Pattern of antimicrobial resistance of Gram-negative bacilli in surgical site infections in in-patients and out-patients at an apex trauma Center: 2013–2016

Nidhi Bhardwaj, Surbhi Khurana, Minu Kumari[1], Rajesh Malhotra[2], Purva Mathur

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Abstract:

INTRODUCTION: Antimicrobial resistance is an increasing problem worldwide especially among the surgical site infections (SSIs). SSI is becoming more serious due to hospital-acquired infections/nosocomial infections, which further leads to the overuse of broad-spectrum antibiotics. To investigate the antimicrobial resistance patterns among Gram-negative bacteria in SSI in in- and out-patients the present study was designed.

METHODOLOGY: During the 4 years (January 2013–December 2016), the antimicrobial resistant pattern was studied in the admitted patients and in the patients who were followed up to the outpatients department (OPD) after discharge. Antimicrobial resistance pattern testing was done by the disk diffusion method on Mueller-Hinton agar and by E-test for ten antibiotics according to The Clinical and Laboratory Standards Institute guidelines for Gram-negative bacilli.

RESULTS: A total of 2,447 strains were isolated from the studied population on over the period of 4 years. Of 2447, 1996 (81%) were isolated from patients who had SSI during the hospital stay, and 451 (18%) were from patients who attended the OPD after discharge. In the outpatients, who followed up in the OPD for the SSI, *Escherichia coli (*148), and *Pseudomonas aeruginosa* (93), whereas in the patients who develop SSI during their hospital stay, *Acinetobacter baumannii* (622), *E. coli* (424), and *Klebsiella pneumoniae* (315) were found to be common. A very high resistance pattern was observed in both the studied groups; however, a higher resistance pattern was seen in in-patients as compared to outpatients.

CONCLUSION: In our study, we have reported resistance pattern in Gram-negative bacteria isolated from the patients who were came for the follow as well as in the inpatients. For the outpatients, it can be concluded that it could be a community-acquired infection which is also an alarming condition for our society.

Key words:

Antimicrobial resistant, in- and out-patients, surgical site infections

Departments of Laboratory Medicine and [1]Surgery, Jai Prakash Narayan Apex Trauma Centre, All India Institute of Medical Sciences, [2]Department of Orthopedics, All India Institute of Medical Sciences, New Delhi, India

Address for correspondence:
Dr. Purva Mathur, Department of Laboratory Medicine, Jai Prakash Narayan Apex Trauma Centre, All India Institute of Medical Sciences, New Delhi - 110 029, India.
E-mail: purvamathur@yahoo.co.in

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Introduction

Antimicrobial resistance is an increasing problem worldwide especially among the surgical site infections (SSIs). SSI is becoming more serious due to hospital-acquired infections/nosocomial infections.[1,2] Hospital-acquired infections are increasing day-by-day because of the severity of illness, length of Intensive Care Unit (ICU) stay, and usage of invasive devices and procedures.[3-5] These infections have been reported to affect approximately 2 million hospitalized patients in the US

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annually and have imposed 57.6 billion dollars in expense to the US health system in 2000.[4,6,7] Patients after surgery are at risk of acquiring hospital-acquired infections which further contributes to higher rates of surgical site rates. A large number of nosocomial infection leads to SSI. SSIs further results in the overuse of broad-spectrum antibiotics. Frequent rational use of these antibiotics results in the resistant to antimicrobial drugs among which high resistant are seen in Gram-negative bacteria. The resistance further leads to serious infections among which SSIs are the most common.[8] Antimicrobial resistance is spreading rapidly among the bacterial population which further made the treatment difficult and challenging especially in surgical and clinical practice.[9] SSI are still remains the major problem in clinical practices and further considering the high level of resistance pattern in SSI patients,[1,10] it is becoming important to identify the resistant pattern among these SSI cases. Most of the studies were evaluated the resistance pattern of the organisms in SSI cases till the hospital stay only but as most of the infections emerges after the discharge which could be community acquired once the patient was discharged from the hospital. It is very important to establish a resistance pattern of SSI in hospital-acquired or community-acquired infections.

