

A tertiary care hospital's drug resistance profile in instances of gastrointestinal and postbiliary surgical-site infections

P.Sailaja ,Yadala Prapurna Chandra ,P.Naresh Babu ,S.Aliya afra

Department of pharmacology

Ratnam Institute of Pharmacy, Pidathapolur (V), Muthukur (M), SPSR Nellore Dt.524001 A.P. Indi

Abstract:

Surgical-site infection (SSI)-associated bacteria in underdeveloped regions are showing signs of increasing medication resistance, which is leading to more severe complications and increased healthcare expenses. The pattern of medication resistance in our SSI-related isolates was our aim in this analysis. Wound swabs were treated using standard aerobic and anaerobic culture for 191 clinically confirmed SSIs (postbiliary tract and postgastrointestinal surgery) during a 2-year period. The Epsilometer was used to determine the minimum inhibitory concentration (MIC) of the antibiotic. According to the criteria, phenotypes of multidrug resistance were identified. There were 5.3% SSIs, mostly caused by *Klebsiella*, *Staphylococcus*, and *Pseudomonas*, with no anaerobes found. Nineteen percent of the *Staphylococcus aureus* bacteria were resistant to methicillin, and a third of those bacteria showed an elevated macrolide minimum inhibitory concentration (MIC). Out of all the Enterobacteriaceae isolates, about 58.2% were found to generate extended-spectrum beta-lactamases. We found isolates that had a higher meropenem MIC. The dangerously increasing proportion of antibiotic resistance in SSI patients is accompanied with MICs that are rapidly nearing resistance in susceptible isolates. Immediate remedial measures are required by law.

Search Terms:

Minimum inhibitory concentration, health care-associated infection, surgical-site infection, extended-spectrum beta-lactamase, and methicillin-resistant *Staphylococcus aureus* Despite being avoidable in over half of instances, surgical-site infections (SSIs) are linked to higher rates of patient morbidity, death, and healthcare-associated costs. Up to 30% of patients in poor and medium income countries who have surgery are affected by surgical site infections (SSIs), making them the most prevalent kind of healthcare-associated illness (HAI). [2] SSI is the second most common kind of healthcare-associated infection (HAI), accounting for up to 20% of all HAIs in developed nations. [5]

Introduction

The average SSI rate here was 4.2%, according to a comprehensive multicentric research that included data from six Indian cities. Bacterial isolates associated with SSIs are typically found in healthcare settings, where medication resistance is prevalent. Drug resistance may be associated with surgery-related variables such as emergency operations and extended surgical prophylaxis. For both patients and businesses, SSIs become more costly and time-consuming as bacteria develop resistance. In the Western world, most SSI isolates are Gram-positive, and a large portion of that population is resistant to drugs.[5] There is a dearth of comparable data from nations with low or medium incomes. three to five The Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License permits others to modify, adapt, and create upon the work non-commercially, provided that proper citation is provided and the new works are licensed under the same terms. This license governs the distribution of articles in this open access journal. less publicized. We analyzed the medication resistance trend and pathogen profile of surgical site infections (SSIs) after biliary and gastrointestinal (GI) surgeries, the two most prevalent procedures in our tertiary care hospital's general surgery department.

