Burden of MDR ESKAPE pathogens in a Tertiary Care Hospital, Nepal

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ABSTRACT

INTRODUCTION

The acronym ESKAPE is used to describe six nosocomial pathogens that exhibit virulence and multidrug resistance, which includes: *Staphylococcus aureus, Klebsiella pneumoniae, Enterococcus faecium, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter spp.*

Among MDR pathogens, ESKAPE pathogens have caused a major concern due to their resistance against antibiotics and other medicine resulting in worse patient outcomes and increased treatment costs.

MATERIAL AND METHODS

A retrospective cross-sectional study was conducted at microbiology laboratory of a tertiary care hospital, Nepal. A total of 6583 samples were processed following standard microbiological procedures. Standard microbiological techniques were used for isolation and identification of pathogens and antibiotic susceptibility test was performed as per clinical and laboratory standard institute (CLSI) guidelines. Phenotypic detection of multidrug resistance (MDR), methicillin resistant *Staphylococcus aureus* (MRSA), and vancomycin resistant *Enterococcus faecium* (VRE) was performed.

RESULTS

During the period, a total of 1583 (24.05%) ESKAPE pathogens were identified. Amongst gram negative ESKAPE pathogens, multidrug resistant (MDR) were more predominant in *Acinetobacter baumannii* (67.70%) followed by *Klebsiella pneumoniae* (65.59%), *Enterobacter species* (49.36%), *Pseudomonas aeruginosa* (46.78%). Similarly, in gram positive ESKAPE pathogens, MDR was found to be *Staphylococcus aureus* (65.35%), and *Enterococcus faecium* (69.23%). MRSA was found to be 42.51% (n=54) and VRE 3.08% (n=2).

CONCLUSION

Due to increasing burden of MDR ESKAPE pathogens in hospital settings, periodic surveillance of resistant bacteria in hospital settings is strongly recommended to minimize the problem by formulating the antibiotic policy and antibiotic stewardship program.

KEYWORDS

MDR, ESKAPE pathogens, Gram negative

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INTRODUCTION

Antibiotic resistance has a direct impact on human health and behavior. Pathogenic microorganisms showing multidrug resistant (MDR) and extensively drug-resistant microorganisms (XDR) resistance to various antimicrobial agents is continuously rising and are often described as a cause of infections with pan-resistant microorganisms also being reported as a cause of severe hospital-acquired infections.[1] Among MDR pathogens, ESKAPE *(Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacterbaumannii, Pseudomonas aeruginosa, Enterobacter species)* pathogens have caused a major concern due to their adeptness at 'escaping' the effects of antimicrobial treatments and the efficient utilization of the commonly observed resistance mechanisms.[2]

Multidrug resistant (MDR) in ESKAPE strains and isolates, which are not resistant to (at least) one representative of each of three categories of antimicrobial compound families; similarly, extreme drug-resistant, (XDR), which are resistant to (at least) one representative of all but very few categories of antimicrobial compound families; and pan-drug resistant (PDR) ones, which are resistant to any of the tested representatives of all known antimicrobial compound families.[3]

The enzyme beta-lactamase produced by the organisms hydrolyze β-lactam ring of antibiotics, which mediate resistance and making the drug in treatment impotent. It is classified into two categories, i.e. Ambler molecular classification scheme and Bush-Jacoby-Medieros functional classification system.[4] Ambler classification scheme divides beta lactamase into four major classes (class A-D), where A, C and D are serine β-lactamase and class B enzyme is MBL. Ambler class B enzyme is characterized by its ability to hydrolyze carbapenems and its resistance to all available beta-lactam but is inhibited in presence of metal chelators.[5]

Extended-spectrum beta-lactamases (ESBLs) are the group of beta-lactamase enzymes, that hydrolyze and cause resistance to the oxyimino-cephalosporins (cefotaxime, ceftazidime, ceftriaxone, cefuroxime and cefepime) and monobactams (aztreonam), but not the cephamycins (cefoxitin and cefotetan) or carbapenems (imipenem, meropenem, and ertapenem), produced by *Escherichia coli and Klebsiella pneumoniae.*[6]

