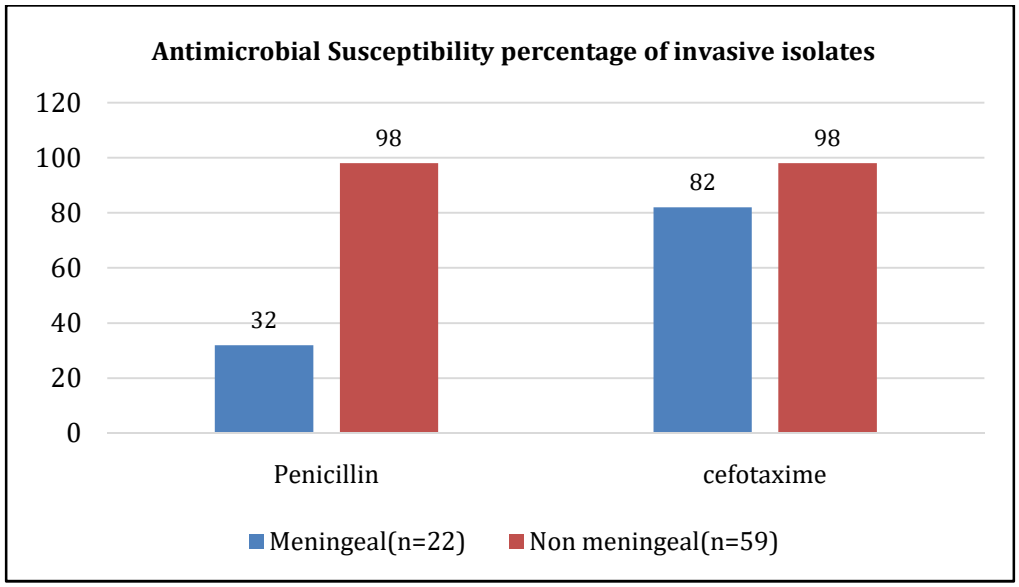


Figure 7.2: Penicillin and cefotaxime antimicrobial susceptibility of invasive isolates of *S. pneumoniae* (n=81)

Table 7.3: Number of invasive isolates susceptible to Erythromycin, Levofloxacin, Linezolid, Vancomycin, Chloramphenicol, Cotrimoxazole

Antibiotics	Number of isolates susceptible n=81(%)
Erythromycin	22(27)
Levofloxacin	79(98)
Linezolid	81(100)
Vancomycoin	81(100)
Chloramphenicol	77 (95)
Cotrimxazole	25(31)

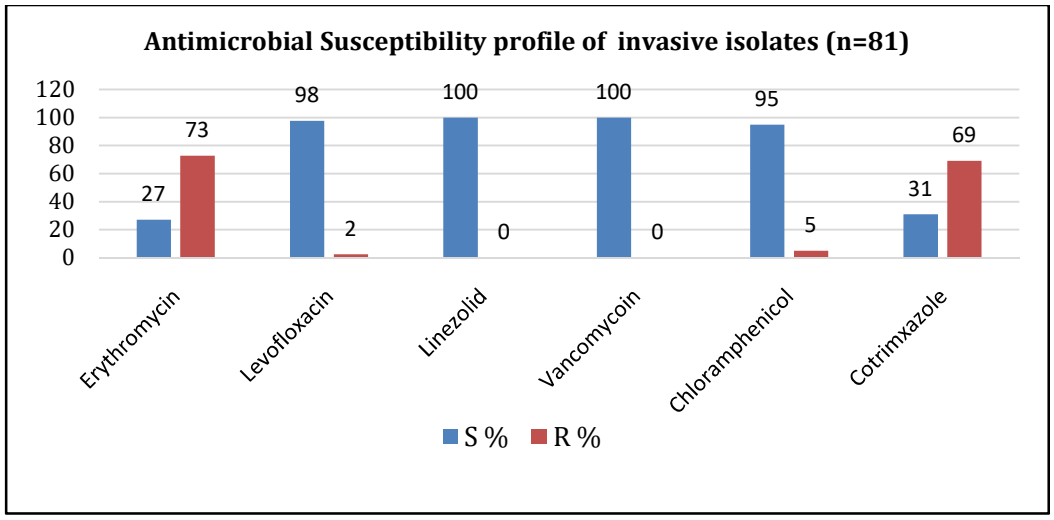


Figure 7.3: Antimicrobial susceptibility profile of invasive isolates of *S. pneumoniae* for antibiotics other than penicillin and cefotaxime (n=81)

Table 7.4: Number of non-invasive isolates susceptible to levofloxacin, erythromycin and penicillin

Antibiotics	No of susceptible isolates (%)
Penicillin(n=16)	16(100)
Erythromycin(n=113)	43(35)
Levofloxacin(n=115)	111(97)

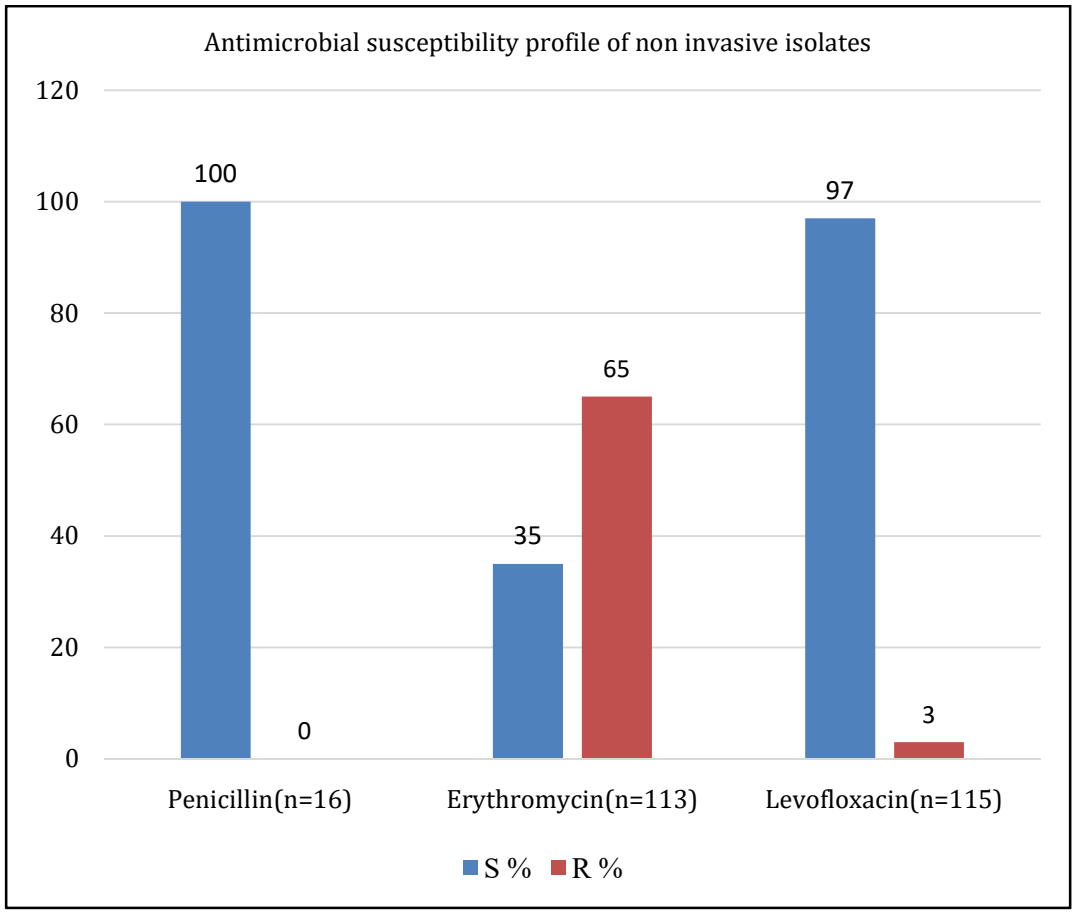


Figure 7.4: Antimicrobial Susceptibility profile of non-invasive isolates (n=128)

Clinical relevance and treatment guidance

The Pneumosil serotype percentage was similar in the invasive and the non-invasive, 44 % and 42% respectively. Serotypes 3, 4 and 18C constitute an additional 10% and 9 % in the invasive and non-invasive isolates of which serotype 18C contributes more than half the number among the 9% in the non-invasive. This denotes the percentage reduction in vaccine serotypes and the increase of non-vaccine serotypes. The impact of the replacement of the PCV13 vaccine by Peumosil (Sii) has to be monitored since serotype 18C is predominant in the non-invasive compared to the invasive isolates. The next predominant non-vaccine serotypes among the invasive isolates were 16F, 35B, 15B, 13 and 34. The antimicrobial non-susceptibility to penicillin and cefotaxime is decreasing gradually. Hence, monotherapy with either of these antibiotics is not recommended for meningeal infections. Current ICMR guidelines of combination therapy (cephalosporins with vancomycin) are recommended. While for non-meningeal infections, penicillin and cephalosporins are observed to be effective.

Chapter 8. Diarrhoeal bacterial pathogens

Number of diarrheal pathogens studied during 2022 was comparatively lesser (0.6%) than the previous years. The isolates belonging to *Vibrio cholerae*, *Campylobacter spp* and *Clostridium difficile* were not reported from any sites. Antimicrobial susceptibility profile (phenotypic) of isolates received from other centres and nodal centre showed a similar trend.

Aeromonas species

Distribution of *Aeromonas spp.* from faeces showed annual increase in the number of positives from n=131 in 2017 to n=164 in 2022. Isolates from faeces and other sources were highly susceptible to cefixime, meropenem and tetracycline. In contrast, % susceptibility to ciprofloxacin was low (7.8% - 8.5%) (Table 8.1).

Year wise distribution of *Aeromonas sp.* from 2017 – 2022 showed an increase in susceptibility to carbapenems (both imipenem and meropenem). Conversely, percentage susceptibility to tetracycline and ciprofloxacin remained the same over the years (Table 8.2 and Figure 8.1).

