



Antimicrobial Resistance in *Enterobacteriaceae* Bacteria Causing Infection in Trauma Patients: A 5-Year Experience from a Tertiary Trauma Center

Omika Katoch¹ Surbhi Khurana¹ Purva Mathur^{1,✉} Rajesh Malhotra²

¹Department of Laboratory Medicine, JPNA Trauma Centre, All India Institute of Medical Sciences, New Delhi, India

²Department of Orthopaedics, JPNA Trauma Centre, All India Institute of Medical Sciences, New Delhi, India

Address for correspondence Purva Mathur, MD, Department of Laboratory Medicine, JPNATC, All India Institute of Medical Sciences, New Delhi 110029, India (e-mail: purvamathur@yahoo.co.in).

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Abstract

Introduction Multiple drug resistance emergences among bacteria at an alarming rate worldwide are posing a serious threat to the treatment benefits that have been achieved with antibiotics. This crisis is due to the inappropriate and overuse of existing antibiotics. We evaluated the antimicrobial resistance pattern of *Enterobacteriaceae* pathogens isolated from intensive care units (ICUs), wards, and outpatient department (OPD) patients.

Objectives The aim of the study is to determine the antimicrobial resistance pattern in bacteria of *Enterobacteriaceae* family.

Material and Methods This is a retrospective study conducted at a tertiary care level-1 trauma center in the capital city of India. We collected all the retrospective data of 5 years from the laboratory information system software of the microbiology laboratory. The retrospective data included patients' details, samples detail, organism's identification, and their antimicrobial susceptibility testing, done by Vitek2 compact system and disk diffusion test according to each year's Clinical and Laboratory Standards Institute (CLSI) guidelines. This study included the interpretation of zone diameters and minimum inhibitory concentrations of all isolates according to CLSI guidelines, 2018.

Results Among all the *Enterobacteriaceae*, *Klebsiella* spp. was the most commonly isolated pathogen, followed by *Escherichia coli* and *Enterobacter* spp. in ICUs and wards, while in OPD patients *E. coli* was the most commonly isolated pathogen, followed by *Klebsiella* spp. and *Enterobacter* spp. *Enterobacteriaceae* isolates remained resistant to all classes of cephalosporins in all settings. In addition, β lactam and β -lactamase inhibitor remained less effective. Carbapenems showed less resistance than quinolones and aminoglycosides. Among the different antimicrobial agents, tigecycline proved most effective in all settings; however, it showed more resistance than other studies.

Conclusion Tigecycline proved effective among different multidrug resistance bacteria. Multidrug resistance in bacteria leads to prolonged hospital stays as well as makes the treatment less cost effective. Proper and judicious use of antimicrobials is the need of the hour.

Keywords

- ▶ tigecycline
- ▶ Vitek2
- ▶ disk diffusion
- ▶ *Enterobacteriaceae*
- ▶ *Klebsiella* spp.
- ▶ *Escherichia coli*
- ▶ antibiotic resistance

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Introduction

Antibiotic resistance is a great threat to patient care. This antibiotic resistance not only increases the total cost of effective treatment but also is associated with a substantial increase in morbidity and mortality in hospitalized patients.¹⁻⁴ Nosocomial infections are one of the main causes of death in trauma patients, and bacteria belonging to family *Enterobacteriaceae* are the most prominent causative agents of these nosocomial infections.^{2,5} Beta lactam antibiotics are usually the first line of treatment used against the infections caused by *Enterobacteriaceae*, however, with time these bugs have evolved by producing extended spectrum of β lactamases (ESBL). The first ESBL producing *Enterobacteriaceae* reported from Germany in 1983 and since then, their incidence has been reported to be increasing rapidly worldwide.⁶ In 1994, the first KPC-producing *Klebsiella pneumoniae* isolate was reported in Japan, which conferred resistance to carbapenems.⁷ In 1999, Martínez-Martínez et al found that the combination of porin loss and the presence of plasmid-mediated β lactamases resulted in carbapenem resistance.⁸ New Delhi metallo- β -lactamase (NDM-1) producing *Enterobacteriaceae* are resistant to all β -lactams and carbapenems.⁹ Unfortunately, today these bugs have started to confer resistance against colistin, which is the last resort against these highly resistant gram-negative pathogens.¹⁰⁻¹²

This study is unique because of its large sample size, different source of samples, patients admitted to different settings (intensive care unit [ICU], ward, and outpatient department

[OPD]) and use of wide range of antimicrobial agents. Very few authors have reported the study with such a large sample size. The present study would help in understanding the antimicrobial resistance pattern in *Enterobacteriaceae* pathogens isolated from different settings of level-1 trauma center over a period of 5 years.

Materials and Methods

Study Period and Place

Retrospective 5 years data (January 2012 to December 2016) was collected from laboratory information system software of microbiology laboratory of 186 bedded tertiary apex trauma center, New Delhi. A total of 6,061 isolates belonging to family *Enterobacteriaceae* were recovered from 5,067 nonrepeated clinical samples. These clinical isolates were recovered from patients' clinical samples received during this study period, namely, blood, urine, body fluid, bone and tissue, tip culture, pus/wound and swab, and respiratory samples. Duplicate samples were excluded from the study. All organisms were not subjected to antimicrobial susceptibility testing (AST) by both methods. Therefore, for accuracy, only those isolates which were subjected to AST by both methods constituted the analysis. Intermediate sensitive isolates were not included in the study. **► Fig. 1** shows the exclusion and inclusion criteria.

Bacterial Identification

All the samples were processed as per standard microbiological methods. Bacterial isolates were identified to species level

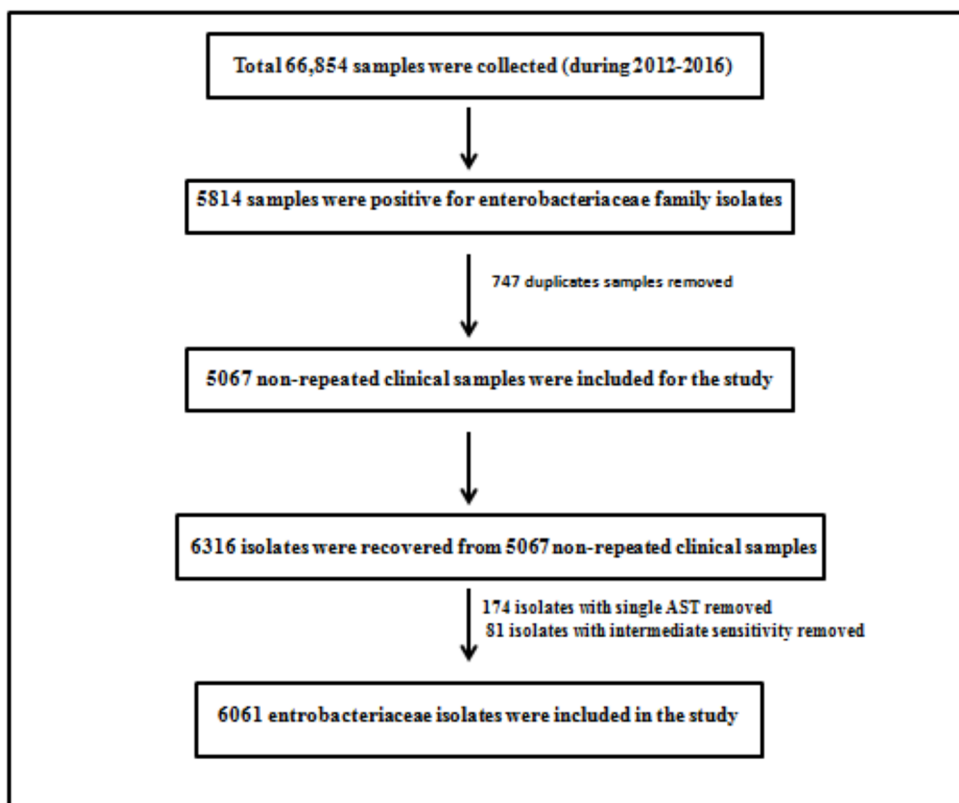


Fig. 1 Exclusion and inclusion criteria included in the study.

by the Vitek2 compact identification system (Biomeriux, France).

Antimicrobial Susceptibility Testing

The antimicrobial susceptibility testing of all isolates was done by the disk diffusion method on Mueller-Hinton agar. Apart from this, the minimum inhibitory concentrations (MICs) were also determined by the Vitek2 compact system (using AST GN cards; Biomeriux, France). The interpretation of zone diameters and MICs was done according to each year's CLSI guidelines.

Escherichia coli ATCC 25922 was taken as the control strains. The following antimicrobials (Himedia, India) were tested: ceftazidime (30 µg), cefotaxime (30 µg), ceftriaxone (30 µg), ceftiofloxacin (30 µg), cefepime (30 µg), piperacillin (100 µg), piperacillin-tazobactam (100/10 µg), ticarcillin-clavulanate (75/10 µg), cefoperazone-sulbactam (75/30 µg), cefepime-tazobactam (30/10 µg), ceftriaxone-sulbactam (30/15 µg), imipenem (10 µg), meropenem (10 µg), ertapenem (10 µg), amikacin (30 µg), gentamicin (10 µg), netilmicin (30 µg), tobramycin (10 µg), tetracycline (30 µg), Trimethoprim-sulfamethoxazole (1.25/24 µg), ciprofloxacin (5 µg), levofloxacin (5 µg), tigecycline (15 µg), nitrofurantoin (300 µg), and chloramphenicol (30 µg).