The most common variant of ESBL is CTX-1 type 10. A variety of carbapenemases has been described belonging to three classes of β-lactamase, the Ambler class A, C and D. This has brought urgent threat in utility of carbapenem in clinical laboratory, which is the major drug used for treatment of serious infections caused by ESBL- producing organisms (particularly, Gram-negative members of ESKAPE pathogens).[7]

The gram-negative ESKAPE organisms, *Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa,* and *Enterobacter* species, constitute an even more worrisome clinical challenge because of their trends in acquiring rapid resistance to the currently available antibiotics. The major underlying resistance mechanisms are antibiotic alteration, bacterial target site modification, decreased intracellular antibiotic accumulation, and biofilm formation.[8]

There are nine vancomycin resistance genes including van A, B, C, D, E, G, L, M, and van N in *Enterococci.* Van A is the most common type worldwide mainly related to vancomycin resistant *Enterococcus faecium,* allowing a great rate of vancomycin and teicoplanin resistance and Van B causes a high degree of vancomycin resistance, yet susceptible to other glycopeptides such as teicoplanin.[9]

Nearly, 25 - 30% of skin or noses of healthy people are colonized by *Staphylococcus aureus.* Methicillin-resistant *Staphylococcus aureus* (MRSA) is resistant to certain antibiotics, such as methicillin, dicloxacillin, oxacillin, cloxacillin, nafcillin, and closely related class of drugs, such as cephalosporins. The possible predisposing factors of MRSA emergence are: consumption of antibiotics without medical prescription, lack of awareness, receipt of antibiotics before coming to the hospital, long duration of hospitalization.[9]

MATERIAL AND METHODS

A retrospective cross-sectional study was conducted at microbiology laboratory of a tertiary care hospital, Nepal. The total of 6583 samples (urine, sputum, swab, blood, pus, endotracheal aspirates, fluid, BAL, biopsy, bile, semen, CVP tip, catheter tip, drain tip, foley's tip, suction tip, CSF) were received from various outpatients and inpatient department. Samples were processed at microbiology laboratory following standard microbiological procedures. Standard microbiological techniques were used for isolation and identification of pathogens. An antibiotic susceptibility test was performed according to the recommended modified Kirby-Bauer disc diffusion method. The diameter of the zone of inhibition in mm was measured and interpreted as sensitive, intermediate, and resistant as per CLSI guidelines 2020.[10] The antibiotics with potency used were as follows: amikacin (30mcg), gentamycin (10 mcg), ciprofloxacin (5 mcg), ceftriaxone (30 mcg), cefotaxime (30 mcg), chloramphenicol (30 mcg), co-trimoxazole (25 mcg), cefixime (5 mcg), cefepime (30 mcg), nitrofurantoin (300 mcg), norfloxacin (10 mcg), nalidixic acid (30 mcg), ofloxacin (5 mcg), meropenem (10 mcg), imipenem (10 mcg), colistin (10 mcg), polymyxin B (100 IU), tigecycline (15 mcg).

RESULTS

Demographic profile of the study population

During the study period, a total of 6583 patients were included into current study. The prevalence of ESKAPE pathogens isolated on the basis of gender distribution was 862 (54.45%) from females and 721 (45.54%) from males. The maximum number of patients infected were of the age group 71-80 years (15.67%) followed by 31-40 years of age (14.91%). On the basis of patient type, the isolation rate of ESKAPE pathogens from in-patients was 67.90% and 32.10% from out-patients (table 1).