Table 8.1: Susceptible pattern of *Aeromonas spp*

AMA	All Specimens n=180	Faeces n=164
Cefixime	146 / 180 (81.1%)	132 / 164 (80.5%)
Ciprofloxacin	14 / 180 (7.8%)	14 / 164 (8.5%)
Imipenem	113 / 180 (62.8%)	104 / 164 (63.4%)
Meropenem	149 / 180 (82.8%)	138 / 164 (84.1%)
Tetracycline	154 / 180 (85.6%)	141 / 164 (86.0%)

Table 8.2: Yearly susceptible trends of *Aeromonas spp* from faeces

AMA	Year 2017	Year 2018	Year 2019	Year 2020	Year 2021	Year 2022
	Total n=131	Total n=114	Total n=170	Total n=77	Total n=179	Total n=164
Cefixime	*0/0	23/36 (63.9)	*0/0	*0/0	*0/0	132 / 164 (80.4)
Imipenem	20/46 (43.5)	53/109 (48.6)	*1/2	*0/0	77/154 (50)	104 / 164 (63.4)
Meropenem	26/48 (54.2)	71/109 (65.1)	*1/2	*0/0	118/153 (77.1)	138 / 164 (84.1)
Tetracycline	104/126 (82.5)	97/113 (85.8)	134/169 (79.3)	58/77 (75.3)	145/178 (81.5)	141 / 164 (85.9)
Ciprofloxacin	8/78 (10.3)	11/112 (9.8)	20/169 (11.8)	4/74 (5.4)	22/177 (12.4)	14 / 164 (8.5)

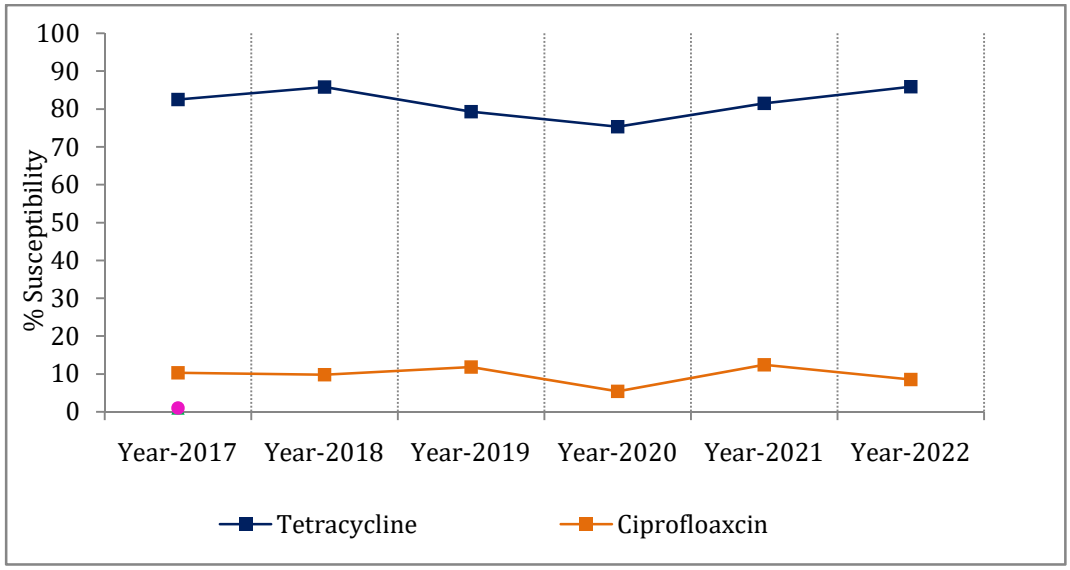


Figure 8.1: Yearly susceptible trends of *Aeromonas spp*

Shigella species

Taxonomic distribution of *Shigella spp.* from 2019 indicated consistently increasing prevalence of *Shigella sonnei* over the dominant *Shigella flexnerii.* Among the 91 isolates characterized, *Shigella flexneri* (56.04% n=51/91) was the dominant species followed by *Shigella sonnei* (42.8% n=39/91) (Table 8.2). Antimicrobial susceptibility profile of *Shigella* spp. showed that *S. sonnei* is highly susceptible (76.9%) to ampicillin while *S. flexnerii* showed only 11.8% susceptibility. Percentage susceptibility to cefixime also showed *S. sonnei* being highly susceptible (79.5%) whereas almost half the numbers of *S. flexnerii* are resistant (46.8%). In contrast, *S. sonnei* is relatively less susceptible to Trimethoprim-sulfamethoxazole (23.1%) while *S. flexnerii* showed 52% susceptibility (Table 8.2).

Year-wise susceptibility trend of *S. flexneri* (2017 -2022) showed declining susceptibility to both ampicillin and cefixime. On the other hand, there is a slight increase in the percentage susceptibility to Trimethoprim-sulfamethoxazole (Table 8.3; Figure 8.2).

Table 8.1: Susceptible pattern of *Shigella* species

AMA	*S.sonnei* n=39	*S.flexneri* n=51	*Shigella spp.* n=*1
Ampicillin	30/39 (76.9)	6/51 (11.8)	*0 / 1 (-)
Cefixime	31/39 (79.5)	25/47 (53.2)	*0 / 1 (-)
Nalidixic acid	*0/4 (-)	*0/8 (-)	%0 / 1 (-)
Trimethoprim-sulfamethoxazole	9/39 (23.1)	26/50 (52)	*1 / 1 (-)

Table 8.2: Yearly susceptible trends of *Shigella flexneri*

AMA	Year 2017	Year 2018	Year 2019	Year 2020	Year 2021	Year 2022
	Total n=89	Total n=47	Total n=95	Total n=55	Total n=37	Total n=51
Ampicillin	40/89 (44.9)	12/47 (25.5)	24/94 (25.5)	9/54 (16.7)	7/37 (18.9)	6/51 (11.8)
Cefixime	56/69 (81.2)	38/46 (82.6)	73/92 (79.3)	45/51 (88.2)	25/37 (67.6)	25/47 (53.2)
Nalidixic acid	0/24 (-)	*0/15	2/35 (5.7)	*2/13	*0/8	*0/8 (-)
Trimethoprim-sulfamethoxazole	7/72 (9.7)	14/47 (29.8)	22/95 (23.2)	9/55 (16.4)	14/37 (37.8)	26/50 (52.0)

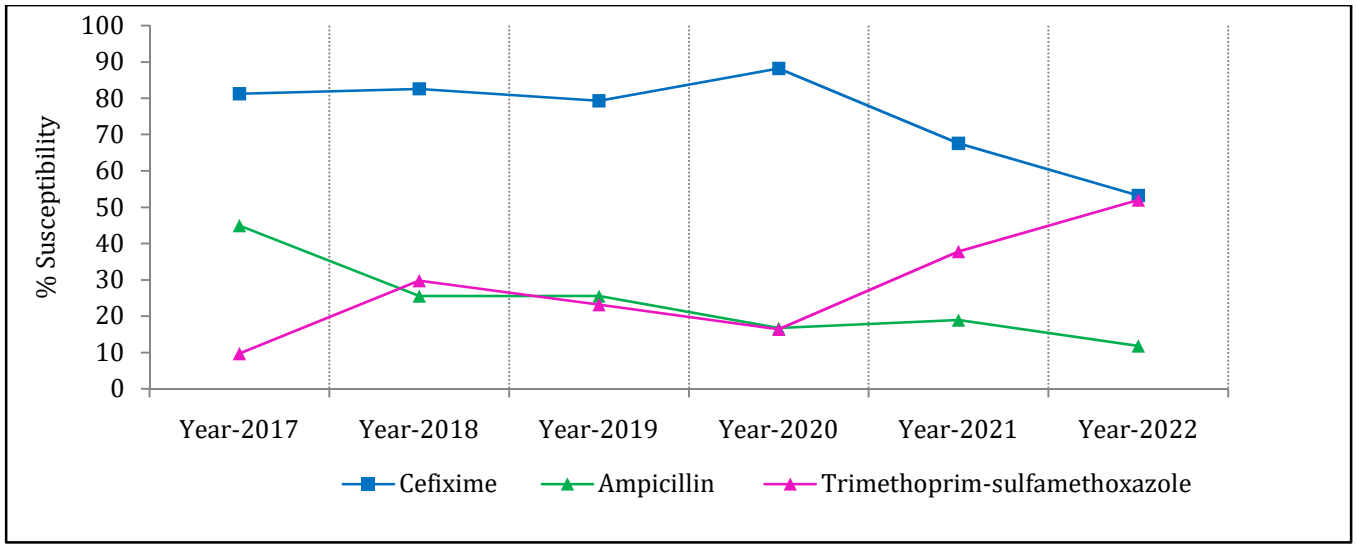


Figure 8.2: Yearly susceptible trends of *Shigella flexneri*

Similarly, the year wise susceptibility trend of *S. sonnei* has been analysed and the data showed a similar trend over the years (2017-2022). The percentage susceptibility remained almost same and were mostly non-susceptible (40-50%) to first line antibiotics such as ampicillin and co-trimoxazole, although a slightly increased co trimoxazole susceptibility is noted, its clinical relevance to repurpose is poor present (Table 8.4; Figure 8.3).

Table 8.4: Yearly susceptible trends of *Shigella sonnei*

AMA	Year 2017	Year 2018	Year 2019	Year 2020	Year 2021	Year 2022
	Total n=52	Total n=26	Total n=57	Total n=*14	Total n= 41	Total n= 39
Ampicillin	35/52 (67.3)	18/24 (75)	42/57 (73.7)	*10/14	22/40 (55)	30 / 39 (76.9)
Cefixime	47/50 (94)	25/26 (96.2)	52/57 (91.2)	*12/13	31/39 (79.5)	31 / 39 (79.5)
Nalidixic acid	*0/8	*0/1	*0/8	*0/0	*0/7 (-)	*0 / 4 (-)
Trimethoprim-sulfamethoxazole	4/52 (7.7)	0/25 (0)	5/57 (8.8)	*1/13	9/41 (22)	9 / 39 (23.1)

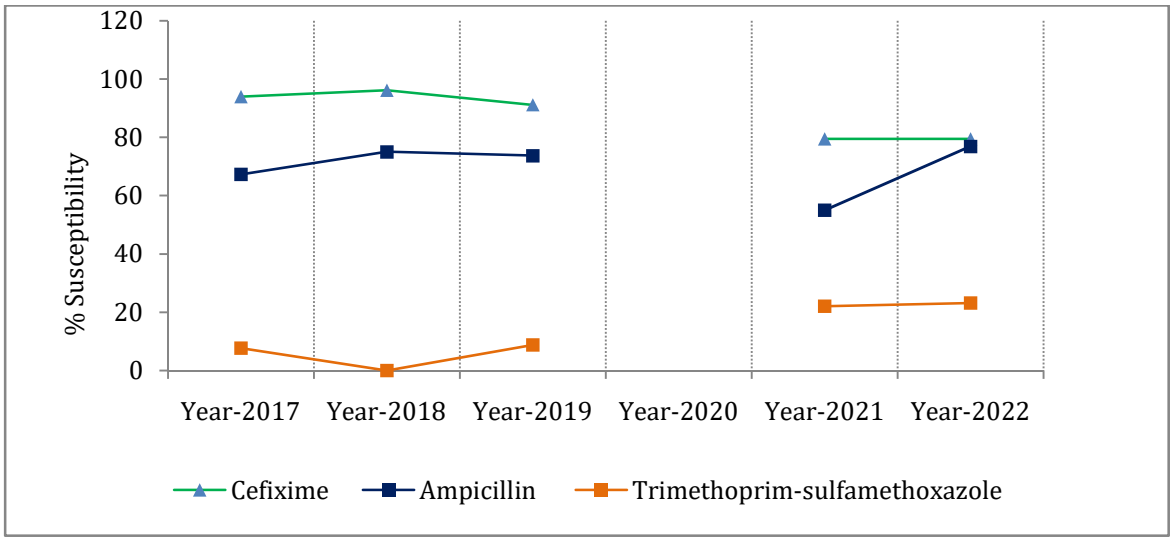


Figure 8.3: Yearly susceptible trends of *Shigella sonnei*

Diarrheagenic *E. coli* (DEC)

A total of n=189 DEC were isolated during 2022. The susceptibility report of DEC showed that isolates being less susceptible to first-line agents such as ampicillin (3.2%), Trimethoprim-sulfamethoxazole (30.1%), Nalidixic acid (9.1%) and cefixime (3.2%) (Table 8.5). Year-wise susceptibility trend from 2019 to 2022 again showed the percentage susceptibility being constant for all four tested antimicrobials (Table 8.6; Figure 8.4).