We interpreted the zone diameters and MICs of the isolates as per CLSI recommendations, 2018.¹³

Statistical Analyses

Statistical analyses were performed using the SPSS software for Windows (SPSS Inc., Chicago, Illinois, United States, version 15.0). The decreased resistance percentage was reported as the resistance percentage difference between the first year (2012) and the last year (2016) of the study.

Results

During the study, a total of 5,067 positive samples were included. The mean age of the patients from whom the samples were received was 32 years (range ± standard deviation [SD]: 1 to 87 ± 15.1 years). In male patients, the mean age was 46 years (range ± SD: 1 to 112 ± 27.11 years) whereas, in female patients, the mean age was found to be 44.5 years with a range of 2 to 96 ± 26.84 years). The difference of the means of the age in male and female patients was found to be statistically significant ($p = 0.002$, 95% confidence interval [CI] = 0.9481–4.2187).

Samples received from ICU (1,472, 29%), wards (2,714, 53.6%), and OPD (881, 17.4%) admitted patients were included in this study. Maximum number of *Enterobacteriaceae* isolates were obtained from patients admitted to general surgical ward (1,254, 25%) followed by neurosurgical ward (1,242, 25%), neurosurgical ICU (739, 15%), polytrauma ICU (733, 14%), and orthopaedics ward (218, 4%). The outpatients contributed about (881) 17% of the samples.

The samples included in our study were blood, urine, body fluid, respiratory samples, bone and tissue, pus/wound and swab, and tip culture. ►Table 1 shows the distribution of clinical samples included in this study. Blood culture yielded

the maximum number of isolates (1,663, 33%), followed by pus/wound and swab (1,317, 26%), urine (849, 17%), respiratory samples (761, 15%), body fluid (268, 5%), bone and tissue (135, 3%), and tip culture samples (74, 1%).

The maximum number of *Enterobacteriaceae* isolates recovered are from wards (3,535, 58.3%), followed by ICUs (1,626, 26.8%), and OPDs (900, 14.8%). In ICUs, *Klebsiella* spp. (815, 50.1%) was found to be the most predominant *Enterobacteriaceae* followed by *E. coli* (371, 22.8%) and *Enterobacter* spp. (135, 8.3%) throughout the study period (►Fig. 2A). In wards also, we found the same pattern except in 2014 and 2015 where *E. coli* was the most prominent (►Fig. 2B). In OPD, *E. coli* was the most predominant *Enterobacteriaceae* (476, 52.8%), followed by *Klebsiella* spp. (166, 18.4%) and *Enterobacter* spp. (77, 8.6%) (►Fig. 2C). For the purpose of conciseness, we concentrate on only predominant *Enterobacteriaceae* isolates, i.e., *Klebsiella* spp. and *E. coli*.

In ICU settings, both *E. coli* and *Klebsiella* spp. isolates showed more than 80% resistance against cephalosporins and quinolones. *E. coli* isolates showed maximum resistance to ciprofloxacin (94.6%), followed by ceftazidime and piperacillin (92%), ticarcillin-clavulanate (84.6%), and levofloxacin (84%). Among carbapenems, *E. coli* isolates showed more resistance against ertapenem (56%), followed by meropenem (36.3%) and imipenem (19.4%). The resistance against amikacin and chloramphenicol in *E. coli* isolates was observed in 38 and 29%, respectively. Among quinolones, *Klebsiella* spp. isolates showed maximum resistance to ciprofloxacin (85%), followed by levofloxacin (77.8%). These isolates also showed resistance against carbapenems; the resistance pattern was the same as observed in *E. coli* isolates, i.e., ertapenem (69%) > meropenem (67.3%) > imipenem (59%). Both *E. coli* and *Klebsiella* spp. isolates showed least resistance to tigecycline; *Klebsiella* spp. isolates showed 16% resistance, while *E. coli* isolated showed less than 1% resistance. All the urine isolates were resistant (98–100%) to nitrofurantoin. The year-wise resistance pattern against different antibiotics of *Enterobacteriaceae* in ICU settings is given in ►Table 2. In wards, *E. coli* showed 90% resistance to cephalosporins, 84% resistance to ceftazidime, and 81% resistance to levofloxacin. Among aminoglycosides, highest resistance was observed against gentamycin (55%), followed by tobramycin

Table 1 Percentage distribution of *Enterobacteriaceae* isolates in different samples during 2012–2016

Samples (N = 5,067)	
	N (%)
Blood	1,663 (33%)
Pus/wound + swab	1,317 (30%)
Urine	849 (17%)
Respiratory	761 (15%)
Body fluid	268 (5%)
Bone + tissue	135 (3%)
Tip culture	74 (1%)

^aN, total number of isolates.

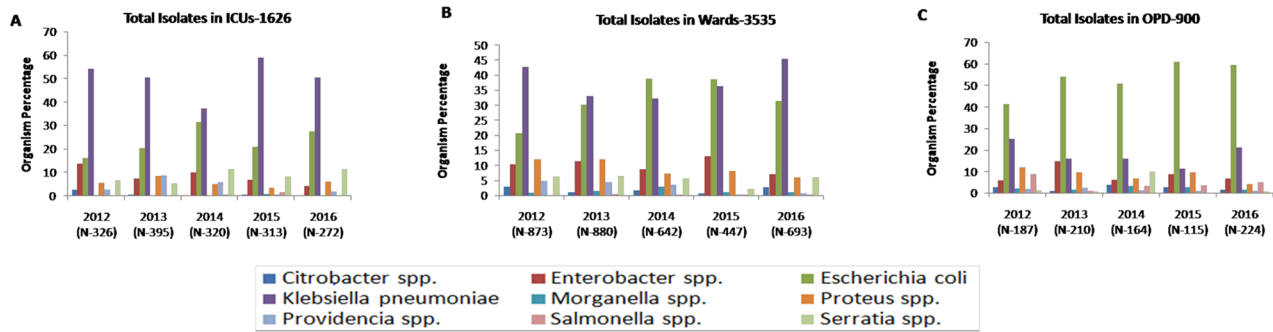


Fig. 2 Yearly distribution of *Enterobacteriaceae* isolates in (A) ICUs, (B) wards, and (C) OPDs. ICU, intensive care unit; OPD, outpatient department.

(41%) and amikacin (27%). Among carbapenems, maximum resistance was observed against ertapenem (46.8%), followed by meropenem (31.8%) and imipenem (16.1%). *Klebsiella* spp. isolates showed 92% resistance to ceftazidime, 89% to ciprofloxacin, and 79% to levofloxacin. Among aminoglycosides, *Klebsiella* spp. showed highest resistance against gentamycin (80%), followed by amikacin (73%). Among carbapenems, resistance against both ertapenem and meropenem was 67% and against imipenem was 53%. The year-wise resistance pattern against different antibiotics of *Enterobacteriaceae* in wards settings is given in ► **Table 3**.

In OPD, *E. coli* showed less than 70% resistance to cephalosporins, resistance against ciprofloxacin and levofloxacin was 79.4 and 69%, respectively. Among aminoglycosides, maximum resistance was seen against gentamycin (44%), followed by tobramycin (31.5%) and amikacin (18.3%). Among carbapenems, maximum resistance was observed against ertapenem (24.5%), followed by meropenem (18.9%) and imipenem (5.3%). *E. coli* showed 17% resistance to chloramphenicol. *Klebsiella* spp. showed 77% resistance to ceftazidime, 70.5% resistance to cefepime, and 65% resistance to levofloxacin. Among carbapenems, maximum resistance was observed against meropenem (59%), followed by imipenem (46.3%) and ertapenem (34%). Among aminoglycosides, maximum resistance seen in *Klebsiella* spp. isolates was against gentamycin (70%), followed by tobramycin (62.6%) and amikacin (64%). ► **Table 4** shows the year-wise resistance pattern against different antibiotics of *Enterobacteriaceae* of OPD patients. We observed least resistance against tigecycline among both *E. coli* and *Klebsiella* spp. (1.5 and 12.6%, respectively).

From 5-years resistance pattern in ICUs, we observed that *E. coli* and *Klebsiella* spp. isolates showed some decrease in resistance percentage against some antimicrobials. About 32% decreased resistance was observed in *E. coli* against meropenem, while against *Klebsiella* spp. isolates it was 34%. Against piperacillin-tazobactam, *E. coli* showed 25% decreased resistance, while *Klebsiella* spp. showed 22%. Both *E. coli* and *Klebsiella* spp. isolates showed 22% decreased resistance against cefoperazone-sulbactam. In addition to these, *Klebsiella* spp. isolates also showed decreased resistance against ceftriaxone (7%), 21% against ciprofloxacin, 12% against ticarcillin-clavulanate, 17% against gentamycin,

3% decreased resistance against imipenem, and 26% against levofloxacin.

In wards also, both *E. coli* and *Klebsiella* spp. isolates showed decreased resistance across the study period. In *E. coli*, maximum decreased resistance was observed against meropenem (27%), followed by gentamicin (18%) and imipenem (6%). In *Klebsiella* spp. maximum decreased resistance was observed against tigecycline (25%), followed by imipenem (21%), meropenem (19%), gentamicin (17%), piperacillin-tazobactam (8%), and ciprofloxacin (6%).

In OPD patients, *E. coli* showed maximum decreased resistance against ticarcillin-clavulanate (41%), followed by ceftazidime (29%), meropenem (23%), gentamycin (20%), chloramphenicol (17.7%), cefoperazone-sulbactam (8%), imipenem (4.2%), and tigecycline (1%). *Klebsiella* spp. isolates showed maximum decreased resistance against levofloxacin (49%), followed by imipenem (39.6%), cefepime (36.1%), and ceftazidime (23.7%).