Table 1. Prevalence of ESKAPE pathogens according to demographic characteristics (n=1583)

Total isolates (n) =1583 (100%)	
Sex-wise	
Male	721 (45.55%)
Female	862 (54.45%)
Patient type	
Inpatient	1075 (67.90%)
Outpatient	508 (32.10%)
Age interval (in years)	
1-10	99 (6.25%)
11-20	51 (3.22%)
21-30	209 (13.20%)
31-40	236 (14.91%)
41-50	161 (10.17%)
51-60	207 (13.08%)
61-70	234 (14.78%)
71-80	248 (15.67%)
>80	138 (8.72%)

Distribution of ESKAPE pathogens in various clinical specimens

Overall, 1583 ESKAPE pathogens were isolated from various clinical specimens. The distribution of ESKAPE pathogens among various clinical specimens is shown in (table 2), with the most prevalent from urine specimens followed by those in sputum, swab, blood, pus, ETA, fluid, BAL, and biopsy.

Analysis of culture positivity of clinical specimens

Out of 6583 clinical specimens processed,1583 (24.05%) ESKAPE pathogens were recovered. The most predominant isolate was *Klebsiella pneumoniae* (n=808, 51.04%) followed by *Pseudomonas aeruginosa* (n=233, 14.72%), Acinetobacter baumannii (n=192, 12.13%), Enterobacter species (n= 158, 9.98%), *Staphylococcus aureus* (n= 127, 8.02%), and *Enterococcus faecium* (n= 65 ,4.11%) (table 2).

Table 2. Distribution of ESKAPE pathogens in various clinical specimens

Sample	E. faecium n (%)	S. aureus n (%)	K. pneumoniae n (%)	A. baumannii n (%)	P. aeruginosa n (%)	Enterobacter species n (%)	Total n (%)
Urine	53	47	422	69	93	73	757 (47.82%)
Sputum	2	12	208	52	77	37	388 (24.51%)
Swab	5	22	39	8	12	11	97 (6.13%)
Blood	3	16	34	14	8	9	84 (5.31%)
Pus	0	19	28	8	16	13	84 (5.31%)
ETA	1	1	42	24	9	1	78 (4.93%)
Fluid	1	4	12	4	5	3	29 (1.83%)
BAL	0	2	10	8	7	1	28 (1.77%)
Biopsy	0	0	4	1	1	2	8 (0.5%)
Bile	0	0	3	2	2	0	7 (0.44%)
Semen	0	4	0	0	1	2	7 (0.44%)
CVC Tip	0	0	2	0	1	3	6 (0.38%)
Catheter Tip	0	0	4	0	0	1	5 (0.32%)
Drain Tip	0	0	0	0	0	2	2 (0.13%)
Foleys Tip	0	0	0	1	0	0	1 (0.06%)
Suction Tip	0	0	0	1	0	0	1 (0.06%)
CSF	0	0	0	0	1	0	1 (0.06%)
Total	65 (4.11%)	127 (8.02%)	808 (51.04%)	192 (12.13%)	233 (14.72%)	158 (9.98%)	1583 (100%)

Abbreviations: *E. faecium, Enterococcus faecium; S. aureus, Staphylococcus aureus; K. pneumoniae, Klebsiellapneumoniae; A. baumannii, Acinetobacterbaumannii; P. aeruginosa, Pseudomonas aeruginosa; ETA, endotracheal aspirate; BAL, bronchoalveolar lavage; CVC, central venous catheter; CSF, cerebrospinal fluid*

Antibiotic resistance pattern of ESKPE pathogens

In the present study, higher level of antimicrobial resistance to most of the antibiotics determined. The ESKAPE group of pathogens showed highest susceptibility to last- resort antimicrobial agents.

A. Antibiotic resistance pattern of *Klebsiella pneumoniae and Enterobacter species*

Regarding Enterobacteriaceae, *Klebsiella pneumoniae* showed higher resistance towards cephalosporins like cefixime (72.77 %), ceftazidime (66.58 %), and ceftriaxone

(65.59 %). Similar resistance rate towards cephalosporins was seen in *Enterobacter* species. However, higher sensitivity was observed to amikacin (61 % to 77 %). Unfortunately, both *Klebsiella pneumoniae* and *Enterobacter* species had significantly increased resistance rate of carbapenems (imipenem, meropenem) and nitrofurantoin (used in urinary isolates).