Table 8.5: Susceptible pattern of DEC

AMA	Faeces
	DEC n=189
Ampicillin	6 / 189 (3.2%)
Cefixime	6 / 189 (3.2%)
Nalidixic acid	15 / 164 (9.1%)
Trimethoprim-sulfamethoxazole	56 / 186 (30.1%)

Table 8.6: Yearly susceptible trend of DEC

AMA	Year-2019	Year-2020	Year-2021	Year-2022
	Total n=134	Total n=102	Total n=88	Total n=189
Ampicillin	6/132 (4.5)	1/102 (1)	0/87 (0)	6/189 (3.2)
Cefixime	17/129 (13.2)	11/100 (11)	12/87 (13.8)	6/189 (3.2)
Nalidixic acid	14/122 (11.5)	11/98 (11.2)	7/87 (8)	15/164 (9.1)
Trimethoprim-sulfamethoxazole	45/133 (33.8)	32/102 (31.4)	32/88 (36.4)	56/186 (30.1)

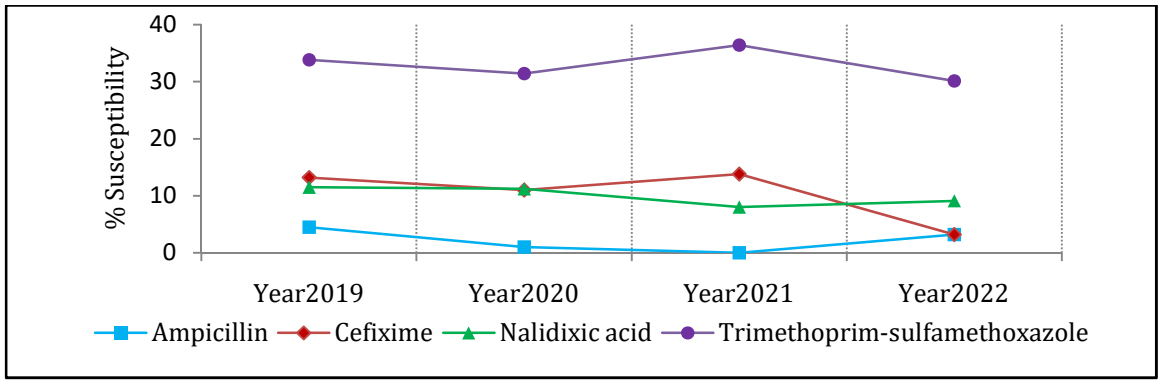


Figure 8.4: Yearly susceptible trend of DEC

Vibrio cholerae

A total of 38 *Vibrio spp.* isolates were reported of which n=32 were phenotypically characterized as *Vibrio cholerae*. Susceptibility to trimethoprim-sulfamethoxazole was found to be the lowest (50%; n=16/32) and thus this antibiotic should not be recommended for treatment (Table 8.7). However, susceptibility to ampicillin (84.4%) and tetracycline (90.6%) are reported to be >80% and can be considered as treatment options. Year-wise susceptibility trend of *V. cholerae* from 2017 to 2022 showed the percentage susceptibility being constant over the years. The susceptibility trend of Trimethoprim-sulfamethoxazole varied from 17% - 50% while susceptibility to ampicillin ranged from 40 – 85% (Table 8.8 and Figure 8.5). High susceptibility was observed for tetracycline (>90%) throughout the study period (2017 – 2022).

Table 8.7: Susceptible pattern of *Vibrio cholerae* and *Vibrio spp*

AMA	*Vibrio cholerae* n=32	*Vibrio spp.* n=*6
Ampicillin	27/32 (84.4)	*3/6 (-)
Nalidixic acid	*0/1 (-)	*0/0 (-)
Tetracycline	29/32 (90.6)	*5/6 (-)
Trimethoprim-sulfamethoxazole	16/32 (50.0)	*3/6 (-)

Table 8.8: Yearly susceptible trends of *Vibrio cholerae*

AMA	Year 2017	Year 2018	Year 2019	Year 2020	Year 2021	Year 2022
	Total n=24	Total n=25	Total n=39	Total n=31	Total n=58	Total n=32
Ampicillin	*17/24 (-)	*17/24 (-)	22/39 (56.4)	*11/28 (-)	44/51 (86.3)	27/32 (84.3)
Tetracycline	19/21 (90.5)	*7/10	36/38 (94.7)	31/31 (100)	55/58 (94.8)	29/32 (90.6)
Nalidixic acid	*1/8	*0/4	*0/5	*1/1	*0/0	*0/1 (-)
Trimethoprim-sulfamethoxazole	*10/24 (-)	*6/24 (-)	18/38 (47.4)	13/31 (41.9)	10/58 (17.2)	16/32 (50.0)

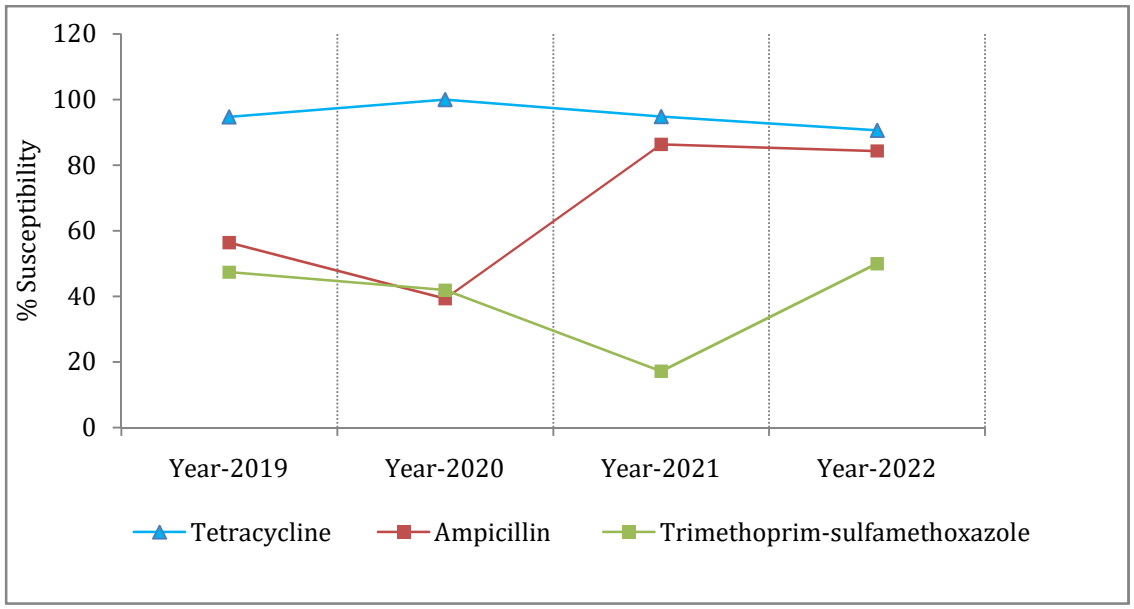


Figure 8.5: Yearly susceptible trends of *Vibrio cholerae*

Increasing resistance to third generation cephalosporins and azithromycin warrants the development of new antibiotics or re-purposing of existing antibiotics as these are among the few therapeutic options left for moderate to severe Shigella infections. Further molecular analysis of *Shigella* isolates showed presence of genes encoding resistance to β-lactams, trimethoprim/sulfamethoxazole, and fluroquinolones. The genotypic presence of AMR genes correlated with the phenotypic AST profile. No significant change in the AMR gene profile was identified. Unlike the global trend of increased XDR incidence and its dissemination, only few cases of XDR isolates are reported from our study.

Clinical relevance and treatment guidance

Continuation of treatment with third generation cephalosporin / azithromycin is suggested after analysing its susceptibility and administration of fluroquinolone may be paused. Reporting of any third-generation cephalosporin / azithromycin resistant isolates of these pathogens may be appropriately communicated to the nodal centres.

AST profile of *V. cholerae* isolates indicates decreased susceptibility to trimethoprim-sulfamethoxazole (50%) and hence is not recommended for treatment. Owing to high susceptibility, ciprofloxacin and tetracycline may be considered as treatment options and azithromycin is recommended only in case if ciprofloxacin / tetracycline resistance is found. In total, with increasing AMR and decreased arsenal of antibiotics together with the paucity of new drugs, continued monitoring of AMR trends among diarrheagenic is critical and every participating centre should watch closely the appearance of resistant isolates and report to the nodal centers appropriately.

Characterisation of resistance mechanism

PCR based molecular testing was applied for the molecular characterization and identification of different strains of *E. coli* namely, Enteroinvasive *Escherichia coli* (EIEC)*/Shigella,* Enterohemorrhagic *Escherichia coli* (EHEC), Enteropathogenic *Escherichia coli* EPEC. PCR positives for *ipaH* &*eaeA*, *stx1 & stx2*, and *bfpA* identified the isolates as EIEC/Shigella, EHEC and EPEC respectively.

PCR based molecular typing for the common resistance mechanism in different diarrheagenic pathogens was done. PCR positive for the amplification of TEM, OXA, *dhfr*, *sul1*, CTX-M *qnrS/B* indicated the resistance to penicillins and early cephalosporins, oxacillin and related anti-staphylococcal penicillins (presence of some OXA, like OXA-48 may also warrant carbapenem resistance), trimethoprim, *sulfonamides and* Extended-spectrum beta-lactamases (ESBLs) activity conferring resistance to most beta-lactam antibiotics, including penicillins, cephalosporins, and the monobactam aztreonam respectively.

Chapter 9. Fungal pathogens

Total number of fungal isolates studied during the year 2022 was 3237 (3%). The antifungal susceptibility testing (AFST) profiling of *Candida* species (*C. tropicalis, C. albicans, C. glabrata, C. parapsilosis, C. auris, C. krusei and C. utilis*) isolated from all specimens revealed 95.5% fluconazole susceptibility in *C. albicans*, 93.5% in *C. tropicalis*, 85.5% in *C. utilis* and 83% in *C. parapsilosis* but only 1.9% in *C. auris;* 98.8% voriconazole susceptibility in *C. krusei,* 94.1% in *C. albicans,* 86.7% in *C. parapsilosis*and 23.1% in *C. auris* (Table 9.1). Notably, more than 95% of *C. albicans* and *C. tropicalis* showed susceptibility to echinocandins. However, *C. auris* showed variable resistance to echinocandins (caspofungin-24.4%, anidulafungin-16.5% and micafungin -5.1%) (Table 9.1).