Discussion

In this study, we evaluated the antimicrobial resistance pattern of *Enterobacteriaceae* in trauma patients. We found that in ICUs and wards, the most common gram-negative pathogens responsible for nosocomial infections were *Klebsiella* spp., followed by *E. coli* and *Enterobacter* spp. These findings are in concordant with other published studies.^{14,15} In OPD patients, the most common gram-negative pathogens responsible for nosocomial infections were *E. coli*, followed by *Klebsiella* spp. and *Enterobacter* spp.

Our study showed *Enterobacteriaceae* isolates from ICUs, wards, and OPD showed high level of resistant to all classes of cephalosporins. In addition, β lactam and β -lactamase inhibitor combination remained less effective. This encouraged therapy with quinolones, aminoglycosides, or carbapenems. However, among quinolones, aminoglycosides, and carbapenems we found least resistance to carbapenems followed by aminoglycosides and quinolones in all settings; this result is in concordant with another study.¹⁶ This shows that the resistance is increasing to currently used antibiotics, and the older drugs may prove as an effective option. Both imipenem and meropenem showed good activity against *Enterobacteriaceae*

Table 2 Antimicrobial resistance pattern of *Enterobacteriaceae* pathogens isolated from ICUs against different antibiotics

Organism name	Year	AMK, N (%)	CEFEP, N (%)	CEFEPTAZ, N (%)	CEFTAZ, N (%)	CEFTRX, N (%)	CEFTRXSUL, N (%)	CHL, N (%)	CIPRO, N (%)	ERTA, N (%)	GENTA, N (%)	IMI, N (%)	LEVO, N (%)	MERO, N (%)	NETIL, N (%)	PIP, N (%)	PIPTAZ, N (%)	TETRA, N (%)	TIC, N (%)	TICLAV, N (%)	TIG, N (%)	TOBRA, N (%)	TMZ, N (%)		
<i>Citrobacter</i> spp.	2012 (8)	8 (100)	8 (100)	8 (100)	8 (100)	8 (100)	NA	2 (25)	8 (100)	1 (14)	8 (100)	2 (25)	2 (25)	2 (25)	8 (100)	8 (100)	0	8 (100)	8 (100)	0	8 (100)	0	8 (100)	NA	
	2013 (1)	0 (0)	0 (0)	0	0	0	NA	NA	0	NA	0	0	0	0	0	1 (100)	0	0	1 (100)	0	0	0	NA	NA	
	2014 (0)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	
	2015 (1)	0 (0)	0 (0)	0 (0)	0	0	0	1 (100)	0	0	1 (100)	0	0	0	0	0	0	0	0	0	0	0	0	NA	1 (100)
	2016 (0)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
<i>Enterobacter</i> spp.	2012 (44)	39 (88)	39 (88)	NA	40 (91)	40 (91)	NA	30 (69)	38 (86)	40 (92)	39 (89)	33 (75)	37 (84)	37 (82)	38 (86)	40 (91)	38 (86)	20 (45)	43 (97)	38 (87)	4 (9)	43 (97)	NA	NA	
	2013 (28)	13 (46)	19 (67)	13 (46)	24 (86)	19 (68)	13 (46)	10 (35)	19 (68)	12 (43)	17 (61)	15 (54)	13 (46)	17 (61)	16 (57)	24 (86)	15 (52)	14 (50)	28 (100)	20 (70)	4 (13)	28 (100)	0 (0)		
	2014 (31)	20 (65)	22 (71)	20 (63)	23 (74)	24 (77)	23 (74)	10 (31)	21 (68)	22 (71)	23 (74)	17 (55)	21 (68)	18 (58)	21 (69)	24 (86)	19 (61)	0 (0)	NA	26 (84)	5 (17)	NA	24 (77.4)		
	2015 (21)	8 (40)	13 (63)	6 (29)	15 (70)	18 (88)	8 (40)	11 (50)	11 (50)	10 (46)	13 (60)	3 (16)	11 (50)	3 (15)	13 (60)	14 (65)	5 (26)	21 (100)	0 (0)	13 (61)	2 (11)	NA	10 (50)		
	2016 (11)	5 (46)	4 (36)	6 (55)	6 (55)	6 (55)	6 (55)	4 (36)	6 (55)	0 (0)	6 (55)	4 (36)	4 (36)	6 (55)	5 (46)	6 (55)	6 (55)	NA	NA	6 (50)	0 (0)	0 (0)	0 (0)		
	2012 (52)	17 (33)	39 (75)	NA	46 (88)	47 (90)	NA	10 (20)	49 (94)	9 (17)	27 (52)	11 (21)	11 (21)	44 (85)	29 (56)	16 (30)	39 (75)	44 (85)	50 (96)	35 (67)	0	52 (100)	NA	NA	
<i>Escherichia coli</i>	2013 (80)	26 (33)	66 (82)	22 (28)	76 (95)	73 (91)	37 (46)	20 (25)	72 (90)	21 (26)	51 (64)	11 (14)	67 (84)	41 (51)	26 (33)	65 (81)	51 (64)	70 (88)	78 (97)	75 (94)	1 (1)	80 (100)	0 (0)	0 (0)	
	2014 (100)	33 (33)	77 (77)	34 (34)	85 (85)	94 (94)	48 (48)	22 (22)	94 (94)	62 (62)	62 (62)	27 (27)	70 (70)	41 (41)	33 (33)	87 (87)	55 (55)	NA	NA	84 (84)	1 (1)	NA	83 (83.8)		
	2015 (65)	32 (49)	57 (88)	33 (51)	63 (97)	65 (100)	46 (70)	23 (36)	65 (100)	49 (76)	50 (77)	6 (9)	64 (99)	9 (14)	34 (53)	64 (99)	34 (53)	NA	NA	59 (91)	0 (0)	NA	47 (72.3)		
	2016 (74)	34 (46)	69 (93)	26 (35)	71 (96)	71 (96)	44 (60)	33 (44)	71 (96)	66 (89)	60 (81)	17 (23)	66 (89)	18 (24)	36 (48)	73 (99)	37 (50)	NA	NA	61 (83)	0 (0)	NA	56 (75)		
	2012 (176)	148 (84)	162 (92)	NA	169 (96)	171 (97)	NA	116 (66)	171 (97)	128 (73)	158 (90)	121 (90)	162 (92)	144 (82)	160 (91)	169 (96)	153 (87)	118 (67)	IR	172 (98)	42 (24)	174 (99)	NA		
	2013 (199)	167 (84)	187 (94)	151 (76)	187 (94)	189 (95)	159 (80)	111 (56)	185 (93)	109 (55)	169 (85)	123 (85)	169 (85)	161 (81)	165 (83)	191 (96)	153 (77)	107 (54)	IR	189 (94)	34 (17)	199 (100)	0 (0)		
<i>Klebsiella pneumoniae</i>	2014 (119)	88 (74)	104 (87)	87 (73)	104 (87)	112 (94)	88 (74)	48 (40)	95 (80)	83 (70)	94 (79)	71 (60)	75 (63)	90 (76)	83 (70)	105 (88)	91 (76)	0 (0)	IR	106 (89)	19 (16)	NA	94 (79.6)		
	2015 (184)	96 (52)	166 (90)	94 (51)	158 (86)	166 (90)	132 (72)	101 (55)	145 (79)	118 (64)	134 (73)	75 (41)	138 (75)	88 (48)	107 (58)	169 (92)	132 (71)	NA	160 (87)	21 (12)	NA	145 (80.1)			
	2016 (137)	122 (89)	126 (92)	104 (76)	132 (95)	123 (90)	119 (87)	92 (67)	104 (76)	121 (88)	100 (73)	90 (66)	66 (66)	66 (48)	127 (93)	136 (99)	89 (65)	NA	117 (86)	19 (14)	0 (0)	112 (82)			
	2012 (0)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	IR	NA	NA		
	2013 (0)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	IR	NA	NA		
<i>Morganella</i> spp.	2014 (0)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	IR	NA	NA		
	2015 (2)	2 (100)	0	0	2 (100)	0	2 (100)	0	2 (100)	0	2 (100)	0	2 (100)	0	2 (100)	2 (100)	2 (100)	0	NA	2 (100)	IR	NA	2 (100)		
	2016 (0)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	IR	NA	NA		

(continued)

Table 2 (continued)