Furthermore, notable increased alarming resistance was found to colistin, polymyxin B, and tigecycline in both *Klebsiella pneumoniae* and *Enterobacter* species (table 3).

B. Antibiotic resistance pattern of *Acinetobacter baumannii*
Higher resistance was seen to cephalosporins- cefixime (61.25 %), ceftazidime (60.42 %), and ceftriaxone (57.29%) and carbapenems (imipenem (58.33%), and meropenem (55.73%). However, significantly decreased resistance was found in aminoglycosides (amikacin (25 %, and gentamycin (28.65 %).

In addition, increasing trends of resistance to tigecycline, colistin, polymyxin B, and piperacillin-tazobactam have been identified (table 3).

C. Antibiotic resistance pattern of *Pseudomonas aeruginosa*
In contrast to *Klebsiella pneumoniae and Acinetobacter baumannii,* carbapenem (imipenem (35.62 %), meropenem (36.05 %) and nitrofurantoin (33.48) %) resistant was slightly decreased. Although, similar pattern of resistance to aminoglycosides, cephalosporins and piperacillin- tazobactam have been observed.

Tobramycin (82.40%) and aztreonam (62.66%) were shown to be effective against *Pseudomonas* isolates. The resistance pattern of colistin (4.29 %) and polymyxin B (4.72%) was slightly acceptable in contrast to *Klebsiella pneumoniae, Enterobacter species, and Acinetobacter baumannii* (table 3).

Table 3. Antibiotic resistance pattern of gram-negative isolates of ESKAPE Pathogens

Antibiotic Category	Antibiotics	*K. pneumoniae(n=808)*		*A. baumannii(n=192)*		*P. aeruginosa(n=233)*		*Enterobacter species (n=158)*	
		Sensitive n (%)	Resistant n (%)	Sensitive n (%)	Resistant n (%)	Sensitive n (%)	Resistant n (%)	Sensitive n (%)	Resistant n (%)
Aminoglycoside	AK	493 (61.01)	315 (38.99)	144 (75.00)	48 (25.00)	147 (63.09)	86 (36.91)	123 (77.85)	35 (22.15)
	G	384 (47.52)	424 (52.48)	137 (71.35)	55 (28.65)	116 (49.79)	117 (50.21)	93 (58.86)	65 (41.14)
	TOB**					192 (82.40)	41 (17.60)		
Penicillin + β- lactamase inhibitors	AMC	356 (44.06)	452 (55.94)	152(70.17)	40 (20.83)	48 (20.60)	185 (79.40)	65 (41.14)	93 (58.86)
3rd generation cephalosporins	CFM	220 (27.23)	588 (72.77)	36 (18.75)	156 (61.25)	84 (36.05)	149 (63.95)	47 (29.75)	111 (70.25)
	CAZ	270 (33.42)	538 (66.58)	76 (39.58)	116 (60.42)	115 (49.36)	118 (50.64)	38 (24.05)	120 (75.95)
	CTR	278 (34.41)	530 (65.59)	82 (42.71)	110 (57.29)	114 (48.93)	119 (51.07)	53 (33.54)	105 (66.46)
3rd generation cephalosporins + β-lactamase inhibitors	CFS	379 (46.91)	429 (53.09)	122 (63.54)	70 (36.46)	156 (66.95)	77 (33.05)	87 (55.06)	71 (44.94)
Folate pathway inhibitors	COT	319 (39.49)	489 (60.51)	93 (48.44)	99 (51.56)	96 (41.20)	137 (58.80)	99 (62.66)	59 (37.34)
Fluroquinolones	CIP	304 (37.62)	504 (62.38)	110 (57.29)	82 (42.71)	131 (56.22)	102 (43.78)	90 (56.96)	68 (43.04)
	NX *	403 (49.88)	405 (50.12)	62 (32.29)	130 (67.71)	105 (45.06)	128 (54.94)	99 (62.66)	59 (37.34)
	OF *	405 (50.12)	403 (49.88)	67 (34.89)	125 (65.11)	94 (40.34)	139 (59.66)	85 (53.79)	73 (46.21)
Polymyxins	CL	708 (87.62)	100 (12.38)	172 (89.59)	20 (10.41)	223 (95.71)	10 (4.29)	153 (96.84)	5 (3.16)
	PB	700 (86.63)	108 (13.37)	170 (88.54)	22 (11.46)	222 (95.28)	11 (4.72)	150 (94.94)	8 (5.06)
Carbapenems	IPM	348 (43.07)	460 (56.93)	80 (41.67)	112 (58.33)	150 (64.38)	83 (35.62)	105 (66.46)	53 (33.54)
	MRP	408 (50.49)	400 (49.51)	85 (44.27)	107 (55.73)	149 (63.95)	84 (36.05)	108 (68.36)	50 (31.64)
Nitrofurans	NIT *	341 (42.20)	467 (57.80)	67 (34.89)	125 (65.11)	155 (66.52)	78 (33.48)	89 (56.33)	69 (43.67)
Glycylcyclines	TGC	632 (78.22)	176 (21.78)	170 (88.54)	22 (11.46)	-	-	150 (94.94)	8 (5.06)
Monobactams	AZT **					146 (62.66)	87 (37.34)		
Extended spectrum penicillin + β-lactamase inhibitors	PIT	393 (48.64)	415 (51.36)	138 (71.88)	54 (28.12)	174 (74.68)	59 (25.32)	109 (68.98)	49 (31.02)