C. parapsilosis which is generally reported as less susceptible to echinocandins, exhibited significant susceptibility to echinocandins (caspofungin-97.5%, anidulafungin- 98.3% and micafungin - 97.7%) in the present study (Table 9.1). Interestingly, *C. utilis*, an emerging fungal pathogen, was found susceptible to all major classes of antifungals (i.e., caspofungin 95.2% and fluconazole 85.5%). Although two most common human fungal pathogens(*C. albicans* and *C. tropicalis*) showed the azole susceptibility in > 90%, increasing resistance rate over the recent years among these species is a major health concern (Table 9.1-9.3). *C. tropicalis* isolated from blood was more susceptible to anidulafungin (97.4 %) compared to isolates obtained from urine (90%) (Table 9.2 and 9.3). Further, decrease in antifungal susceptibility to majority of the antifungals among *C. albicans, C. tropicalis, C. parapsilosis* and *C. glabrata* needs to be cautiously monitored.

The antifungal susceptibility testing (AFST) profiling across different locations of *Aspergillus* species isolated from all specimens was mentioned in Table 9.4. *A. flavus* and *A. fumigatus* were among the leading moulds isolated from clinical samples.

Table 9.1: Susceptible pattern of *Candida* species isolated from all samples

AMA	*Candida* tropicalis n=733	*Candida albicans* n=719	*Candida glabrata* n=322	*Candida parapsilosis* n=322	*Candida auris* n=164	Candida krusei n=86	*Candida utilis* n=63
Anidulafungin	253/264 (95.8)	203/207 (98.1)	147/156 (94.2)	117/119 (98.3)	66/79 (83.5)	51/54 (94.4)	*20/20
Caspofungin	697/722 (96.5)	692/713 (97.1)	218/320 (68.1)	312/320 (97.5)	121/160 (75.6)	45/85 (52.9)	59/62 (95.2)
Fluconazole	685/733 (93.5)	686/718 (95.5)	216/280 (77.1)	263/317 (83)	3/161 (1.9)	10/85 (11.8)	53/62 (85.5)
Micafungin	507/512 (99)	393/397 (99)	211/228 (92.5)	210/215 (97.7)	111/117 (94.9)	55/63 (87.3)	*21/21
Voriconazole	299/531 (56.3)	672/714 (94.1)	248/314 (79)	274/316 (86.7)	37/160 (23.1)	84/85 (98.8)	44/62 (71)

Table 9.2: Susceptible pattern of *Candida* species isolated from blood

AMA	*Candida* tropicalis n=349	*Candida parapsilosis* n=234	*Candida albicans* n=212	*Candida glabrata* n=123	*Candida auris* n=108	*Candida utilis* n=58	Candida krusei n=47
Anidulafungin	147/151 (97.4)	83/84 (98.8)	99/101 (98)	55/58 (94.8)	44/53 (83)	*18/18 (-)	33/36 (91.7)
Caspofungin	331/346 (95.7)	227/233 (97.4)	204/210 (97.1)	77/122 (63.1)	74/104 (71.2)	56/57 (98.2)	20/46 (43.5)
Fluconazole	322/349 (92.3)	181/231 (78.4)	201/212 (94.8)	66/96 (68.8)	0/105 (0)	50/57 (87.7)	6/47 (12.8)
Micafungin	275/277 (99.3)	152/157 (96.8)	159/160 (99.4)	79/86 (91.9)	75/80 (93.8)	*19/19 (-)	36/42 (85.7)
Voriconazole	152/245 (62)	193/229 (84.3)	193/210 (91.9)	89/118 (75.4)	23/105 (21.9)	42/57 (73.7)	45/46 (97.8)

* Less than 20 samples

Table 9.3: Susceptible pattern of *Candida* species isolated from Urine

AMA	*Candida* tropicalis n=120	*Candida albicans* n=111	*Candida glabrata* n=53	*Candida auris* n=*22	*Candida parapsilosis* n=*15
Anidulafungin	27/30 (90)	33/33 (100)	25/29 (86.2)	*10/11	*5/5 (-)
Caspofungin	111/116 (95.7)	106/111 (95.5)	30/53 (56.6)	18/22 (81.8)	*14/14 (-)
Fluconazole	112/120 (93.3)	105/111 (94.6)	41/46 (89.1)	*0/22	*13/15 (-)
Micafungin	99/100 (99)	91/91 (100)	44/49 (89.8)	*18/19	*12/12 (-)
Voriconazole	65/96 (67.7)	103/110 (93.6)	40/53 (75.5)	*2/21	*13/15 (-)

* Less than 30 samples

Table 9.4: Susceptible pattern of *Aspergillus* species isolated from all samples across different locations

	Aspergillus flavus				*Aspergillus fumigatus*			
AMA	Total n=264	OPD n=133	Ward n=113	ICU n=*18	Total n=183	OPD n=70	Ward n=73	ICU n=40
Amphotericin B	231/263 (87.83)	113/132 (85.60)	100/113 (88.49)	*18/18 (100)	126/182 (69.23)	55/70 (78.57)	46/72 (63.88)	25/40 (62.50)
Caspofungin	228/230 (99.13)	117/119 (98.31)	96/96 (100)	*15/15 (100)	175/177 (98.87)	68/68 (100)	70/72 (97.22)	37/37 (100)
Itraconazole	255/257 (99.22)	128/130 (98.46)	109/109 (100)	*18/18 (100)	174/181 (96.13)	69/70 (98.57)	67/72 (93.05)	38/39 (97.43)
Posaconazole	206/225 (91.55)	94/107 (87.85)	96/102 (94.11)	*16/16 (100)	149/160 (93.12)	53/55 (96.36)	61/68 (89.70)	35/37 (94.59)
Voriconazole	263/264 (99.62)	132/133 (99.24)	113/113 (100)	*18/18 (100)	180/182 (98.90)	70/70 (100)	70/72 (97.22)	40/40 (100)

** Less than 20 samples*

Invasive infections due to multidrug-resistant *C. auris* continue to be reported across many centers. *C. auris* was isolated from seven centres, highest number of *C. auris* isolates were from New Delhi (RC6=28), followed by Kolkata (RC8=16) and Chennai (RC10). Echinocandin resistant *C. auris* was isolated from three centres (Figure 9.1). Susceptibility trends of seven *Candida* species have been shown in figure 9.2.

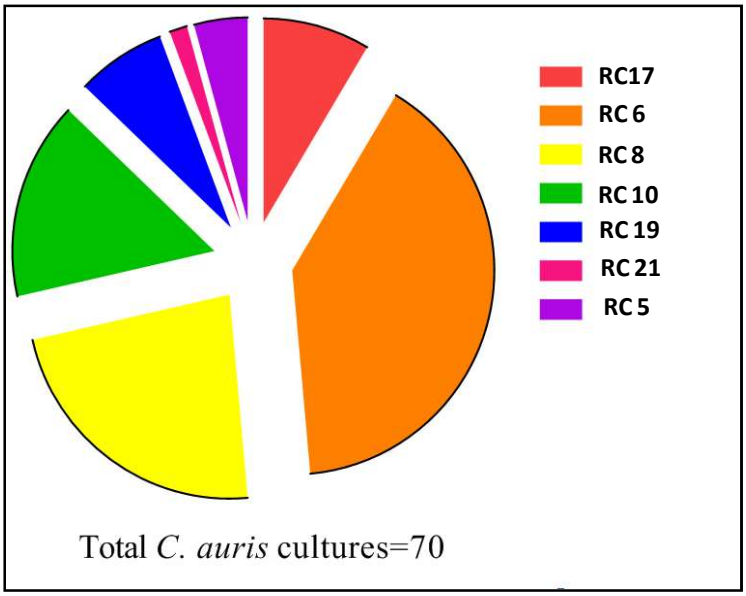
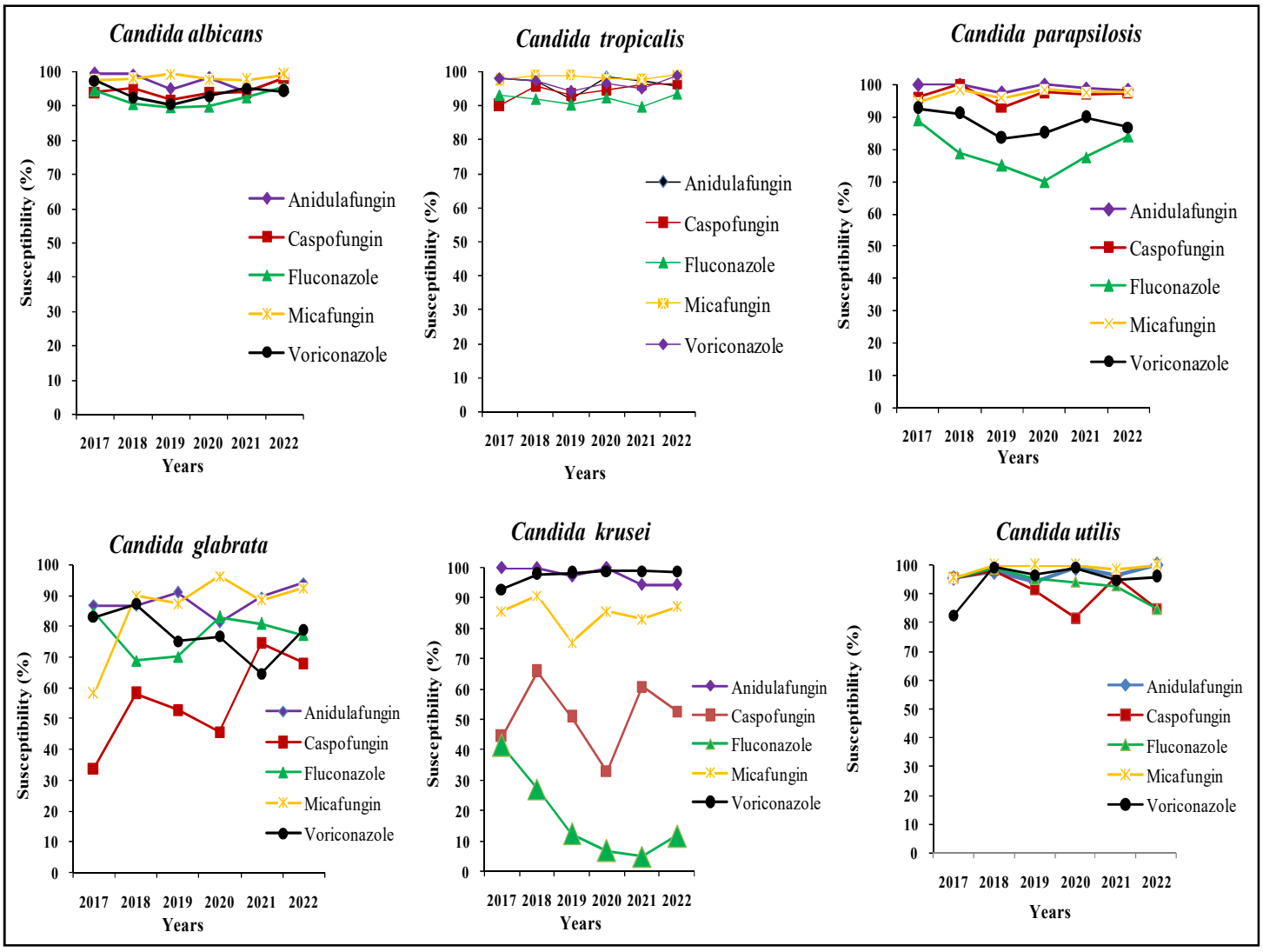