Year	AMIK, N (%)	CEFER, N (%)	CEFEPTAZ, N (%)	CEFOSUL, N (%)	CEFOT, N (%)	CEFOX, N (%)	CEFTAZ, N (%)	CEFTRX, N (%)	CEFTRXSUL, N (%)	CHL, N (%)	CIPRO, N (%)	ERTIA, N (%)	GENTA, N (%)	IMI, N (%)	LEVO, N (%)	MERO, N (%)	NETIL, N (%)	PIP, N (%)	PIPTAZ, N (%)	TETRA, N (%)	TIC, N (%)	TICLAV, N (%)	TIG, N (%)	TOBRA, N (%)	TMZ, N (%)
<i>Proteus</i> spp.	2012 (17)	11 (63)	17 (100)	NA	NA	2 (14)	15 (88)	17 (100)	NA	11 (67)	17 (100)	NA	9 (50)	0 (0)	13 (77)	9 (53)	17 (100)	5 (31)	0 (0)	IR	14 (82)	6 (36)	IR	17 (100)	NA
	2013 (33)	13 (38)	29 (89)	4 (13)	24 (73)	9 (26)	26 (79)	20 (61)	4 (13)	24 (74)	15 (46)	33 (100)	18 (55)	2 (6)	18 (55)	21 (64)	28 (85)	7 (21)	1 (3)	IR	33 (100)	14 (43)	IR	33 (100)	0 (0)
	2014 (15)	11 (73)	12 (80)	1 (7)	9 (63)	5 (36)	12 (80)	8 (53)	2 (13)	12 (80)	13 (87)	0 (0)	12 (80)	6 (39)	12 (80)	6 (40)	14 (93)	6 (40)	0 (0)	IR	NA	8 (53)	IR	NA	14 (93.3)
	2015 (10)	0 (0)	3 (30)	0	2 (22)	0	3 (30)	0	0	8 (80)	3 (30)	0	2 (20)	3 (30)	0	3 (30)	0	3 (30)	0	IR	NA	0	IR	NA	4 (40)
	2016 (16)	5 (31)	3 (19)	1 (6)	10 (60)	NA	6 (38)	7 (44)	2 (13)	2 (15)	9 (56)	0 (0)	6 (38)	3 (19)	10 (60)	1 (6)	6 (38)	1 (6)	1 (6)	IR	0 (0)	1 (6)	IR	0 (0)	6 (35.7)
<i>Providencia</i> spp.	2012 (8)	7 (88)	5 (57)	NA	NA	7 (85)	7 (88)	7 (88)	NA	8 (100)	4 (50)	NA	7 (88)	6 (75)	4 (50)	1 (13)	7 (88)	7 (88)	6 (7.5)	IR	6 (80)	8 (100)	IR	8 (100)	NA
	2013 (34)	23 (68)	23 (67)	28 (83)	31 (92)	20 (60)	26 (76)	26 (76)	28 (83)	23 (69)	28 (82)	0 (0)	28 (82)	9 (27)	29 (85)	21 (62)	25 (74)	22 (65)	13 (38)	IR	13 (38)	27 (79)	IR	34 (100)	0 (0)
	2014 (18)	17 (94)	17 (94)	13 (72)	17 (94)	14 (78)	18 (100)	17 (94)	15 (83)	13 (71)	17 (94)	18 (100)	18 (100)	17 (94)	17 (94)	13 (72)	18 (100)	17 (94)	17 (94)	IR	NA	18 (100)	IR	NA	7 (41.2)
	2015 (1)	1 (100)	1 (100)	0	1 (100)	0	1 (100)	0	0	1 (100)	1 (100)	0	1 (100)	0	1 (100)	0	1 (100)	0	0	IR	NA	1 (100)	IR	NA	NA
	2016 (4)	1 (33)	1 (33)	1 (33)	0 (0)	NA	1 (33)	1 (33)	1 (33)	0 (0)	1 (33)	0 (0)	1 (33)	0 (0)	1 (33)	1 (33)	1 (33)	1 (33)	1 (33)	IR	0 (0)	1 (33)	IR	0 (0)	1 (25)
<i>Salmonella</i> spp.	2012 (0)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	2013 (0)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	2014 (1)	1 (100)	1 (100)	0	1 (100)	0	1 (100)	1 (100)	0	0	0	0	1 (100)	0	0	0	0	0	0	0	0	0	0	0	0
	2015 (4)	1 (25)	0	0	0	0	0	0	0	1 (25)	0	1 (25)	0	1 (25)	0	1 (25)	0	1 (25)	0	0	0	0	0	0	0
	2016 (0)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	0
<i>Serratia</i> spp.	2012 (21)	17 (81)	14 (65)	NA	NA	IR	18 (86)	18 (86)	NA	6 (30)	14 (67)	NA	8 (38)	5 (25)	13 (62)	9 (45)	14 (67)	21 (100)	18 (86)	7 (35)	18 (86)	21 (100)	11 (50)	18 (86)	NA
	2013 (20)	11 (55)	12 (62)	6 (29)	10 (50)	IR	17 (85)	15 (75)	6 (29)	2 (10)	7 (37)	0 (0)	6 (30)	4 (21)	3 (15)	7 (35)	15 (75)	15 (75)	2 (11)	0 (0)	19 (93)	15 (74)	2 (11)	18 (92)	0 (0)
	2014 (36)	28 (78)	29 (81)	1 (4)	33 (91)	IR	32 (89)	30 (83)	4 (11)	9 (25)	15 (42)	12 (33)	5 (14)	13 (37)	8 (22)	9 (25)	27 (74)	28 (78)	0 (0)	0 (0)	NA	24 (67)	8 (32)	NA	15 (41.7)
	2015 (25)	2 (8)	8 (32)	4 (17)	25 (100)	IR	12 (48)	20 (80)	3 (12)	4 (16)	8 (32)	25 (100)	1 (4)	6 (22)	3 (13)	4 (16)	21 (83)	8 (32)	7 (28)	0 (0)	NA	8 (32)	4 (17)	NA	1 (4)
	2016 (30)	26 (85)	26 (85)	3 (11)	27 (90)	IR	29 (96)	29 (96)	19 (63)	9 (29)	12 (40)	0 (0)	8 (26)	0 (0)	23 (75)	0 (0)	29 (96)	29 (96)	2 (8)	0 (0)	0 (0)	29 (96)	2 (7)	0 (0)	0 (0)

Abbreviations: AMIK, amikacin; CEFER, cefepime; CEFEPTAZ, ceftazidime; CEFOSUL, cefoperazone-sulbactam; CEFOT, cefotaxime; CEFOX, ceftiofur; CEFTAZ, ceftazidime; CEFTRX, ceftroxime; CEFTRXSUL, ceftriaxone-sulbactam; CHL, chloramphenicol; CIPRO, ciprofloxacin; ERTIA, ertapenem; GENIA, gentamicin; IMI, imipenem; IR, intrinsic resistance; LEVO, levofloxacin; MERO, meropenem; NA, not applicable; NETIL, netilmicin; PIP, piperacillin; PIPTAZ, piperacillin-tazobactam; TETRA, tetracycline; TIC, ticarcillin-clavulanate; TIG, tigecycline; TOBRA, tobramycin; TMZ, trimethoprim/sulfamethoxazole.
 Note: N denotes the number of isolates.

Table 3 Antimicrobial resistance pattern of Enterobacteriaceae pathogens isolated from wards against different antibiotics