To keep this in mind, the present study was designed to investigate the antimicrobial resistance patterns among Gram-negative bacteria in SSIs in in- and out-patients.

Case History

During a 4-year study, from January 2013 to December 2016, we studied pattern of antimicrobial resistance in SSI from outpatients and inpatients, received in the clinical microbiology laboratories.

Bacterial isolates

The Gram-negative bacilli in this study were recovered from clinical samples of SSI from our hospital and patients population was divided into two groups: in- and out-patients.

Inpatients

Gram-negative bacilli were isolated from the patients who develop SSI after the surgery and Pus/wound sample was collected from the surgical site.

Outpatients

Patients after surgery were followed up after discharge, and sample was collected when patients attended the OPD for follow-up. Gram-negative isolates were identified by standard microbiological methods.

The identification was confirmed for all isolates by the Vitek 2 identification cards (Biomerix, France). All the strains were stocked at −70°C for further analysis in stocking beads (Microbank, Pro-Lab Diagnostics, and Richmond Hill, Canada).

Antimicrobial susceptibility testing

The antimicrobial susceptibility testing of Gram-negative was performed by the disk diffusion method on Mueller-Hinton agar according to the recommendations of the Clinical and Laboratory Standards Institute (CLSI). The following antibiotics were tested: Amikacin (AMK) (30 µg), Cefepime (CFPM) (30 µg), Cefoperazone/Sulbactam (CPZ/SUL) (75/30 µg), Ceftazidime (CAZ) (30 µg), Chloramphenicol (CAM) (30 µg), Ciprofloxacin (CIP) (5 µg), Imipenem (IPM) (10 µg), Netilmycin (NET) (30 µg), Piperacillin/Tazobactam (PIT) (100 µg/10 µg), and Tigecycline (TGC) (15 µg). The MIC was determined by E-test for all the above antimicrobials; performed according to manufacturer's recommendations (Biomeriux Ltd., formerly AB Biodisk, Sweden). The inhibition zone diameters and MIC breakpoints were adopted according to CLSI guidelines for Gram-negative bacilli.

Results

A total of 2447 strains were isolated from the studied population over the period of 4 years. Of 2447, 1996 (81%) were isolated from patients who had SSI during the hospital stay, and 451 (18%) were from patients who attended the outpatients department (OPD) after discharge. In the outpatients, who followed up in the OPD for the SSI, *Escherichia coli* (148) and *Pseudomonas aeruginosa* (93) were observed to be the most common isolate followed by *Klebsiella pneumoniae* (58), *Acinetobacter baumannii* (49), *Enterobacter cloacae* (42), and *Proteus mirabilis* (40), whereas in the patients who develop SSI during their hospital stay, *A. baumannii* (622), *E. coli* (424) *and K. pneumoniae* (315) were found to be commonly followed by *P. aeruginosa* (298), *E. cloacae* (137) during 2013–2016. All the organisms were isolated from pus and wound. Distribution of Gram-negative organisms during the study period is shown in Table 1.

Antimicrobial Resistance patterns of Gram-negative bacteria in surgical site infections resistance pattern in outpatients

A high level of the resistant pattern was observed in the patients who were followed up for the SSI after discharge. The highest resistance by *A. baumannii* was seen followed by *K. pneumonia*, *E. coli* and *P. aeruginosa* against AMK, CFPM, CPZ/SUL, CAZ, CAM, CIP, IPM, NET, and PIT. Resistance to TGC was least in all organisms isolated from a sample taken from OPD patients. Only *P. aeruginosas* showed high resistance in TGC. Among the isolates obtained from the OPD patient *A. baumannii*, *E. cloacae*, *K. pneumonia*, *E. coli* and *P. aeruginosa* shown a very high resistance to above-mentioned antibiotics. The detailed resistant pattern of these organisms are shown in Table 2.