Figure 9.1: Distribution of *C. auris*



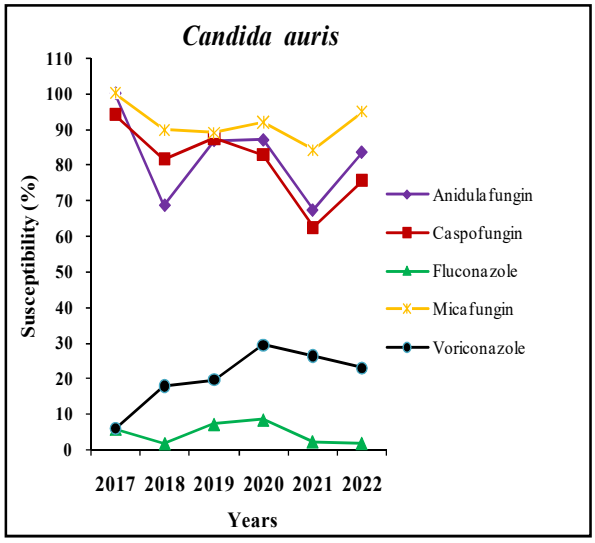


Figure 9.2: Susceptibility trends over the years in seven major yeasts species

Clinical relevance and treatment guidance

Following the earlier trend, *C. tropicalis* and *C. albicans* were reported as leading candidemia agents, followed by *C. glabrata* and *C. parapsilosis*. Resistance rate against echinocandins was below 5% for most of the species, making them the most suitable drugs for treatment. Fluconazole resistance was also below 10% for the two foremost causing agents. High levels of voriconazole resistance in *C. albicans* need to be closely examined. Lesser isolates of *C. parapsilosis* were found to be resistant against fluconazole compared to last year (17% vs. 22%). *C. auris* being multidrug resistant showed near complete resistance (88%) against fluconazole and up to 25% resistance against caspofungin. Among emerging *Candida* species, decreasing isolation rate of *C. utilis* was reported consecutively for last two years, however comparable isolation trend was observed for *Wickerhamomyces anomalus*. Looking at the susceptibility patterns of different *Candida* species, echinocandins and fluconazole remain the best options for the management of these infections.

As per the susceptibility patterns, echinocandins and fluconazole seem to be the best treatment option for *C. albicans* and *C. tropicalis* infections. Although fluconazole resistance was towards the lower side in *C. parapsilosis* spp. this year, still either echinocandins or voriconazole can be recommended in the infections caused by these species. Declining susceptibility of *C. glabrata* to caspofungin and fluconazole justifies micafungin, anidulafungin and voriconazole as better treatment option against *C. glabrata* infections. Echinocandins (more specifically anidulafungin) and voriconazole are the suitable treatment choices for invasive infections due to *C. krusei. C. auris* infections with near complete resistance to azoles can be better treated with echinocandins as suggested by the antibiogram of the current report. Emerging pathogenic yeasts, *C. utilis* and *W. anomalus*, can be effectively treated with azoles and echinocandins.

The increasing prevalence and azoles resistance in *Meyerozyma guilliermondii* in our study is concomitant with the published data. This surge can further complicate the clinical scenario leading to treatment failure or recurrence. Two important attributes of fluconazole resistance (ergosterol content reduction and biofilm formation) were represented in the present report. Thorough investigations into the drug resistance mechanisms are hence justified.

Characterisation of resistance mechanism

The *in vitro* AFST was performed according to CLSI guideline by using M27 microbroth dilution method on 87 isolates against multiple azoles, amphotericin B and two echinocandins. Epidemiological cutoff values (ECVs) were implemented according to the CLSI M57S guideline to identify non- wildtype strains (Table 9.3). Only 2 isolates (10-03-01-56 and 10-11-09-22) had fluconazole MICs (8 and 16 mg/L) and originated from Qatar and The Netherlands, respectively. The *W. anomalus ERG11* gene was located and subsequently aligned to *C. albicans ERG11*. Isolate 10-11-09-22 harbored an I469L

substitution, while no substitutions were found in the other fluconazole resistant isolate. The *ERG11* I469L substitution was in a hotspot region of *C. albicans*. To investigate the potential impact of this substitution on fluconazole resistance, an *ERG11* homology model was constructed, based on a *Saccharomyces cerevisiae CYP51* template with a 70.65% sequence identify and a MolProbity Score of 1.14. The I469 position is in close proximity to the heme-binding site, which is also used by azole derivatives. No substitutions solely present in fluconazole resistant isolates were found for *UPC2* and *ERG3.* With nucleotide blast, efflux transcription factors *TAC1* and *MRR1* could not be identified based on orthologous *C. albicans* genes.

Table 9.3: *In Vitro* AFST metrics for *W. anomalus* (n=87), according to CLSI M27 standard in RPMI-1640 media.

Antifungal	Range (mg/L)	GM (mg/L)	MIC_{50} (mg/L)	MIC_{90} (mg/L)	*n* resistant (%)
AMB (n=87)	0.016-2	0.24	0.25	0.5	1 (1.1)
FLU (n=87)	0.5-16	1.71	2	4	2 (2.3)
ITC (n=87)	0.016-1	0.21	0.25	0.5	1 (1.1)
VOR (n=87)	0.03-0.5	0.09	0.125	0.125	0 (0)
ISA (n=49)	0.031-0.125	0.06	0.063	0.063	0 (0)
AFG (n=48)	≤0.008-0.12	0.04	0.031	0.12	0 (0)
MFG (n=50)	≤0.008-0.032	0.01	0.016	0.031	0 (0)

AMB, amphotericin B; FLU, fluconazole; ITC, itraconazole; VOR, voriconazole; ISA, isavuconazole; AFG, anidulafungin; MFG, micafungin; GM, geometric mean; MIC, minimal inhibitory concentration.

In the present study, the specific, reproducible, and sensitive high resolution STR type scheme for *W. anomalus* was demonstrated. This assay includes amplification of six markers which consists of two multiplex PCRs. The total genotyping of 90 *W. anomalus* isolates identified 38 different genotypes, unveiling four simultaneous outbreak events across Indian hospitals. Further, STR and WGS SNP genotyping correlating well indicates the high resolution of this STR typing scheme. Interestingly, the construction of an ERG11 homology model with SWISS MODEL based on yeast (*Saccharomyces cerevisiae*), a significant role of the I469L substitution in fluconazole resistance was demonstrated.

Chapter 10.Healthcare Associated Infections

This report provides comprehensive details of blood stream infections (BSIs) and Urinary tract infections (UTIs), and Ventilator Associated Pneumonia (VAP) reported from January, 2022 to December, 2022 from a network of 39 hospitals across India. The network hospitals in this report are part of the ICMR's AMR network and hospitals which have voluntarily joined the network. The methodology, SOPs and trainings modules for HAI surveillance are provided on our website www.haisindia.com. During the period from January, 2022 to December, 2022, a total of 106 ICUs from the 39 Centres reported Healthcare Associated Infections (HAI) rates to our centralized database. Medical and Neonatal ICUs accounted for 17.9 and 14.2 % of the total ICUs in our network. Six (5.7%) ICUs in the network during this period were dedicated COVID ICUs.

The cumulative patient days for the network for this period was 3, 12,310. A total of 1, 03,079 Central line days and 1, 67,272 urinary catheter days were reported during this period. A total of 1,747 episodes of blood stream infections and 539 episodes of urinary tract infections were reported, accounting for the total BSI rate to be 5.08 per 1,000 patient days and total UTI rate to be 1.63 per 1,000 patient days. A fatal outcome (14-day outcome) was reported in 44.3% of BSIs and 23.2% UTI cases. However, this is not the attributable BSI or UTI mortality, since other predisposing factors, underlying critical illness and other infections also contribute to patient's mortality in the ICUs.

Gram-negative bacteria (GNB) accounted for 74.4% of all BSI cases; 8.6% were due to *Candida* sp. For UTI, GNB accounted for 57.7% cases. *Klebsiella* spp. (30.4%) was the most common GNB and *Enterococcus* spp. (52%) was the most common Gram-positive cocci (GPC) causing BSIs. 75% of *Klebsiella pneumoniae* and 88% of *Acinetobacter baumannii* causing BSIs were imipenem resistant. Nearly 87% of *Staphylococcus aureus* and around 42% of *Enterococcus faecium* causing BSIs were respectively oxacillin and vancomycin resistant.

The focus of this network has been on generation of quality assured HAI data and to assess the impact of infection prevention and control on the rates of HAIs. The network hospitals reported AMR according their own running systems (Manual/ Automated) and not all hospitals used the same set of antimicrobials. Moreover, speciation was not done uniformly by all hospitals; several of the organisms were identified only till genus level. Efforts will be made to strengthen and homogenize AMR reporting across the network and to ensure that the HAI causing strains are also made part of the Quality Assurance work of ICMR so that AMR data is quality assured.

The AMR-HAI burden is an important metric, considering the fact that ICUs are the hot beds for AMR infections, which may cause adverse outcomes. ICU- based surveillance, coupled with IPC will help in the reduction of overall AMR in individual hospitals.