Organism name	Year	AMK, N (%)	CEFEP, N (%)	CEFEPTAZ, N (%)	CEFOSUL, N (%)	CEFOT, N (%)	CEFOX, N (%)	CEFTAZ, N (%)	CEFTRX, N (%)	CEFTRXSUL, N (%)	CHL, N (%)	CIPRO, N (%)	ERT, N (%)	GENTA, N (%)	IMI, N (%)	LEVO, N (%)	MERO, N (%)	NETIL, N (%)	PIP, N (%)	PIPTAZ, N (%)	TETRA, N (%)	TIC, N (%)	TICLAV, N (%)	TIG, N (%)	TOBRA, N (%)	TMZ, N (%)	
Citrobacter spp.	2012 (25)	18 (73)	14 (57)	0 (0)	17 (69)	0 (0)	18 (73)	18 (73)	19 (76)	0 (0)	15 (60)	15 (58)	16 (63)	18 (73)	13 (50)	7 (28)	10 (39)	17 (67)	19 (76)	15 (60)	4 (17)	23 (92)	21 (85)	0 (0)	25 (100)	0 (0)	
	2013 (9)	5 (55)	5 (55)	6 (71)	5 (55)	7 (82)	6 (64)	7 (82)	7 (82)	6 (71)	6 (71)	5 (55)	7 (75)	5 (55)	2 (27)	4 (46)	5 (55)	5 (55)	5 (60)	5 (55)	5 (50)	6 (67)	7 (73)	0 (0)	9 (100)	0 (0)	
	2014 (10)	3 (31)	3 (31)	3 (31)	4 (38)	4 (36)	5 (50)	5 (50)	4 (38)	4 (36)	2 (23)	2 (19)	6 (56)	4 (38)	1 (14)	1 (13)	1 (6)	2 (23)	4 (44)	4 (38)	0 (0)	0 (0)	5 (50)	0 (0)	0 (0)	0 (0)	0 (0)
	2015 (3)	2 (50)	1 (33)	0 (0)	1 (40)	1 (40)	0 (0)	1 (33)	2 (67)	0 (0)	1 (25)	2 (60)	1 (25)	2 (50)	1 (33)	2 (50)	1 (33)	2 (50)	1 (17)	0 (0)	0 (0)	0 (0)	2 (50)	0 (0)	0 (0)	0 (0)	0 (0)
	2016 (18)	5 (30)	10 (55)	5 (25)	11 (60)	18 (100)	0 (0)	12 (68)	12 (68)	12 (65)	12 (65)	12 (65)	10 (55)	7 (39)	3 (15)	5 (28)	3 (17)	7 (40)	13 (70)	8 (44)	0 (0)	0 (0)	13 (70)	0 (0)	0 (0)	0 (0)	3 (17)
	2012 (89)	57 (64)	59 (66)	0 (0)	61 (68)	0 (0)	IR	68 (76)	69 (77)	0 (0)	36 (41)	60 (67)	39 (44)	61 (68)	46 (52)	53 (60)	54 (61)	58 (65)	73 (82)	55 (62)	40 (45)	75 (84)	76 (85)	7 (8)	89 (100)	0 (0)	
Enterobacter spp.	2013 (99)	51 (52)	57 (58)	44 (44)	60 (61)	70 (71)	IR	73 (74)	68 (69)	58 (59)	58 (59)	53 (54)	41 (41)	58 (59)	41 (41)	47 (47)	40 (40)	59 (60)	77 (78)	55 (56)	32 (32)	84 (85)	76 (77)	4 (4)	95 (96)	0 (0)	
	2014 (56)	27 (48)	36 (64)	29 (51)	30 (54)	38 (68)	IR	42 (75)	30 (54)	38 (68)	25 (45)	28 (50)	31 (55)	35 (63)	24 (42)	17 (31)	23 (41)	30 (54)	39 (69)	31 (55)	0 (0)	0 (0)	41 (74)	1 (2)	0 (0)	0 (0)	
	2015 (58)	31 (54)	32 (56)	6 (11)	24 (41)	36 (62)	IR	43 (74)	41 (71)	26 (44)	27 (47)	30 (52)	24 (41)	39 (68)	15 (25)	27 (46)	15 (25)	26 (45)	38 (65)	26 (44)	0 (0)	0 (0)	41 (70)	0 (0)	0 (0)	0 (0)	
	2016 (49)	24 (48)	20 (41)	18 (37)	21 (42)	20 (41)	IR	22 (45)	21 (42)	22 (44)	15 (30)	19 (39)	30 (61)	24 (48)	13 (26)	20 (40)	15 (30)	20 (41)	22 (44)	21 (42)	0 (0)	0 (0)	24 (48)	5 (10)	0 (0)	17 (35)	
	2012 (180)	50 (28)	124 (69)	0 (0)	86 (48)	4 (2)	85 (47)	153 (85)	160 (89)	0 (0)	34 (19)	166 (92)	47 (26)	118 (66)	32 (18)	149 (83)	83 (46)	40 (22)	164 (91)	76 (42)	157 (87)	171 (95)	169 (94)	9 (5)	178 (99)	0 (0)	
	2013 (264)	58 (22)	219 (83)	71 (27)	121 (46)	216 (82)	153 (58)	232 (88)	230 (87)	116 (44)	116 (44)	116 (44)	243 (92)	161 (61)	48 (18)	206 (78)	121 (46)	74 (28)	246 (93)	116 (44)	214 (81)	259 (98)	253 (96)	1 (0.3)	264 (100)	0 (0)	
Escherichia coli	2014 (248)	62 (25)	174 (70)	62 (25)	82 (33)	208 (84)	149 (60)	193 (78)	82 (33)	208 (84)	42 (17)	218 (88)	117 (47)	124 (50)	42 (17)	188 (76)	64 (26)	87 (35)	181 (73)	107 (43)	0 (0)	0 (0)	181 (73)	2 (1)	0 (0)	0 (0)	
	2015 (172)	53 (31)	136 (79)	52 (30)	83 (48)	151 (88)	0 (0)	146 (85)	139 (81)	96 (56)	60 (35)	151 (88)	120 (70)	86 (50)	26 (15)	146 (85)	34 (20)	50 (29)	151 (88)	101 (59)	0 (0)	0 (0)	139 (81)	7 (4)	0 (0)	0 (0)	
	2016 (216)	69 (32)	179 (83)	71 (33)	102 (47)	192 (89)	0 (0)	179 (83)	192 (89)	117 (54)	63 (29)	197 (91)	153 (71)	104 (48)	26 (12)	188 (87)	41 (19)	63 (29)	194 (90)	106 (49)	0 (0)	0 (0)	166 (77)	89 (41)	0 (0)	147 (68)	
	2012 (371)	301 (81)	341 (92)	0 (0)	308 (83)	0 (0)	289 (78)	352 (95)	349 (94)	0 (0)	193 (52)	341 (92)	223 (60)	338 (91)	237 (64)	312 (84)	286 (77)	289 (78)	356 (93)	293 (79)	249 (67)	IR	371 (100)	111 (30)	371 (100)	0 (0)	
	2013 (290)	206 (71)	267 (92)	168 (58)	229 (79)	247 (85)	238 (82)	273 (94)	273 (94)	186 (64)	186 (64)	186 (64)	171 (59)	229 (79)	165 (57)	200 (69)	215 (74)	223 (77)	273 (94)	220 (76)	136 (47)	IR	281 (97)	78 (27)	290 (100)	0 (0)	
	2014 (206)	122 (59)	167 (81)	136 (66)	148 (72)	187 (91)	161 (78)	173 (84)	148 (72)	187 (91)	97 (47)	183 (89)	146 (71)	157 (76)	103 (50)	150 (73)	138 (67)	161 (78)	173 (88)	150 (73)	0 (0)	IR	177 (86)	29 (14)	0 (0)	0 (0)	
Klebsiella pneumoniae	2015 (162)	115 (71)	149 (92)	78 (48)	125 (77)	147 (91)	0 (0)	152 (94)	152 (94)	117 (72)	91 (56)	144 (89)	118 (73)	122 (75)	45 (85)	84 (52)	118 (73)	156 (96)	120 (74)	0 (0)	0 (0)	IR	152 (94)	8 (5)	0 (0)	0 (0)	
	2016 (313)	238 (76)	269 (86)	200 (64)	257 (82)	297 (95)	0 (0)	285 (91)	285 (91)	238 (76)	160 (51)	269 (86)	247 (74)	231 (43)	135 (81)	182 (58)	257 (82)	297 (95)	222 (71)	222 (71)	0 (0)	IR	282 (90)	16 (5)	0 (0)	194 (62)	
	2012 (8)	3 (33)	4 (44)	0 (0)	6 (78)	0 (0)	6 (78)	4 (56)	4 (56)	0 (0)	3 (38)	6 (78)	0 (0)	5 (67)	3 (33)	4 (56)	5 (67)	5 (63)	2 (25)	6 (71)	7 (88)	6 (75)	IR	6 (75)	IR	6 (75)	0 (0)
	2013 (13)	5 (38)	5 (40)	4 (30)	7 (56)	0 (0)	11 (88)	8 (63)	8 (64)	4 (30)	4 (30)	4 (30)	13 (100)	7 (50)	4 (31)	10 (75)	7 (50)	6 (44)	8 (63)	4 (27)	13 (100)	11 (83)	10 (75)	IR	13 (100)	0 (0)	
	2014 (18)	10 (53)	6 (35)	1 (7)	10 (53)	12 (64)	18 (100)	13 (71)	10 (53)	12 (64)	12 (64)	12 (64)	9 (50)	13 (71)	1 (7)	13 (71)	2 (12)	12 (64)	5 (29)	4 (24)	0 (0)	0 (0)	10 (53)	IR	0 (0)	0 (0)	
	2015 (5)	1 (25)	1 (13)	1 (17)	1 (14)	2 (33)	0 (0)	1 (25)	1 (17)	1 (13)	0 (0)	0 (0)	2 (38)	1 (25)	1 (13)	2 (38)	1 (13)	2 (33)	1 (25)	1 (25)	0 (0)	0 (0)	1 (25)	IR	0 (0)	0 (0)	
2016 (7)	4 (50)	5 (75)	4 (50)	5 (75)	5 (75)	0 (0)	5 (75)	5 (75)	5 (75)	5 (75)	2 (33)	5 (75)	0 (0)	4 (50)	5 (75)	2 (25)	5 (75)	5 (75)	4 (50)	0 (0)	0 (0)	5 (75)	IR	0 (0)	7 (100)		

(continued)

Table 3 (continued)