*Used in urinary isolates
**Used in *P. aeruginosa*

Abbreviations: AK, amikacin; G, gentamycin; TOB, tobramycin; AMC, amoxycillin-clavulanic acid; CFM, cefixime; CAZ, ceftazidime; CTR, ceftriaxone; CFS, cefoperazone-sulbactam; COT, cotrimoxazole; CIP, ciprofloxacin; NX, norfloxacin; OF, ofloxacin; CL, colistin; PB, polymyxin B; IPM, imipenem; MRP, meropenem; NIT, nitrofurantoin; TGC, tigecycline; AZT, aztreonam; PIT, piperacillin-tazobactam

D. Result of MDR, MRSA, and VRE isolates
In the present study, resistance to ≥ three antimicrobial agents (MDR) were found in 60.89 % of gram-negative ESKAPE isolates (n=1391). Multidrug resistant (MDR) were more predominant in *Acinetobacter baumannii* (67.70%) followed by *Klebsiella pneumoniae* (65.59%), *Enterobacter species* (49.36%), *Pseudomonas aeruginosa* (46.78%). Similarly, in gram positive ESKAPE pathogens, MDR *Staphylococcus aureus* was found to be (65.35%), and *Enterococcus faecium* (69.23%). In the present study,

methicillin-resistant *Staphylococcus aureus* (MRSA) was found to be 42.51% (n=54) and *vancomycin resistant Enterococcus faecium* (VRE) 3.08% (n=2).

E. Resistance pattern of *Staphylococcus aureus and Enterococcus faecium*

Table 4 shows the antibiotic resistance pattern of Gram-positive ESKAPE pathogens; *Staphylococcus* showed significant resistance to ampicillin (77.17%), azithromycin (86.61%), clindamycin (77.95%), erythromycin (77.95%), and penicillin G (94.49%). However; linezolid, teicoplanin, vancomycin, doxycycline, cloxacillin were found to be more susceptible.

Similarly, *Enterococcus faecium* achieved remarkable resistance pattern to azithromycin (86.15%), clindamycin (83.08%), erythromycin (83.08%), and penicillin G (93.85%). The sensitivity towards vancomycin (3.08%), teicoplanin (26.15%), linezolid (3.08%), cloxacillin (38.46%), and ampicillin (33.85%) were identified.

Nitrofurantoin was found to be effective against (25.20% to 29.24%) of urinary isolates in both gram-positive ESKAPE pathogens.