This HAI Surveillance work is primarily ICU based, considering the high rate of device utilization in the ICUs. The most common ICUs represented in this network are Medical, Neonatal, Paediatric Medical and Surgical ICUs. Six ICUs during the reporting year were

converted to COVID ICUs. The distribution of ICUs is shown in table 10.1. This surveillance focused on BSIs (Primary and secondary BSIs) and UTIs (Catheter associated and non-catheter associated). Blood and urine cultures were taken into consideration for fulfilling the surveillance definitions (www.haisindia.com). The distribution of organisms from blood and urine cultures is shown in table 10.2. *Enterobacterales* were the most common, followed by non fermenting Gram-negative bacteria. The denominators for calculation of HAI rates during this period are shown in Table 10.3

Table 10.1: Distribution of ICUs in the network

Name of ICU	Number (Percentage)
Medical ICU	19 (17.9)
Neonatal ICU	15 (14.2)
Pediatric Medical ICU	11 (10.4)
Surgical ICU	10 (9.4)
COVID ICU	6 (5.7)
Medical/Surgical ICU	8 (7.5)
Cardiothoracic Surgical ICU	2 (1.9)
High Dependency Unit	4 (3.8)
Respiratory ICU	3 (2.8)
Cardiac ICU	2 (1.9)
Gastrointestinal ICU	1 (0.9)
Oncologic Medical ICU	1 (0.9)
Oncologic Surgical ICU	1 (0.9)
Pediatric Medical/Surgical ICU	5 (4.7)
Neurosurgical ICU	2 (1.9)
Trauma ICU	16 (15.1)
Total	**106**

Table 10.2: Specimen wise distribution of major groups of organisms isolated from BSIs and UTIs

Isolate	Culture Positive					
	Total n = 2,286		Blood n = 1,747		Urine n = 539	
	n	%	n	%	n	%
Enterobacterales	821	35.9	607	34.7	214	39.7
NF-GNB	715	31.3	627	35.9	88	16.3
Enterococci	251	11.0	154	8.8	97	18.0
Candida sp.	271	11.9	150	8.6	121	22.4
Staphylococci	143	6.3	137	7.8	6	1.1
Others	85	3.7	72	4.1	13	2.4

Table 10.3: Denominator Data

Indicator	Number
Patient days	**3,12,310**
Central line days	**1,03,079**
Urinary catheter days	**1,67,272**

Network Level BSI data

A total of 1,585 cases of BSIs were reported by the network. The distribution (types) of BSI cases is shown in table 10.4. The total BSI rate in our network was 5.08/1,000 patient days, with the CLABSI rate being 6.7/ 1,000 central line days. The rates of BSIs, Primary BSIs, CLABSIs and Secondary BSIs are shown in Table 10.5. The rates of total BSIs were compared against different types of ICUs, since the morbidity of patients varies with the different types of ICUs. Table 10.6 compares the rates of BSIs across the different ICU types in our network. Of the 1,747 cases of BSIs, males accounted for 63%, as shown in table 10.7. However, no interpretation can be made from this data. It may reflect a higher admission rate in the ICUs.

Table 10.4: Types of BSI cases

Type of BSI cases	No. of BSI cases (%)
CLABSI	686 (43.3)
Non-CLABSI	691 (43.6)
Secondary BSI	208 (13.1)
Total	**1,585**

Table 10.5: BSI rates

Indicator	Rates
Total BSI rate(per 1,000 patient days)	**5.08**
Primary BSI rate (per 1,000 patient days)	**4.41**
CLABSI rate(per 1,000 central line days)	**6.66**
Secondary BSI rate (per1,000 patient days)	**0.67**

Table 10.6: Distribution of BSI cases by ICUs

Type of ICUs	No. of BSI cases (Percentage)	Total BSI rate (per 1,000 patient days)
Medical ICU	398 (25.1)	6.43
Neonatal ICU	373 (23.5)	5.3
Medical/Surgical ICU	191 (12.1)	5.95
Surgical ICU	110 (6.9)	5.75
Trauma ICU	263 (16.6)	5.9
COVID ICU	10 (0.6)	4.5
Pediatric Medical ICU (PICU)	80 (5.0)	3.74
Gastrointestinal ICU	15 (0.9)	3.82
Respiratory ICU	4 (0.3)	3.21
High Dependency Unit (HDU)	19 (1.2)	1.48
Oncologic Surgical ICU	23 (1.5)	7.53
Oncologic Medical ICU	23 (1.5)	7.27
CardiothoracicSurgical ICU	14 (0.9)	3.48
Pediatric Medical/Surgical ICU	48 (3.0)	2.84
Cardiac ICU	12 (0.8)	3.43
Neurosurgical ICU	2 (0.1)	0.23
Total	**1,585**	

Table 10.7: Distribution of BSI cases by gender and age

Gender	No. of BSI cases (%)
Males	965 (62.9)
Females	569 (37.1)
Total	**1,534**

	Median (Years)	Range (Years)
Age of males	32	0–93
Age of females	25	0–98

Table 10.8 shows the duration of stay in the ICUs and the duration between ICU admission and the development of BSI. The duration of ICU stay is a risk factor for development of HAIs. Some patients had a very prolonged ICU stay and invariably, the BSI cases were found more in patients who had a longer ICU stay, across all ICU types. The 14-day mortality in cases of BSIs was 44.3%. This may not be the actual attributable mortality, since severe primary illness or other underlying co-morbidities may be contributing to the fatal outcome. Nearly 40% of BSI cases were discharged at 14-day. Table 10.9 shows the short-term outcomes of BSI cases. A total of 1,747 pathogens were isolated from the BSI cases. Gram-negative organisms predominated as the cause of BSIs in our network, as shown in Table 10.10.

Table 10.8: Median and range of ICU stay for BSI cases

	Median (Days)	Range (Days)
Duration of stay in unit	18	3–413
Duration between date of admission and date of event	7	3- 235

Table 10.9: Outcomes of BSIs

14-dayoutcome	No. of BSI cases (%)
Died	680 (44.3)
Discharged	623 (40.6)
LAMA	58 (3.8)
Transferred to other hospital	54 (3.5)
Unknown	119 (7.8)
Total	**1,534**

Table 10.10: Distribution of organisms causing BSIs

S.No.	Type of organisms	Number (%)
1	Gram- negative organisms	1,300 (74.4)
2	Gram -positive organisms	296 (16.9)
3	Fungal Pathogens	151 (8.6)
Total		**1,747**

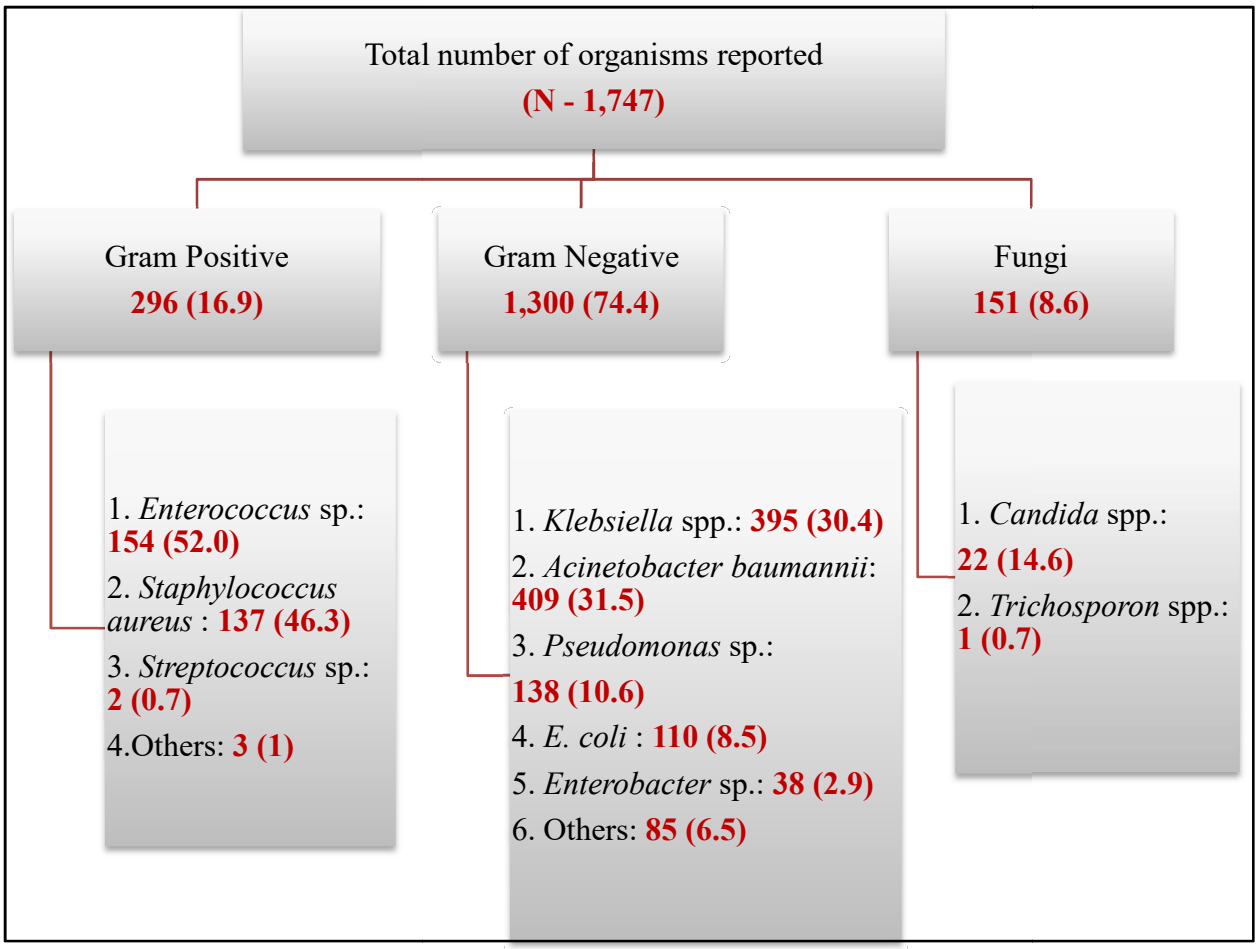


Figure 10.1: Distribution of organisms causing BSIs

The genus level distribution in Gram-negative and Gram-positive organisms and species distribution of *Candida* causing overall BSIs is shown in tables 10.11-10.13. *Enterococcus* spp. was the most common Gram-positive organism; *Klebsiella* sp was the most common Gram-negative organism and *Candida tropicalis* was the most common fungal pathogen.

Table 10.11: Distribution of Gram-positive organisms causing BSIs (Total BSIs)

S.No.	Name of organism	Number (%)
1	*Enterococcus sp.*	154 (9.0)
2	*Staphylococcus aureus*	137 (7.8)
3	*Streptococcus sp.*	2 (0.1)
4	*Others*	3 (0.2)
Total Gram-positive organisms		**296 (16.9)**

Table 10.12: Distribution of Gram-negative organisms causing BSI (Genus level)

S.No.	Name of organism	Number (%)
1	*Klebsiella sp.*	395 (22.6)
2	*Acinetobacter sp.*	409 (23.4)
3	*Pseudomonas sp.*	138 (7.9)
4	*Escherichia sp.*	110 (6.3)
5	*Enterobacter sp.*	38 (2.2)
6	*Burkholderia sp.*	57 (3.3)
7	*Stenotrophomonas sp.*	22 (1.3)
8	*Serratia sp.*	28 (1.6)
9	*Elizabethkingia sp.*	18 (1.0)
10	*Others*	85 (4.9)
Total Gram-negative organisms		**1,300 (74.4)**

Table 10.13: Distribution of *Candida* sp. causing BSIs

S.No.	Name of organism	Number(%)
1	*Candidatropicalis*	39 (2.2)
2	*Candida sp.*	22 (1.3)
3	*Candidaparapsilosis*	19 (1.1)
4	*Candida auris*	15 (0.9)
5	*Candida albicans*	30 (1.7)
6	OtherCandida	25 (1.4)
7	*Trichosporonsp.*	1 (0.1)
Total		**151 (8.6)**

Central line associated blood stream infections (CLABSIs) data

The denominator in cases of CLABSI is taken as the central line days. The risk of developing CLABSIs varies with the position of the Central lines. Table 10.14 shows the locations of Central lines in our surveillance data. Even in CLABSIs, Gram-negative pathogens predominated over Gram-positives. A high proportion of CLABSIs were caused due to Candida spp. in our network. The distribution of organisms, Gram-positive, Gram-negative and *Candida* species causing CLABSIs is shown in tables 10.15-10.18.