Resistance pattern in inpatients

As compared to the outpatient population, inpatients population showed a high number of organisms isolated from the surgical site and very high resistance was seen in this group of the population. Among the total isolated (1996) obtained from inpatients *A. baumannii*, *Aeromonas hydrophilla*, *Citrobacter fruendii*, *E. cloacae*, *E. coli*, *K. pneumoniae*, *Morganella morganii*, *P. mirabilis*, *Providencia stuartii*, and *P. aeruginosa* were found to be common isolates and showed high resistance among these organism. *A. baumannii* showed 97% resistance to CAZ and CFPM (Cefepime); 95% to PIT; 94% and 91% to AMK and CAM, respectively. Similar high resistance by *E. coli* for CIP (92%) and CAZ (90%); *K.pneumoniae* showed 88% resistance to CAZ, 85% to CEPM, 81% to NET and CIP; *P. aeruginosa* showed 89% resistance to CAM. The detailed resistant pattern of these organisms is shown in Table 3.

Table 1: Distribution of organisms over the period of 4 years

	2013		2014		2015		2016		Total
	Out patients, *n* (%)	In patients, *n* (%)	Out patients, *n* (%)	In patients, *n* (%)	Out patients, *n* (%)	In patients, *n* (%)	Out patients, *n* (%)	In patients, *n* (%)	
Acinetobacter baumannii	15 (11)	21 (3)	15 (12)	162 (34)	5 (6)	108 (31)	14 (11)	141 (28)	481
Acinetobacter lwoffii	-	3 (0.4)	1 (0.8)	2 (0.4)		3 (1)		1	10
Aeromonas hydrophilla	1 (1)	13 (2)		9 (2)				1	24
Citrobacter amalonaticus	-	-	-	-	-	-	1 (0.8)	-	1
Citrobacter fruendii	-	4 (2)	1 (0.8)	7 (1.4)	2 (2.5)	3 (1)	-	15 (3)	32
Citrobacter koseri	-	-	2 (1)	2 (0.4)	-	-	-	3 (0.7)	7
Enterobacter aerogenes	3 (2)	1					1 (0.8)	4 (0.7)	9
Enterobacter cloacae	17	56 (8)	6 (5)	24 (5)	8 (10)	37 (10)	11 (9)	20 (4)	179
Enterobacter gergoviae	-	-	-	1	-	-	-	-	1
Escherichia coli	42 (31)	125 (18)	43 (36)	91 (19)	26 (32)	90 (26)	37 (31)	118 (23)	572
Klebsiella pneumoniae	14 (10)	118 (17)	18 (15)	60 (12)	8 (10)	40 (12)	18 (15)	97 (19)	373
Morganella morganii		1		7 (1.5)		2 (0.5)		1	11
Proteus mirabilis	14 (10)	34 (5)	8 (7)	13 (2)	11 (14)	14 (4)	7 (6)	23 (4.5)	124
Providencia rettgeri	-	-	1 (0.8)	-	1 (1.25)	-	-	1	3
Providencia stuartii	-	13 (2)	1 (0.8)	1	-	-	2 (1.6)	-	17
Pseudomonas aeruginosa	28 (20)	81 (12)	19 (16)	88 (18)	19 (23)	49 (14)	27 (22)	80 (16)	391
Pseudomonas luteola	-	2	-	1	-	-	1 (0.8)	-	4
Pseudomonas putida	-	3 (0.4)	-	-	-	1	-	-	4
Pseudomonas stutzeri	-	1	-	-	-	-	-	-	1
Serratia fonticala	-	1	1 (0.8)	-	-	-	-	-	2
Serratia marcescens	-	6 (10.8)	1 (0.8)	1	-	-	-	2 (0.3)	10
Sphingomonas paucimobillis	-	-	-	-	-	-	1 (0.8)	-	1
Total	134	673	117	469	80	347	120	507	2447