Organism name	Year	AMK, N (%)	CEFE, N (%)	CEFTAZ, N (%)	CEFTRXSUL, N (%)	CEFTRX, N (%)	CHL, N (%)	CIPRO, N (%)	ERT, N (%)	GENTA, N (%)	IMI, N (%)	LEVO, N (%)	MERO, N (%)	NETIL, N (%)	PIP, N (%)	PIPTAZ, N (%)	TETRA, N (%)	TICLAV, N (%)	TIG, N (%)	TOBRA, N (%)	TMZ, N (%)
<i>Proteus</i> spp.	2012 (104)	66 (63)	62 (60)	74 (71)	76 (73)	70 (67)	79 (76)	26 (25)	56 (54)	17 (16)	72 (69)	49 (47)	87 (84)	35 (34)	8 (8)	61 (59)	56 (54)	IR	104 (100)	0 (0)	
	2013 (106)	42 (40)	86 (81)	88 (83)	76 (72)	35 (33)	75 (71)	0 (0)	71 (67)	18 (17)	78 (74)	41 (39)	88 (83)	29 (27)	11 (10)	61 (58)	34 (32)	IR	106 (100)	0 (0)	
	2014 (46)	20 (43)	31 (68)	38 (82)	19 (41)	21 (46)	23 (51)	34 (73)	0 (0)	35 (75)	13 (29)	29 (62)	14 (30)	38 (82)	3 (7)	IR	15 (33)	IR	0 (0)	0 (0)	
	2015 (36)	16 (45)	26 (71)	25 (70)	26 (72)	0 (0)	26 (71)	31 (86)	0 (0)	23 (64)	0 (0)	26 (72)	0 (0)	31 (86)	4 (11)	4 (11)	IR	7 (20)	IR	0 (0)	
	2016 (41)	22 (54)	25 (60)	29 (71)	27 (67)	2 (6)	29 (71)	18 (44)	0 (0)	28 (69)	7 (18)	29 (71)	1 (3)	29 (71)	9 (23)	1 (3)	IR	2 (6)	IR	0 (0)	30 (73)
	2012 (42)	31 (73)	27 (64)	31 (73)	34 (80)	0 (0)	15 (36)	38 (90)	0 (0)	37 (87)	8 (18)	34 (82)	26 (63)	35 (84)	29 (68)	6 (15)	32 (77)	32 (75)	IR	42 (100)	0 (0)
<i>Providencia</i> spp.	2013 (39)	26 (67)	26 (66)	35 (91)	36 (93)	23 (59)	32 (81)	9 (22)	32 (81)	18 (47)	33 (84)	29 (75)	31 (79)	27 (70)	24 (61)	39 (100)	32 (83)	IR	39 (100)	0 (0)	
	2014 (22)	17 (77)	14 (62)	17 (77)	17 (77)	20 (89)	15 (67)	18 (83)	0 (0)	17 (77)	10 (44)	12 (54)	17 (78)	17 (77)	17 (77)	IR	15 (70)	IR	0 (0)	0 (0)	
	2015 (1)	1 (50)	0 (0)	1 (50)	0 (0)	0 (0)	1 (50)	1 (100)	0 (0)	1 (50)	0 (0)	1 (50)	0 (0)	1 (50)	0 (0)	1 (50)	0 (0)	IR	0 (0)	0 (0)	
	2016 (5)	2 (40)	0 (0)	2 (40)	2 (40)	0 (0)	0 (0)	4 (80)	0 (0)	4 (80)	2 (40)	4 (80)	2 (40)	2 (40)	2 (40)	2 (40)	2 (40)	2 (40)	IR	0 (0)	0 (0)
<i>Salmonella</i> spp.	2012 (6)	0 (43)	0 (0)	0 (6)	0 (7)	0 (8)	0 (21)	0 (50)	0 (25)	0 (7)	0 (7)	0 (7)	0 (20)	0 (27)	0 (10)	0 (0)	0 (21)	0 (38)	0 (8)	0 (0)	
	2013 (4)	0 (0)	0 (0)	3 (67)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (17)	0 (0)	0 (0)	1 (17)	3 (83)	0 (0)	0 (0)	0 (0)	
	2014 (1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (17)	0 (0)	0 (0)	0 (17)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (17)	0 (0)	0 (0)	0 (0)	
	2015 (1)	0 (20)	0 (0)	0 (40)	0 (40)	0 (0)	0 (0)	1 (60)	0 (0)	1 (60)	0 (0)	0 (20)	0 (0)	0 (0)	0 (40)	0 (40)	0 (0)	0 (40)	0 (0)	0 (0)	0 (0)
	2016 (2)	0 (15)	0 (8)	0 (0)	0 (0)	0 (0)	0 (8)	0 (15)	0 (0)	1 (46)	0 (0)	0 (8)	0 (0)	0 (0)	0 (15)	0 (0)	0 (0)	0 (8)	0 (0)	0 (0)	0 (0)
	2012 (54)	49 (91)	44 (82)	40 (74)	51 (94)	14 (26)	46 (85)	18 (32)	22 (40)	21 (38)	8 (15)	26 (49)	12 (23)	46 (85)	39 (73)	8 (15)	15 (27)	42 (78)	0 (0)	52 (97)	0 (0)
<i>Serratia</i> spp.	2013 (56)	18 (32)	31 (55)	42 (75)	38 (68)	21 (38)	18 (32)	18 (32)	22 (40)	12 (21)	14 (25)	17 (30)	20 (35)	29 (51)	41 (74)	18 (33)	31 (56)	39 (70)	0 (0)	46 (83)	56 (100)
	2014 (35)	14 (41)	17 (48)	18 (50)	7 (21)	16 (47)	8 (24)	14 (41)	12 (33)	3 (8)	3 (8)	9 (25)	4 (10)	18 (50)	4 (10)	0 (0)	0 (0)	16 (45)	1 (3)	0 (0)	0 (0)
	2015 (9)	1 (11)	4 (44)	4 (44)	0 (0)	3 (38)	4 (43)	4 (44)	0 (0)	0 (0)	0 (0)	2 (22)	0 (0)	5 (50)	8 (88)	5 (50)	0 (0)	6 (67)	0 (0)	0 (0)	0 (0)
	2016 (42)	23 (54)	28 (67)	28 (67)	28 (67)	21 (50)	16 (38)	24 (57)	0 (0)	11 (27)	1 (3)	24 (58)	0 (0)	28 (67)	25 (60)	13 (31)	0 (0)	25 (60)	10 (23)	0 (0)	0 (0)

Abbreviations: AMK, amikacin; CEFE, cefepime; CEFTAZ, ceftazidime; CEFOT, cefotaxime; CEFOX, ceftaxime; CEFOSUL, ceftiozone-sulbactam; CEFOTI, cefotaxime; CEFOT, cefotaxime; CEFOT, cefotaxime; CEFOSUL, ceftiozone-sulbactam; CEFOTI, cefotaxime; CEFOX, ceftaxime; CEFTAZ, ceftazidime; CEFTRXSUL, ceftriaxone-sulbactam; CHL, chloramphenicol; CIPRO, ciprofloxacin; ERTA, eripenem; GENTA, gentamicin; IMI, imipenem; IR, intrinsic resistance; LEVO, levofloxacin; MERO, meropenem; NETIL, netilmicin; PIP, piperacillin; PIPTAZ, piperacillin-tazobactam; TETRA, tetracycline; TIC, ticarcillin-clavulanate; TIC, tigecycline; TOBRA, tobramycin; TMZ, trimethoprim/sulfamethoxazole.
 Note: N denotes the number of isolates.

Table 4 Antimicrobial resistance pattern of Enterobacteriaceae pathogens isolated from OPD patients against different antibiotics