Table 10.14: Location of Central lines

Location of central line	No. of CLABSI cases (%)	TotalBSI rate (per 1,000 central line days)
Jugular	509 (68.5)	6.09
Subclavian	117 (13.6)	1.32
Umbilical	65 (7.5)	0.84
Brachial	21 (2.4)	0.21
Femoral	59 (6.9)	0.58
Other	9 (1.0)	0.16
Total	**861**	

**Multiple central lines possible in a single patient*

Table 10.15: Distribution of organisms causing CLABSIs

S.No.	Name of organism	Number (%)
1	Gram positive organisms	131 (16.9)
2	Gram-negative organisms	550 (70.9)
3	Fungal pathogens	95 (12.2)
Total organisms		**776**

Table 10.16: Distribution of Gram-positive organisms causing CLABSIs

S. No.	Name of organism	Number (%)
1	*Enterococcus sp.*	84 (10.8)
2	*Staphylococcussp.*	44 (5.7)
3	*Others*	3 (0.4)
Total Gram-positive organisms		**131 (16.9)**

Table 10.17: Distribution of Gram-negative organisms causing CLABSIs (Genus level)

S.No.	Name of organism	Number (Percentage)
1	*Klebsiella spp.*	159 (20.5)
2	*Acinetobacter sp.*	163 (21.0)
3	*Burkholderia spp.*	48 (6.2)
4	*Pseudomonas spp.*	38 (4.9)
5	*Escherichia sp.*	41 (5.3)
6	*Enterobacter spp.*	24 (3.1)
7	*Stenotrophomonas spp.*	12 (1.5)
8	*Serratia spp.*	13 (1.7)
9	*Elizabethkingia spp.*	6 (0.8)
10	*Providencia spp.*	3 (0.4)
11	*Others*	43 (5.5)
Total Gram-negative organisms		**550 (70.9)**

Table 10.18: Distribution of *Candida* sp causing CLABSIs

S. No.	Name of organism	Number (%)
1	*Candida tropicalis*	29 (3.7)
2	*Candida sp.*	11 (1.4)
3	*Candida auris*	14 (1.8)
4	*Candida albicans*	16 (2.1)
5	*Candida parapsilosis*	12 (1.5)
6	*Candida glabrata*	9 (1.2)
7	*Candida pelliculosa*	1 (0.1)
8	Other Candida	3 (0.4)
Total		**95 (12.2)**

Data of Primary Non-CLABSIs

Non-CLABSI Primary BSIs are the BSI cases for which no secondary sources are traced and that do not have a central line in place for >/= two calendar days. The organism distribution of Non- CLABSI Primary BSIs is shown in tables 10.19-10.22.

Table 10.19: Distribution of organisms causing Non-CLABSI primary BSIs

S.No.	Name of organism	Number (%)
1	Gram-positiveorganisms	148 (20.2)
2	Gram-negativeorganisms	539 (73.6)
3	Fungi	45 (6.2)
Total		**732**

Table 10.20: Distribution of gram-positive organisms causing Non-CLABSI Primary BSIs

S.No.	Name of organism	Number (%)
1	*Staphylococcussp.*	86 (11.7)
2	*Enterococcussp.*	60 (8.2)
3	*Streptococcus sp.*	2 (0.3)
Total Gram-positive organisms		**148 (20.2)**

Table 10.21: Distribution of Gram-negative organisms causing Non-CLABSI Primary BSIs (Genus level)

S.No.	Name of organism	Number (%)
1	*Klebsiella pneumoniae*	151 (20.6)
2	*Acinetobacter baumannii*	122 (16.7)
3	*Escherichia coli*	59 (8.1)
4	*Pseudomonas aeruginosa*	47 (6.4)
5	*Enterobacter sp.*	10 (1.4)
6	*Stenotrophomonas sp.*	8 (1.1)
7	*Burkholderia sp.*	7 (1.0)
8	*Serratia sp.*	10 (1.4)
9	*Citrobacter sp.*	18 (2.5)
10	*Elizabethkingia sp.*	10 (1.4)
11	*Proteus sp.*	3 (0.4)
12	*Others*	94 (12.8)
Total Gram-negative organisms		**539 (73.6)**

Table 10.22: Distribution of *Candida* sp. causing non-CLABSI Primary BSIs

S.No.	Name of organism	Number (%)
1	*Candida tropicalis*	6 (0.8)
2	*Candida parapsilosis*	5 (0.7)
3	*Candida spp.*	11 (1.5)
4	*Candida auris*	1 (0.1)
5	*Candida albicans*	10 (1.4)
6	Other candida	11 (1.5)
7	*Trichosporon sp.*	1 (0.1)
Total		**45 (6.1)**

Data of Secondary BSIs

Secondary BSIs are those cases of BSIs in which a source of infection is found at some other body site and bacteremia is secondary to a primary source. The organism distribution in cases of secondary BSIs is shown in tables 10.23-10.26.

Table 10.23: Distribution of organisms causing Secondary BSI

S. No.	Name of organism	Number (%)
1	Gram-positive organisms	17 (7.1)
2	Gram-negative organisms	211 (88.3)
3	*Candida* sp.	11 (4.6)
Total		**239**

Table 10.24: Distribution of Gram-positive organisms causing Secondary BSI

S.No.	Name of organism	Number (%)
1	*Staphylococcus sp.*	7 (2.9)
2	*Enterococcus sp.*	10 (4.2)
Total Gram-positive organisms		**17 (7.1)**

Table 10.25: Distribution of Gram-negative organisms causing Secondary BSIs (Genus level)

S.No.	Name of organism	Number (%)
1	*Acinetobacter sp.*	95 (39.7)
2	*Klebsiella sp.*	61 (25.5)
3	*Enterobacter sp.*	4 (1.7)
4	*Pseudomonas sp.*	26 (10.9)
5	*Escherichia sp.*	10 (4.2)
6	*Stenotrophomonas sp.*	2 (0.8)
7	*Burkholderia sp.*	2 (0.8)
8	*Proteus sp.*	1 (0.4)
9	*Elizabethkingia sp.*	2 (0.8)
10	*Serratia sp.*	5 (2.1)
11	Others	3 (1.2)
Total Gram-negative organisms		**211 (88.3)**

Table 10.26: Distribution of *Candida* spp. causing Secondary BSIs

S.No.	Name of organism	Number (%)
1	*Candida albicans*	4 (1.7)
2	*Candida tropicalis*	4 (1.7)
3	*Candida glabrata*	1 (0.4)
4	*Candida parapsilosis*	2 (0.8)
Total		**11 (4.6)**

AST in isolates causing BSIs

A high rate of resistance was seen against third generation cephalosporins, carbapenems, fluoroquinolones and aminoglycosides in *Klebsiella pneumoniae, E. coli* and *Acinetobacter baumannii* causing BSIs. The rate of resistance in *Pseudomonas aeruginosa* was less as compared to these. Minocycline and Tigecycline appear to be a promising alternative in *Klebsiella* and *Acinetobacter* sp (Table 10.27). Almost 40% strains of *E. faecium* causing BSIs were vancomycin resistant.

Table 10.27: % Susceptibility of Gram-negative organisms causing BSIs in HAI Surveillance Network

Antibiotics	*Klebsiella pneumoniae* (N = 345)	*Escherichia coli* (N = 110)	*Acinetobacter baumannii* (N = 409)	*Pseudomonas aeruginosa* (N = 106)
Amoxicillin-Clavulanate	25.8	26.4	26.7	8
Amikacin	35.5	65.0	15.5	51
Ampicillin	4.7	14.5	4.0	-
Cefazolin	3.0	10.4	6.4	50.0
Cefepime	13.2	17.3	7.6	43.6
Cefotaxime	8.8	7.3	4.9	-
Ceftazidime	7.1	13.4	8.7	35.4
Ceftriaxone	8.1	12.3	8.1	54.5
Ciprofloxacin	20.4	25.7	14.2	51.0
Colistin	53.1	52.8	66.6	43.8
Ertapenem	20.2	22.7	22.2	-
Gentamicin	29.4	47.0	12.9	48.0
Imipenem	25.0	42.1	11.7	49.5
Levofloxacin	16.7	21.3	11.6	45.8
Meropenem	27.3	48.0	11.2	55.0
Minocycline	11.4	13.4	46.1	75.0
Netilmicin	14.28	57.1	3.6	5.5
Piperacillin	17.6	-	1.4	68.4
Tetracycline	3.1	8.6	13.5	-
Tigecycline	14.2	28.4	67.7	-
Tobramycin	30	-	4.0	33.7

Table 10.28: % Susceptibility of *Enterococcus species* causing BSI, 2022

Antibiotics	*Enterococcus faecalis* (N = 28)	*Enterococcus faecium* (N = 89)	*Enterococcus spp.* (N = 35)
Ampicillin	45.8	4.1	30.0
Ciprofloxacin	16.0	7.4	21.4
Gentamicin	16.7	25.0	1/1 (100)
Linezolid	92.6	67.8	80.0
Teicoplanin	80.0	45.2	34.5
Vancomycin	74.0	57.1	79.4
Tetracycline	33.3	14.3	62.5

Table 10.29: % Susceptibility of *Staphylococcus aureus* causing BSIs, 2022

Antibiotics	*Staphylococcus aureus (N = 137)*
Erythromycin	18.5
Ciprofloxacin	23.8
Oxacillin	12.3
Clindamycin	38.3
Trimethoprim/Sulfamethoxazole	47.5
Tetracycline	34.5
Teicoplanin	42.0
Linezolid	87
Vancomycin	100

Urinary Tract Infections (UTI) data

A total of 505 cases of UTIs were reported. The distribution and profile of UTIs is shown in table 10.30. The catheter associated UTI (CAUTI) rate was 2.76/1,000 urinary catheter days, as shown in table 10.31. The rates of total UTIs were compared against different types of ICUs, since the morbidity of patients varies with the different types of ICUs. Table 10.32 compares the rates of UTIs across the different ICU types in our network.