Table 4. Antibiotic resistance pattern of gram-positive isolates of ESKAPE pathogens

Antibiotic category	Antibiotics	*S. aureus (n=127)*		*E. faecium (n=65)*	
		Sensitive n (%)	Resistant n (%)	Sensitive n (%)	Resistant n (%)
β-lactam antibiotics-aminopenicillin	AMP	29 (22.83)	98 (77.17)	43 (66.15)	22 (33.85)
Macrolides	AZM	17 (13.39)	110 (86.61)	9 (13.85)	56 (86.15)
	E	28 (22.05)	99 (77.95)	11 (16.92)	54 (83.08)
Lincosamide	CD	28 (22.05)	99 (77.95)	11 (16.92)	54 (83.08)
β-lactam antibiotics-penicillin	COX	92 (72.44)	35 (27.56)	40 (61.64)	25 (38.46)
Folate pathway inhibitors	COT	75 (59.06)	52 (40.94)	12 (18.46)	53 (81.54)
Tetracyclines	DOX	117 (92.13)	10 (7.87)	37 (56.92)	28 (43.08)
	TE	98 (77.16)	29 (22.84)	26 (40.00)	39 (60.00)
Oxazolidinones	LZ	124 (97.63)	3 (2.37)	63 (96.92)	2 (3.08)
Nitrofurans	NIT *	95 (74.80)	32 (25.20)	46 (70.76)	19 (29.24)
Fluroquinolones	NX *	76 (59.84)	51 (40.16)	36 (55.38)	29 (44.62)
	OF *	58 (45.67)	69 (54.33)	23 (35.38)	42 (64.62)
Benzylpenicillin	P	7 (5.51)	120 (94.49)	4 (6.15)	61 (93.85)
Glycopeptides	TEI	115 (90.55)	12 (9.45)	48 (73.85)	17 (26.15)
	VA	125 (98.42)	2 (1.58)	63 (96.92)	2 (3.08)

*Used in urinary isolates.

Abbreviations: AMP, ampicillin; AZM, azithromycin; E, erythromycin; CD, clindamycin; COX, cloxacillin, COT, cotrimoxazole; DOX, doxycycline; TE, tetracycline; LZ, linezolid; NIT, nitrofurantoin; NX, norfloxacin; OF, ofloxacin; P, penicillin G; TEI, teicoplanin; VA, vancomycin

DISCUSSION

Antibiotic resistance in ESKAPE pathogens is a major burden in Nepal in treating health-care associated infections (HAIs).[11] WHO has categorized ESKAPE pathogens under critical priority list posing of high clinical concern in both community transmission risk and nosocomial infections.[12]

In the present study, the proportion of female patients (54.45%) infected were higher than male and the maximum number of patients infected with were of 71-80 years, a similar study conducted by Bhatta et al.[13] This may be due to several risk factors associated with age, immune status.

Among Gram-negative ESKAPE pathogens; MDR *Acinetobacter baumannii* was found to be 67. 70% (n=130) to most of antibiotics tested with increasing trends of carbapenem and 3rd generation cephalosporins being more than 50%. A similar study conducted by Mahto et al[14], Pandey et al[7], Flores-Paredes et. al[1] This finding limits the treatment option of *Acinetobacter baumannii* infections and restricted use of last-resort drugs.

Acinetobacter. baumannii showed 90% of susceptibility to colistin, polymyxin B, and tigecycline. Therefore, these drugs could be the potentially useful for treatment. In spite of that, colistin has not been used in clinical setting for several years due to its high level of toxicity.[1] and high level of resistance has been reported (28%) in Nepalese chicken.[15] However; polymyxin B resistance (29%) has been documented in *Pseudomonas* species in Nepal[16] and vigorously used in veterinary medicine to promote the growth of livestock/poultry.[17] FDA has banned the use of medically important drugs for animal growth promotion CDC.[18] Due to these consequences, coexistence of MDR infection and MDROs in food chain may exacerbate antimicrobial resistance problem leading to emergence of pan-drug-resistant organism.[15]

Regarding tigecycline, some data suggest that it is one of the potential drugs of choice for the treatment of hospital-acquired pneumonia caused by MDR *Acinetobacter baumannii*. In addition, tigecycline treatment may be required longer duration to insure better clinical outcomes.[19]