Table 2: Antimicrobial resistant pattern of Gram-negative bacteria isolated from surgical site infection of outpatients

Organisms (*n*)	AMK, *n* (%)	CFPM, *n* (%)	CPZ/SUL, *n* (%)	CAZ, *n* (%)	CAM, *n* (%)	CIP, *n* (%)	IPM, *n* (%)	NET, *n* (%)	PIT, *n* (%)	TGC, *n* (%)
Acinetobacter baumannii (49)	38 (78)	40 (82)	28 (57)	37 (76)	39 (80)	38 (78)	3 (67)	27 (55)	35 (71)	6 (12)
Enterobacter cloacae (42)	17 (40)	11 (26)	12 (29)	16 (38)	9 (21)	11 (26)	23 (55)	12 (29)	12 (29)	4 (10)
Escherichia coli (148)	23 (16)	107 (22)	52 (35)	112 (76)	21 (14)	97 (66)	10 (7)	26 (18)	47 (32)	4 (3)
Klebsiella pneumoniae (58)	29 (50)	34 (59)	32 (55)	39 (67)	30 (52)	35 (60)	15 (26)	33 (57)	31 (53)	9 (16)
Proteus mirabilis (40)	17 (43)	19 (48)	6 (15)	27 (68)	23 (58)	22 (55)	10 (25)	15 (38)	2 (5)	21 (53)
Pseudomonas aeruginosa (93)	38 (41)	32 (34)	22 (24)	40 (43)	69 (74)	37 (40)	23 (25)	31 (33)	0	77 (83)

AMK = Amikacin, CFPM = Cefepime, CPZ/SUL = Cefoperazone/sulbactam, CAZ = Ceftazidime, CAM = Chloramphenicol, CIP = Ciprofloxacin, IPM = Imipenem, NET = Netilmycin, PIT = Piperacillin/tazobactam, TGC = Tigecycline

Table 3: Antimicrobial resistant pattern of Gram-negative bacteria isolated from surgical site infection of inpatients

Organisms (*n*)	AMK, *n* (%)	CFPM, *n* (%)	CPZ/SUL, *n* (%)	CAZ, *n* (%)	CAM, *n* (%)	CIP, *n* (%)	IPM, *n* (%)	NET, *n* (%)	PIT, *n* (%)	TGC, *n* (%)
Acinetobacter baumannii (622)	584 (94)	603 (97)	546 (88)	601 (97)	568 (91)	485 (78)	574 (92)	386 (62)	594 (95)	138 (22)
Aeromonas hydrophilla (23)	9 (39)		21 (91)	18 (78)	23 (100)	16 (70)	9 (39)	5 (22)	15 (65)	
Citrobacter fruendii (29)	14 (48)	19 (66)	21 (72)	23 (79)	15 (52)	15 (52)	7 (24)	15 (52)	15 (52)	3 (10)
Enterobacter cloacae (137)	70 (51)	80 (58)	78 (57)	93 (68)	46 (34)	7 (53) 3	45 (33)	88 (64)	74 (54)	7 (5)
Escherichia coli (424)	124 (29)	346 (82)	204 (48)	380 (90)	118 (28)	390 (92)	80 (19)	149 (35)	243 (57)	7 (2)
Klebsiella pneumoniae (315)	222 (70)	267 (85)	241 (77)	277 (88)	162 (51)	255 (81)	169 (54)	254 (81)	240 (76)	39 (12)
Morganella morganii (11)	6 (55)	5 (45)	6 (55)	8 (73)	6 (55)	8 (73)	8 (73)	6 (55)	5 (45)	4 (36)
Proteus mirabilis (84)	34 (40)	58 (69)	17 (20)	65 (77)	42 (50)	54 (64)	19 (23)	62 (74)	9 (11)	63 (75)
Providencia stuartii (16)	7 (44)	7 (44)	9 (56)	9 (56)	10 (63)	9 (56)	2 (13)	7 (44)	5 (31)	13 (81)
Pseudomonas aeruginosa (298)	156 (52)	175 (59)	195 (65)	184 (62)	265 (89)	190 (64)	158 (53)	185 (62)	3 (1)	197 (66)