Table 10.30: Type of UTI cases

Type of UTI cases	No. of UTI cases (%)
CAUTI (catheter associated UTIs)	462 (91.5)
Non-CAUTI	43 (8.5)
Total	**505**

Table 10.31: UTI rates

S.No.	Indicator	Rates
1	UTI incidence rate (per1,000patientdays)	**1.62**
2	CAUTI rate(per1,000urinarycatheterdays)	**2.76**

Table 10.32: Distribution of UTI cases by ICUs

Type of ICUs	No. of UTI cases (%)	UTI Rate (per 1000 patient days)
Medical/Surgical ICU	85 (16.8)	2.65
Neonatal ICU	4 (0.8)	0.1
Medical ICU	138 (27.3)	2.23
Surgical ICU	15 (3.0)	0.78
Pediatric Medical ICU	13 (2.6)	0.61
COVID ICU	1 (0.2)	0.45
Gastrointestinal ICU	2 (0.4)	0.51
High Dependency Unit	31 (6.1)	2.42
Oncologic Medical ICU	20 (4.0)	6.32
Respiratory ICU	2 (0.4)	1.6
Trauma ICU	163 (32.3)	2.83
Cardiac ICU	2 (0.4)	0.57
Cardiothoracic Surgery ICU	4 (0.8)	0.99
Neurosurgical ICU	3 (0.6)	0.35
Oncologic Surgical ICU	15 (3.0)	4.91
Pediatric Medical/Surgical ICU	7 (1.4)	0.41
Total	**505**	

Table 10.33: Distribution of UTI cases by Gender and Age

Gender	No. of UTI cases (%)
Males	264 (55.6)
Females	211 (44.4)
Total	**475**

	Median	Range
Age of males	42	0 – 87
Age of females	46	0 – 86

Table 10.34 shows the duration of stay in the ICUs and the duration between ICU admission and the development of UTI. The duration of ICU stay is a risk factor for development of HAIs. Some patients had a very prolonged ICU stay and the UTI cases were found more in patients who had a longer ICU stay, across all ICU types. The 14-day mortality in cases of UTI was 23.2%. This may not be the actual attributable mortality, since severe primary

illness or other underlying co-morbidities may be contributing to the fatal outcome. 22.3% of UTI cases were discharged at 14-day. Table 10.35 shows the short- term outcomes of UTI cases. A total of 539 pathogens were isolated from the UTI cases. Gram-negative organisms predominated as the cause of UTIs in our network, as shown in Table 10.36-10.38.

Table 10.34: Duration between ICU admission and development of UTI

	Median	Range
Duration of stay in unit	21	3–381
Duration between date of admission and date of event	11	3–272

Table 10.35: Outcome of UTI cases

14-day outcome	No. of UTI cases (%)
Died	110 (23.2)
Discharged	106 (22.3)
LAMA	16 (3.4)
Still in surveillance unit	148 (31.2)
Transferred to other hospital	2 (0.4)
Transferred to other ward/unit within the hospital	88 (18.5)
Unknown	5 (1.1)
Total	**475**

Table 10.36: Distribution of organisms causing UTI

S.No.	Name of organism	Number (Percentage)
1	Gram- negative organisms	311 (57.7)
2	Gram-positive organisms	103 (19.1)
3	Candida sp∞	125 (23.2)
Total		**539**

∞ *In this surveillance network, Candida sp. was also included, in order to understand the epidemiology and significance of Candiduria.*

Table 10.37: Distribution of organisms causing UTI (Genus level)

S. No.	Name of organism	Number (%)
1	*Candida spp.*	121 (22.4)
2	*Escherichia spp.*	86 (16)
3	*Enterococcus spp.*	97 (18)
4	*Klebsiella spp.*	98 (18.2)
5	*Pseudomonas spp.*	59 (10.9)
6	*Acinetobacter spp.*	25 (4.6)
7	*Proteus spp.*	7 (1.3)
8	*Enterobacter spp.*	9 (1.7)
9	*Myroides spp.*	4 (0.7)
10	*Providencia spp.*	8 (1.5)
11	*Others*	25 (4.6)
Total		**539 (100)**

Table 10.38: Distribution of organisms (species level) causing UTI

S.No.	Name of organism	Number (%)
1	*Escherichia coli*	86(16.0)
2	*Klebsiella pneumoniae*	85(15.8)
3	*Candida spp.*	47(8.7)
4	*Enterococcus spp.*	20(3.7)
5	*Pseudomonas aeruginosa*	56(10.4)
6	*Candida albicans*	22(4.0)
7	*Enterococcus faecium*	57(10.6)
8	*Candida tropicalis*	29(5.4)
9	*Acinetobacter baumannii*	23(4.3)
10	*Enterococcus faecalis*	20(3.7)
11	*Pseudomonas spp.*	3 (0.6)
12	*Candida auris*	8 (1.5)
13	*Proteus mirabilis*	6 (1.1)
14	*Candida glabrata*	9 (1.7)
15	*Others*	68(12.6)
Total		**539**

AST of organisms causing UTI

A high rate of resistance was seen against third generation cephalosporins, carbapenems, fluoroquinolones, colistin, and aminoglycosides in *Klebsiella pneumoniae, E. coli* and *Acinetobacter baumannii* and *Pseudomonas aeruginosa* causing UTIs; nearly 60% isolates of *Enterococcus faecium* were vancomycin resistant.

Table 10.39: % Susceptibility of Gram-negative organisms causing UTIs in HAI Surveillance Network

Antimicrobials	Organisms			
	Klebsiella pneumoniae (N=85)	*Escherichia coli (N=86)*	*Acinetobacter baumannii (N=25)*	*Pseudomonas aeruginosa (N=56)*
	% Susceptible			
Amikacin	5.6	57.0	8.0	28.6
Ampicillin	-	3.0	-	1/1 (100)
Cefazolin	-	2.3	-	-
Cefepime	-	7.0	-	16.0
Cefotaxime	-	1.2	-	-
Ceftazidime	-	1.2	-	10.7
Ceftriaxone	-	5.8	-	-
Ciprofloxacin	4.0	3.5	4.0	19.6
Colistin	8.0	23.2	24.0	35.7
Ertapenem	-	24.4	-	-
Gentamicin	12.0	40.7	12.0	30.4
Imipenem	4.0	29.0	4.0	17.9
Levofloxacin	4.0	3.5	4.0	12.5
Meropenem	4.0	33.7	4.0	25.0
Minocycline	28.0	8.1	28.0	-
Netilmicin	-	66.7	-	10.7
Piperacillin	-	-	-	7.7
Piperacillin/Tazobactam	8.0	1.2	8.0	28.6
Tetracycline	4.0	4.7	4.0	-
Tigecycline	33.3	16.3	33.3	-
Tobramycin	8.0	33.3	8.0	12.5
Amoxicillin/Clavulanate	-	22.2	-	-

Table 10.40: % Susceptibility of *Enterococcus species* causing UTI, 2022

Antimicrobials	Organisms		
	Enterococcus faecalis (N=20)	*Enterococcus faecium (N=57)*	*Enterococcus spp. (N=20)*
	% Susceptible		
Ampicillin	30.0	3.4	20.0
Ciprofloxacin	5.0	-	5.0
Linezolid	65.0	50.9	65.0
Nitrofurantoin	45.0	12.3	35.0
Teicoplanin	50.0	22.8	5.0
Tetracycline	13.3	24.1	-
Vancomycin	80.0	42.1	65.0
Fosfomycin	71.4	66.7	-

Table 10.41: % Susceptibility of Staphylococcus *aureus* causing UTI, 2022

Antimicrobials	Organisms:*Staphylococcus aureus (N=6)*∞
	(% Susceptible)
Clindamycin	16.7
Erythromycin	33.3
Linezolid	33.3
Rifampicin	16.7
Teicoplanin	33.3
Tetracycline	50.0
Tigecycline	50.0
Trimethoprim/Sulfamethoxazole	16.7
Vancomycin	100

∞ *numbers too low*

Ventilator Associated Pneumonia (VAP) data

Surveillance for VAP was started towards the end of 2022 using tailor made definitions for Indian ICUs. The definitions are being validated against the currently used global criteria for ventilator associated events. The data (table 10.42-10.45) below shows the preliminary findings from a few hospitals in the network.

Table 10.42: ICU-wise distribution of total patient days and ventilator days

Type of ICUs	Patient Days	Ventilator Days
Medical ICU	18,448	6609
Neurosurgical ICU	9,926	4675
Medical/Surgical ICU	6,635	2716
Gastrointestinal ICU	4,080	696
Surgical ICU	3,346	753
Cardiac ICU	3,108	720
HDU	3,093	81
Neuro Surgery ward	2,605	808
Pediatric ICU	2,400	263
Covid ICU	1,765	87

Table 10.43: Demographic details of VAP Patients under HAI surveillance network, 2022

S. No.	Features	Patient no. (%) (N=82)
1.	**Gender** ▪ Male ▪ Female	 62 (75.6) 20 (24.3)
2.	**Age: median (range)** ▪ <=18 ▪ >18	46.2 (13 – 86) years 7 (8.5) 75 (91.5)
3.	**Time to infection** ▪ Within 7 days ▪ 7 – 14 days ▪ 14 - 21 days ▪ 21+ days	 50 (61.0) 16 (19.5) 9 (11.0) 7 (8.5)
4	**Outcome** **14-day Outcome** ▪ Still in a surveillance unit ▪ Died ▪ Transferred to another ward/unit within the hospital ▪ Discharged ▪ LAMA ▪ Transferred to other hospitals ▪ Unknown **Final Outcome** ▪ Died ▪ Discharged ▪ LAMA ▪ Transferred to other Hospital ▪ Unknown	 24 (29.3) 30 (36.6) 18 (21.9) 3 (3.6) 2 (2.4) 1 (1.2) 4 (4.9) 37 (45.1) 23 (28.0) 4 (4.9) 1 (1.2) 17 (20.7)

Table 10.44: Distribution of organisms isolated from VAP Patients

Organism	Count	Percent
Acinetobacter spp.	31	32.3
Klebsiella spp.	31	32.3
Pseudomonas spp.	13	13.5
Staphylococcus aureus	8	8.3
Stenotrophomonas maltophilia	4	4.2
Escherichia coli	5	5.2
Burkholderia cepaciae	1	1.0
Enterobacter cloacae	1	1.0
Providencia stuartii	1	1.0
Serratia marcescens	1	1.0
Total	**96**	

Table 10.45: % Susceptibility of Gram-negative organisms isolated from VAP patients

	Enterobacterales (N = 37)	*Acinetobacter baumannii (N = 31)*	*Pseudomonas aeruginosa (N = 13)*
Antibiotics	*S (%)*	*S (%)*	*S (%)*
Amoxicillin-Clavulanate	6.7	32.1	33.3
Amikacin	6.7	29.2	57.1
Ampicillin	6.7	29.2	57.1
Cefazolin	6.7	8.3	57.1
Cefepime	0.0	20.8	38.5
Cefotaxime	0.0	0.0	57.1
Ceftazidime	3.8	8.3	30.0
Ceftriaxone	6.7	12.5	57.1
Ciprofloxacin	3.2	11.8	20.0
Colistin	95.4	92.3	100.0
Gentamicin	3.2	29.4	50.0
Imipenem	0.0	16.7	27.3
Levofloxacin	0.0	18.5	33.3
Meropenem	3.4	20.0	33.3
Minocycline	30.8	25.0	57.1
Netilmicin	0.0	29.2	0.0
Piperacillin	0.0	29.2	57.1
Tetracycline	10.0	22.2	57.1
Tigecycline	6.7	50.0	-
Tobramycin	0.0	29.2	66.7

Annexure I

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CMC, Vellore
JIPMER, Puducherry
PGIMER, Chandigarh

Regional Centers

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AIIMS Jodhpur
Apollo Hopsital, Chennai
Assam Medcial College and Hospital, Assam
IPGMER, Kolkata
JPN Apex Trauma Center, New Delhi
KGMU, Lucknow
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