In this study, multidrug resistant *Klebsiella pneumoniae* composed of 65.59% (n=530), Farhadi M. et.al reported 58% of MDR *Klebsiella pneumoniae* from Iran[20] which is consistent with this study. On the contrary, Pandey et. al reported 32.2% from Nepal.[7] Arbune et al reported 24.4% MDR amongst *Klebsiella pneumoniae* isolates from Romania.[21] Outstandingly, a study conducted in Ethiopia documented 95.5% of MDR *Klebsiella pneumoniae* isolates[22], which is far higher than that observed in our study.

Higher resistance of MDR *Klebsiella pneumoniae* has been reported against aminoglycosides, 3rd generation cephalosporins, fluoroquinolones, carbapenems, and piperacillin- tazobactam. However; more than 90 % of MDR isolates were found to be susceptible against colistin, polymyxin B. Our findings were in harmony with other studies conducted in Nepal.[7, 22]

The multidrug resistance rate of *Enterobacter* species was 49.36% (n=78). Which is far higher than other study conducted by Pandey et. al[7] (0.9%), and El-Kady et.al reported 17.4%.[8] No cases of MDR *Enterobacter* species reported by Pathak et.al.[23]

At the current situation, MDR Enterobacter species are exponentially increasing worldwide.[24] In present study, high level of resistance documented to 3rd generation cephalosporins, fluoroquinolones, carbapenems, and piperacillin- tazobactam. whilst, low resistance pattern to tigecycline (5.06%), polymyxin B (5.06%) and colistin (3.16%) were recorded, compatible to a previous study by Pandey et al.[7]

Multidrug resistance in *Pseudomonas aeruginosa* (46.78%) was found to be similar by Pathak et.al [23] but alarmingly high (76.2%) in a study conducted in nosocomial isolates by Shrestha et al. [25] and relatively similar to a study in Egypt (42.4%).[26] However, certain data revealed lower MDR *Pseudomonas aeruginosa* (10.7%), (12.4%). [8,27]

The last resort drugs (colistin and polymyxin B) were found to be more susceptible to treat *Pseudomonas* infections. Carbapenems and monobactams were reported as less susceptible.

Among Gram positive ESKAPE pathogens, *Staphylococcus aureus* (66.14%) was found to be the commonest organism. Our study is supported by Pandey et.al.[7] This may be due to the involvement of wide range of infection.

The prevalence of MDR *Staphylococcus aureus*, and MRSA was 65.35%, and 42.51% respectively. Which is strongly co-related with a study done by Pandey et.al.7 But the study conducted by Sanjana et.al.[28] reported MDR *Staphylococcus aureus* 25.4 % which is lower than our study but MRSA was 39.6% which is analogous to our study. The increasing trend of MDR *Staphylococcus aureus* and MRSA might be the misuse of antibiotics and dissemination of MRSA in health care settings.

The increasing concern of VRE poses a serious threat due to the possible transmission of VRE to *Staphylococcus aureus.* In the present study, 69.23% of MDR *Enterococcus faecium* was reported and VRE was found to be 3.08%. which is lower than other study done in Nepal.[28,29.]

This study reveals the high prevalence of MDR resistance among the ESKAPE pathogens which accounts for high critical alert for dissemination of antibiotic resistance in health care facility. This study will be helpful for clinicians for proper formulation of antibiotic policy and antibiotic stewardship program to identify the most suitable antibiotics for the treatment of infected patients by prescribing most suitable antimicrobial agents at the right dose and period.

CONCLUSION

The increasing trend of multidrug resistance bacteria worldwide is a serious concern. Periodic tracing and surveillance of resistant bacteria in hospital settings is strongly recommended to minimize the problem by formulating the antibiotic policy and antibiotic stewardship program.

To elucidate the genetic mechanism underlying the resistant phenotypes, molecular methods are recommended and large-scale study is required to determine the national status of ESKAPE pathogens.

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CONFLICT OF INTEREST

None

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