AMK = Amikacin, CFPM = Cefepime, CPZ/SUL = Cefoperazone/sulbactam, CAZ = Ceftazidime, CAM = Chloramphenicol, CIP = Ciprofloxacin, IPM = Imipenem, NET = Netilmycin, PIT = Piperacillin/tazobactam, TGC = Tigecycline

Discussion

Antimicrobial resistance in surgical sites is emerging problem worldwide, which further result in increased hospital stay of the patients and mortality. SSI is the most common problem in hospital after surgery further increasing resistance to the antibiotics are of major concern. In the present study, resistance pattern was studied in SSI patients.[8-10] A total of 451 isolates were found in the patients who had SSI after discharge, and a very high number of SSI isolates ($n = 1996$) were reported in the admitted patients. Similarly, we have reported the difference in antibiotic-resistant in SSI group of patients. In the present study, *A. baumannii, C. fruendii, E. cloacae, E. coli, K. pneumoniae, P. mirabilis, Providencia stuartii*, and *P. aeruginosa* showed high resistance to most of the antibiotics tested in the study; *A. baumannii* showed 97% resistance to CAZ and CEPM; 95% to PIT; 94% and 91% to AMK and CAM, respectively whereas in the outpatients *Acinetobacter baumannii* showed 76% resistance to CAZ and 82% to CEPM; 71% to PIT; 71% and 80% to AMK and CAM, respectively. Similarly, high resistance by *E. coli* for CIP (92%) and CAZ (90%); *K. pneumoniae* showed 88% resistance to CAZ, 85% to CEPM, 81% to NET and CIP; *P. aeruginosa* showed 89% resistance to CAM. Whereas, in outpatients, *E. coli* for CIP (66%) and CAZ (76%); *K. pneumoniae* showed 67% resistance to CAZ, 59% to CEPM, 57% to NET, and 60% to CIP; *P. aeruginosa* showed 74% resistance to CAM.

Increasing pattern in antimicrobial drugs are increasing worldwide in a study published in 2016 by published in 2016 by Krunal Shah reported decreased level of IPM from 94.25% to 36.17% over the period of 2½ years, however in contrast to our they have reported increased level of susceptibility in AMK from 29.31% to 40.42%.[11] A study by Chandra Prakash Bhatt in 2014 showed similar results for Gram-negative isolates on SSI, *Acinetobacter* spp., *K. pneumoniae*, *E. coli*, and *P. aeruginosa* and they have also reported a high level of resistance to the antibiotics tested in the study.[12] They have found 73.91% resistance to CIP, but in contrast, they have found AMK sensitive to Gram-negative bacteria. Raza *et al*.[12] showed that 96/120 (80%) sample was culture positive out of them 58.33% were Gram-negative bacilli.[13] A very high level of resistance was observed in the admitted patients, especially in ICU patients who are due to nosocomial infection by another study.[14] Antimicrobial resistance pattern for SSI patients for each hospital is important for the appropriate treatment of the patients and to control the nosocomial infection in the hospital setting.

Conclusion

In our study, we have reported resistance pattern in Gram-negative bacteria isolated from the patients who were came for the follow, so it can be concluded that it could be a community-acquired infection which is also an alarming condition for our society. Society needs to control the commercially available antibiotics in the market. Our data suggest the high level of resistance in SSI in- and out-patients. Surveillance of SSI is important to understand the magnitude of the problem and find out appropriate preventive methods.

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Conflicts of interest

There are no conflicts of interest.

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