Organism name	Year	AMK, N (%)	CEFEP, N (%)	CEFTAZ, N (%)	CEFRX, N (%)	CEFTRXSUL, N (%)	CHL, N (%)	CIPRO, N (%)	ERTA, N (%)	GENTA, N (%)	IMI, N (%)	LEVO, N (%)	MERO, N (%)	NETIL, N (%)	PIP, N (%)	PIPTAZ, N (%)	TETRA, N (%)	TIC, N (%)	TICLAV, N (%)	TIG, N (%)	TOBRA, N (%)	TMZ, N (%)
<i>Citrobacter</i> spp.	2012 (5)	3 (60)	2 (40)	3 (60)	3 (75)	NA	2 (40)	1 (25)	1 (100)	NA	2 (40)	0 (0)	0 (0)	2 (50)	2 (0)	1 (25)	1 (25)	3 (60)	2 (50)	0 (0)	3 (100)	NA
	2013 (2)	1 (50)	NA	2 (100)	2 (100)	NA	1 (100)	1 (50)	2 (100)	3 (60)	1 (50)	1 (50)	1 (50)	1 (50)	1 (50)	1 (50)	2 (100)	2 (100)	2 (100)	0 (0)	1 (100)	NA
	2014 (6)	0 (0)	0 (0)	1 (16.7)	1 (16.7)	0 (0)	0 (0)	0 (0)	0 (0)	1 (50)	0 (0)	0 (0)	0 (0)	0 (0)	0 (100)	0 (0)	NA	NA	0 (0)	0 (0)	4 (100)	1 (16.7)
	2015 (3)	1 (33.3)	0 (0)	0 (0)	0 (0)	0 (0)	1 (50)	1 (50)	1 (50)	0 (0)	0 (0)	1 (33.3)	0 (0)	1 (33.3)	1 (100)	0 (0)	NA	NA	1 (33.3)	0 (0)	NA	1 (33.3)
	2016 (3)	0 (0)	0 (0)	2 (66.)	2 (66.)	3 (100)	1 (33.)	2 (66.7)	0 (0)	0 (0)	1 (33.3)	0 (0)	0 (0)	0 (0)	2 (33.3)	2 (0)	0 (0)	NA	2 (66.7)	0 (0)	NA	0 (0)
	2017 (11)	5 (50)	6 (54.6)	6 (60)	7 (63.6)	NA	4 (44.)	6 (54.6)	1 (100)	5 (45.5)	4 (36.4)	4 (36.4)	4 (36.4)	4 (36.4)	5 (45.5)	4 (40)	4 (40)	6 (60)	3 (50)	2 (25)	6 (100)	NA
<i>Enterobacter</i> spp.	2012 (31)	6 (19.4)	5 (16.1)	4 (13.3)	4 (12.9)	5 (20)	3 (10.)	4 (13.3)	0 (0)	4 (12.9)	0 (0)	4 (12.9)	4 (12.9)	2 (7.1)	11 (35.5)	4 (13.8)	1 (16.7)	1 (14.3)	11 (35.5)	1 (3.5)	1 (100)	NA
	2013 (10)	3 (33.3)	6 (60)	6 (60)	7 (70)	4 (40)	2 (25)	5 (50)	1 (50)	6 (60)	2 (20)	3 (30)	2 (20)	3 (60)	6 (60)	3 (30)	NA	NA	7 (70)	0 (0)	7 (100)	7 (70)
	2014 (10)	5 (50)	5 (50)	7 (70)	5 (71.4)	3 (30)	2 (22.)	5 (50)	2 (66.)	6 (60)	0 (0)	4 (40)	1 (10)	4 (40)	7 (70)	3 (30)	NA	NA	8 (80)	0 (0)	NA	6 (66.7)
	2015 (15)	6 (40)	6 (40)	5 (33.3)	5 (33.3)	6 (40)	4 (30.8)	3 (20)	4 (30.8)	5 (37.7)	3 (20)	4 (28.6)	3 (20)	6 (40)	6 (40)	5 (33.3)	NA	NA	6 (42.9)	1 (7.1)	NA	3 (37.5)
	2016 (77)	15 (19.5)	36 (61)	57 (79.2)	62 (81.6)	NA	18 (23.3)	61 (82.4)	6 (15.8)	6 (15.8)	42 (55)	6 (8)	58 (77.3)	27 (35)	10 (16.7)	13 (28.3)	54 (80.6)	60 (89.6)	72 (93)	1 (2)	50 (100)	NA
	2017 (113)	16 (14.2)	68 (72.3)	87 (77)	82 (72.6)	18 (26.9)	5 (10.4)	94 (83.2)	12 (16)	12 (16)	62 (54.9)	7 (6.2)	77 (68.8)	27 (24)	20 (18)	37 (33)	39 (84.8)	48 (96)	99 (88)	1 (1)	25 (100)	NA
<i>Escherichia coli</i>	2012 (83)	7 (8.4)	44 (53.7)	48 (60.8)	50 (63.3)	11 (13.4)	2 (7.1)	59 (74.7)	15 (33.3)	31 (37.8)	4 (4.9)	45 (54.9)	11 (13.8)	13 (20)	43 (52.4)	16 (19.5)	NA	NA	53 (64)	1 (0.9)	75 (100)	52 (65)
	2013 (70)	15 (21.4)	51 (75)	41 (58)	28 (65.1)	28 (41.8)	5 (7)	57 (81.4)	23 (48.9)	26 (37)	3 (4)	52 (77.6)	9 (12.9)	16 (27.6)	26 (75.4)	26 (75.4)	NA	NA	39 (56)	0 (0)	NA	47 (69.1)
	2014 (34)	86 (67.7)	28 (21.7)	67 (50)	103 (82.4)	53 (41.7)	8 (6)	107 (82.3)	61 (70.9)	47 (35)	5 (3.8)	96 (75.6)	16 (12)	30 (23.3)	112 (87.5)	46 (35.9)	NA	NA	69 (52)	0 (0)	NA	65 (60.8)
	2015 (47)	42 (89.3)	NA	42 (89.1)	40 (88.9)	NA	26 (72.2)	42 (91.3)	14 (70)	42 (91.3)	33 (69.6)	42 (89)	33 (75)	32 (88.9)	35 (97.2)	20 (80)	21 (56.8)	IR	31 (96.9)	7 (26.9)	42 (100)	NA
	2016 (33)	24 (72.7)	5 (23.8)	26 (79)	18 (54.6)	6 (28.6)	8 (32)	18 (56.3)	9 (39.1)	12 (37.5)	15 (46)	25 (76)	16 (51.6)	14 (42.4)	26 (78.8)	13 (40.6)	3 (30)	IR	27 (81.8)	6 (21.4)	10 (100)	NA
	2017 (26)	13 (50)	18 (69.2)	20 (76)	16 (61.5)	13 (50)	6 (46.2)	12 (46.2)	5 (33.3)	14 (53.9)	11 (42)	16 (61.6)	12 (46.2)	11 (55)	15 (57.7)	14 (53.9)	NA	IR	17 (65.4)	4 (18.2)	52 (100)	13 (54.2)
<i>Klebsiella pneumoniae</i>	2012 (13)	7 (53.9)	8 (61.5)	9 (67)	4 (66.7)	8 (61.5)	4 (57.1)	9 (69.2)	4 (44.4)	9 (69.2)	4 (30.8)	6 (46.1)	5 (38.5)	6 (60)	11 (84.6)	8 (66.7)	NA	IR	9 (75)	1 (8.3)	NA	6 (50)
	2013 (25)	25 (53.2)	29 (61.7)	31 (65.4)	38 (82.6)	36 (76.6)	25 (69.4)	39 (83)	80 (75)	39 (83)	14 (30)	19 (40)	32 (68.1)	37 (78.7)	41 (72.1)	31 (72.1)	NA	IR	42 (91.3)	3 (7)	NA	26 (63.4)
	2014 (47)	42 (89.3)	NA	42 (89.1)	40 (88.9)	NA	26 (72.2)	42 (91.3)	14 (70)	42 (91.3)	33 (69.6)	42 (89)	33 (75)	32 (88.9)	35 (97.2)	20 (80)	21 (56.8)	IR	31 (96.9)	7 (26.9)	42 (100)	NA

(continued)

Table 4 (continued)

Organism name	Year	AMK, N (%)	CEFEP, N (%)	CEFEPTAZ, N (%)	CEFOSUL, N (%)	CEFOT, N (%)	CEFOX, N (%)	CEFTAZ, N (%)	CEFTRX, N (%)	CEFTRXSUL, N (%)	CHL, N (%)	CIPRO, N (%)	ERTA, N (%)	GENTA, N (%)	IMI, N (%)	LEVO, N (%)	MERO, N (%)	NETIL, N (%)	PIP, N (%)	PIPTAZ, N (%)	TETRA, N (%)	TIC, N (%)	TICLAV, N (%)	TIG, N (%)	TOBRA, N (%)	TMZ, N (%)
<i>Morganella</i> spp.	2012 (4)	1 (25)	3 (100)	2 (50)	2 (50)	2 (50)	2 (50)	2 (50)	2 (50)	1 (33.3)	2 (50)	2 (50)	2 (50)	2 (50)	2 (50)	2 (50)	2 (50)	1 (25)	2 (50)	1 (25)	2 (66.7)	3 (75)	2 (66.7)	IR	1 (100)	NA
	2013 (3)	1 (33.3)	3 (100)	2 (66.7)	1 (33.3)	1 (33.3)	1 (33.3)	1 (33.3)	1 (33.3)	0 (0)	1 (50)	3 (100)	NA	1 (33.3)	1 (33.3)	2 (66.7)	2 (66.7)	0 (0)	2 (66.7)	1 (33.3)	1 (100)	1 (100)	2 (66.7)	IR	1 (100)	NA
	2014 (5)	0 (0)	1 (100)	2 (40)	2 (40)	2 (40)	2 (40)	2 (40)	2 (40)	0 (0)	0 (0)	2 (40)	1 (100)	2 (40)	0 (0)	2 (40)	1 (20)	0 (0)	0 (0)	0 (0)	NA	NA	2 (40)	IR	NA	2 (50)
	2015 (3)	2 (66.7)	2 (100)	2 (66.7)	2 (66.7)	1 (50)	2 (100)	NA	2 (66.7)	1 (50)	0 (0)	2 (66.7)	3 (100)	3 (100)	1 (33.3)	2 (66.7)	1 (33.3)	2 (100)	2 (66.7)	2 (66.7)	NA	NA	2 (66.7)	IR	NA	3 (100)
	2016 (3)	2 (66.7)	1 (100)	3 (100)	3 (100)	3 (100)	3 (100)	3 (100)	3 (100)	3 (100)	1 (50)	3 (100)	NA	3 (100)	3 (100)	3 (100)	3 (100)	3 (100)	3 (100)	2 (66.7)	2 (66.7)	NA	3 (100)	IR	NA	1 (100)
<i>Proteus</i> spp.	2012 (22)	10 (45.5)	6 (31.6)	13 (59.1)	13 (61.9)	13 (61.9)	13 (61.9)	13 (61.9)	13 (61.9)	NA	12 (66.7)	NA	0 (0)	8 (36.4)	3 (13.6)	11 (50)	6 (28.6)	11 (61.1)	6 (31.6)	2 (12.5)	6 (46.2)	5 (52.9)	11 (61.1)	IR	12 (100)	NA
	2013 (20)	4 (20)	3 (15)	13 (65)	11 (55)	11 (55)	11 (55)	11 (55)	11 (55)	0 (0)	10 (52.6)	NA	NA	9 (45)	0 (0)	12 (60)	5 (26.3)	14 (70)	3 (15.8)	1 (5.6)	5 (83.3)	9 (52.9)	IR	12 (100)	NA	
	2014 (11)	3 (45.5)	5 (45.5)	7 (63.6)	7 (63.6)	7 (63.6)	7 (63.6)	7 (63.6)	7 (63.6)	0 (0)	2 (28.6)	6 (54.55)	0 (0)	5 (45.5)	3 (27.3)	3 (27.3)	3 (27.3)	7 (63.6)	2 (18.2)	0 (0)	IR	2 (18.2)	IR	24 (100)	8 (80)	
	2015 (11)	4 (50)	4 (57.1)	6 (54.6)	2 (66.7)	2 (66.7)	2 (66.7)	2 (66.7)	2 (66.7)	0 (0)	6 (66.7)	4 (54.55)	NA	6 (54.6)	0 (0)	4 (40)	0 (0)	4 (57.1)	0 (0)	0 (0)	IR	1 (10)	IR	NA	7 (63.6)	
	2016 (9)	7 (77.8)	4 (66.7)	7 (77.8)	5 (71.4)	5 (71.4)	5 (71.4)	5 (71.4)	5 (71.4)	1 (11.1)	7 (87.5)	5 (50)	NA	6 (85.7)	3 (42.9)	7 (87.5)	1 (12.5)	7 (77.8)	3 (33.3)	1 (12.5)	IR	1 (11.1)	IR	NA	5 (83.3)	
	2017 (3)	1 (33.3)	1 (100)	1 (33.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	NA	NA	2 (66.7)	NA	1 (33.3)	1 (33.3)	0 (0)	1 (50)	1 (50)	0 (0)	0 (0)	IR	1 (33.3)	IR	1 (100)	NA	
<i>Providencia</i> spp.	2012 (3)	3 (60)	2 (100)	4 (80)	4 (80)	4 (80)	4 (80)	4 (80)	4 (80)	0 (0)	0 (0)	4 (80)	0 (0)	4 (80)	1 (20)	4 (80)	4 (80)	3 (60)	3 (60)	1 (20)	IR	3 (60)	IR	3 (100)	NA	
	2013 (5)	1 (50)	2 (100)	1 (50)	1 (50)	1 (50)	1 (50)	1 (50)	1 (50)	0 (0)	0 (0)	1 (50)	NA	1 (50)	0 (0)	1 (50)	0 (0)	1 (50)	1 (50)	1 (50)	IR	1 (50)	IR	4 (100)	1 (50)	
	2014 (2)	0 (0)	NA	0 (0)	NA	NA	NA	NA	NA	0 (0)	NA	1 (100)	NA	0 (0)	NA	1 (100)	0 (0)	NA	0 (0)	0 (0)	IR	0 (0)	IR	NA	0 (0)	
	2015 (1)	0 (0)	NA	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	NA	1 (100)	NA	0 (0)	NA	1 (100)	0 (0)	NA	0 (0)	0 (0)	IR	0 (0)	IR	NA	0 (0)	
	2016 (0)	0 (0)	NA	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (100)	NA	2 (100)	0 (0)	2 (100)	0 (0)	0 (0)	0 (0)	0 (0)	IR	0 (0)	IR	NA	0 (0)	
	2017 (2)	0 (0)	1 (20)	1 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (100)	NA	2 (100)	0 (0)	2 (100)	0 (0)	0 (0)	0 (0)	0 (0)	IR	0 (0)	IR	NA	0 (0)	
<i>Salmonella</i> spp.	2012 (16)	6 (42.9)	2 (18.2)	1 (7.1)	1 (7.1)	1 (7.1)	1 (7.1)	1 (7.1)	1 (7.1)	1 (0)	3 (21.4)	1 (50)	3 (25)	1 (7.1)	1 (7.1)	1 (7.1)	1 (7.1)	2 (20)	3 (27.3)	1 (10)	0 (0)	3 (37.5)	1 (7.7)	NA	NA	
	2013 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (50)	0 (0)	0 (0)	0 (0)	1 (50)	0 (0)	NA	NA	
	2014 (5)	0 (0)	1 (33.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)	0 (0)	NA	1 (20)	0 (0)	NA	1 (20)	
	2015 (4)	1 (25)	NA	2 (50)	2 (66.7)	2 (66.7)	2 (66.7)	2 (66.7)	2 (66.7)	0 (0)	0 (0)	2 (50)	NA	3 (75)	0 (0)	0 (0)	0 (0)	0 (0)	2 (50)	2 (50)	NA	2 (50)	0 (0)	NA	0 (0)	
	2016 (11)	0 (0)	1 (9.1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0)	2 (18.2)	NA	3 (33.3)	0 (0)	1 (9.1)	0 (0)	0 (0)	2 (18.2)	0 (0)	NA	1 (10)	0 (0)	NA	2 (20)	

(continued)

Table 4 (continued)

Organism name	Year	AMK, N (%)	CEEP, N (%)	CEFEPTAZ, N (%)	CEFOSUL, N (%)	CEFOT, N (%)	CEFOX, N (%)	CEFTAZ, N (%)	CEFTRX, N (%)	CEFRXSUL, N (%)	CHL, N (%)	CIPRO, N (%)	ERTA, N (%)	GENTA, N (%)	IMI, N (%)	LEVO, N (%)	MERO, N (%)	NETIL, N (%)	PIP, N (%)	PIPTAZ, N (%)	TETRA, N (%)	TIC, N (%)	TICLAV, N (%)	TIG, N (%)	TOBRA, N (%)	TMZ, N (%)
<i>Serratia</i> spp.	2012 (2)	1 (50)	1 (50)	NA	1 (50)	NA	IR	1 (50)	1 (50)	NA	0 (0)	1 (50)	NA	0 (0)	0 (0)	0 (0)	0 (0)	1 (50)	1 (50)	NA	1 (100)	NA	1 (50)	0 (0)	1 (100)	NA
	2013 (1)	0 (0)	0 (0)	NA	0 (0)	NA	IR	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	NA	NA	0 (0)	0 (0)	1 (100)	NA	
	2014 (16)	0 (0)	0 (0)	NA	0 (0)	0 (0)	IR	0 (0)	1 (6.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6.3)	NA	NA	1 (6.3)	0 (0)	NA	NA	
	2015 (0)	1 (100)	1 (100)	NA	NA	NA	IR	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	
	2016 (1)	2 (10)	2 (10)	NA	0 (0)	NA	IR	1 (100)	1 (100)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	NA	0 (0)	1 (100)	1 (100)	NA	NA	1 (100)	0 (0)	NA	NA	

Abbreviations: AMK, amikacin; CEEF, cefepime; CEFEPTAZ, cefepime-tazobactam; CEFOSUL, cefoperazone-sulbactam; CEFOT, cefotaxime; CEFOX, cefoxitin; CEFTAZ, ceftazidime; CEFRXSUL, ceftriaxone-sulbactam; CHL, chloramphenicol; CIPRO, ciprofloxacin; ERTA, ertapenem; GENTA, gentamicin; IMI, imipenem; IR, intrinsic resistance; LEVO, levofloxacin; MERO, meropenem; NA, not applicable; NETIL, netilmicin; PIP, piperacillin; PIPTAZ, piperacillin-tazobactam; TETRA, tetracycline; TIC, tigecycline; OPD, outpatient department; TOBRA, tobramycin; TMZ, Trimethoprim/sulfamethoxazole.
 Note: N denotes the number of isolates.

even when they are producing either ESBLs or Amp C. It was found that meropenem showed $\geq 97.3\%$ sensitivity among *Enterobacteriaceae* isolates while imipenem showed 87.5% sensitivity, showing that meropenem is 4 to 16 times more active than imipenem against *Enterobacteriaceae*.^{17,18} In contrast, we found imipenem more effective than meropenem in all settings. Among aminoglycosides group of antimicrobial agents, less resistance was shown against amikacin than gentamycin; similar results were observed in other published studies.^{19,20} The least resistant was observed against tigecycline (1–15%) among all isolates in all settings. A similar result was found in another study where tigecycline was active against multidrug-resistant *E. coli* and *Klebsiella* spp. isolates.^{21,22}

From 5-year resistance pattern of antimicrobials (►Tables 2-4), we found that *Enterobacteriaceae* isolates showed increased sensitivity against some antimicrobials in all settings. In ICU settings, both *E. coli* and *Klebsiella* spp. isolates showed significant increased sensitivity percentage against β -lactamase inhibitors and carbapenem. *Klebsiella* spp. isolates also showed increased sensitivity against quinolones and aminoglycosides (gentamycin). These results suggest the substantial use of these antibiotics against these pathogens. In wards and OPDs, increased sensitivity was observed across the study period; both pathogens showed increased sensitivity against carbapenems (meropenem, imipenem) and aminoglycosides (gentamycin). *Klebsiella* spp. isolates also showed increased sensitivity against piperacillin-tazobactam, ciprofloxacin, and tigecycline in wards settings. In OPD patients, increased sensitivity against ceftazidime and cefepime was also observed in both pathogens, showing primitive antibiotics like ceftazidime and cefepime can be used as choice of antibiotic against these pathogens in OPD patients, although it is administered intravenously.

Among different classes of antimicrobials, tigecycline proved most effective in all settings. Tigecycline is a potent therapeutic option for multidrug resistance enterobacterial infections. Although tigecycline resistance has been observed, it is still active among *Enterobacteriaceae*. However, increased resistance was observed than other studies which is $< 10\%$.²³⁻²⁶

This study is among the very few studies done in the Indian setting. The large sample size of this study makes its results more reliable. Isolates of *Enterobacteriaceae* included in this study were collected from multiple sources in terms of location of the patients and types of samples. Therefore, the findings can be generalized to a variety of location of patients and samples. However, all the samples were collected from the apex trauma center of a tertiary care center. This limits the generalizability of the study in terms of study settings. The burden, profile, and AST of *Enterobacteriaceae* bacteria isolated from a secondary or primary care setting or from community settings are expected to be different from this study. Hence the interpretation with reference to study setting should be cautiously done.

No intermediate isolate was reported in the study results. This study includes the results based on automated system

(Vitek2 compact system). These need to be validated by molecular methods or by sequencing.

Conclusion

Emergences of multiple drug resistance among bacteria are occurring at an alarming rate worldwide. This crisis is due to the inappropriate and overuse of existing antibiotics and lack of development of new antibiotics.^{27,28} Tigecycline proved to be an effective agent against *Enterobacteriaceae*. Use of tigecycline needs to be strictly monitored to prevent development and dissemination of resistance against it. In addition to curtailing the antibiotic misuse and abuse, it becomes even more important to avoid the emergence of antibiotic resistance by taking measures like strict implementation of infection control guidelines, proper hand hygiene, and antimicrobial stewardship programs that include optimal selection, dose, and duration of treatment.

Ethical Approval

Since this is a retrospective study and the data obtained was from routine laboratory work, this study was exempted from the attainment of ethical approval.

Authors' Contributions

All authors contributed to the conceptualization and implementation of the study. All authors contributed to analyzing the data, writing and reviewing of the manuscript.

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None.

Conflict of Interest

None declared.

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