Methods

Selection of patients

Subjects were recruited continually from the general surgery department (located at both the main hospital complex and one annex hospital inside the city, 6 km distant). People who met the inclusion criteria had to have recently undergone biliary or upper gastrointestinal surgery (e.g., cholecystectomy, appendectomy, gastrojejunostomy, repair of duodenal ulcers, repair of duodenal and intestinal perforations, choledochoduodenostomy, removal of choledochal cysts, Whipple's operation, or partial gastrectomy) and showed signs of surgical site infection (SSI) according to CDC criteria.[1] Medical, laboratory, and epidemiological information was documented upon administration of informed consent. Two swabs were taken from the region that seemed to be contaminated, if any, and then soaked in Amies transport medium. They were then submitted to the bacteriology laboratory in the department as soon as feasible. According to the usual protocol, swabs were inoculated in two sets of standard culture medium (blood agar and MacConkey agar) and then incubated in aerobic and anaerobic (GasPak method) conditions for 48 hours, or until observable growth is seen.[9] Following the guidelines set forth by the Clinical and Laboratory Standards Institute [CLSI], USA, antibiotic susceptibility testing was conducted when growth was detected. Additionally, the Epsilometer test technique (bioMérieux, USA, Durham) was used to verify drug-resistant phenotypes and minimum inhibitory concentration (MIC). According to the advice, certain resistance phenotypes such as ESBL producers, carbapenemase producers, methicillin-resistant *Staphylococcus aureus* (MRSA), and vancomycin-resistant *Enterococci* (VRE) were examined. Isolates of *Enterobacteriaceae* were tested for carbapenemase production using the modified Hodge test (MHT).[10] The procedure was approved by the Institutional Ethics Committee in letter number. MC/119/2007/1128.

Quantity of samples

The sample size was determined using the cross-sectional study formula: $n = Z^2 (1-\alpha)/2 P (1 - P)/d^2$. Here, $Z (1-\alpha)/2$ is the standard normal variate, which is 1.96 at 5% Type I error or . Since our population did not have a published study or pilot study, we assumed that 50% of subjects had drug-resistant isolates, and $d = 7\%$ is the acceptable precision/absolute error. the eleventh

The calculated value of n is 196, according to the formula $(1.96)^2 \times 0.5 (1-0.5)/(0.07)^2$.

length of the follow-upThe two and a half years between June 2014 and November 2015 were the time frame of the research.

Objective

By determining the participants' pathogen profiles and drug-resistant patterns, as measured by major phenotypes, the main goal of the experiment was accomplished.

Statistical Package for the Social Sciences (SPSS) version 23 (IBM, Armonk, NY, USA) was used to examine patterns in a spreadsheet that included patient-specific epidemiological and clinical data. The results of the analysis were then presented using Chi-square and Fisher's exact tests. The analysis focused on several groups linked to SSI and the category values that matched.

Final Product

According to the inclusion criteria used [Table 1 baseline data], out of 3616 surgical patients (postsurgery), about 191 (5.3%) were enrolled as research participants. Out of the 133 SSI individuals, 69.3% were able to get organisms isolated.

Table 2 also shows the bacterial agents that were identified from the people who were part in our research. You can see the key results of the phenotypic drug resistance test in Table 3.

A total of 94 isolates, or 69.11%, exhibited phenotypic drug resistance, as shown in Table 3.

Subject under consideration

Because of the high incidence of bacterial separation when there is chronic antibiotic resistance, our high culture positive rate of 69.6% was comparable to other research [13,14]. The characteristics of the research population (such as the prevalence of concomitant conditions, sex, and age), as well as variations in infection control measures, may account for the observed variation in culture positive among studies and locales. Nonbacterial substances or very particular bacteria might be the cause of negative isolation (30.4%).

In line with other research, the percentage of men who exhibited isolation was much greater (76.5%) than that of females (61.8%).¹² and ¹⁵ Common explanations include a decline in adherence to the prescribed treatment plan, an increase in the number of cases requiring emergency surgery due to factors like accidents, and a rise in smoking rates, which is a major risk factor for surgical site infections.[16]

More patients undergoing emergency procedures compared to elective ones required pathogen isolation ($P = 0.00588$), as seen in Table 1. This is comprehensible

Table 1: Baseline data of the study subjects

	<i>n</i>	Isolation(%)	<i>P</i> (significance=0.05)
Gender			
Female	89	55 (61.8)	0.007152
Male	102	78 (76.5)	
Age(years)			
<30	47	34 (73.3)	0.761994
30–50	116	81 (69.8)	
>50	28	18 (64.3)	
Residence			
Rural	106	73 (68.9)	0.797218
Urban	85	60 (70.6)	
Religion			
Hindu	96	60 (62.5)	0.181565
Muslim	91	62 (68.1)	
Other	4	1(25.0)	
Comorbidity*			
Present	58	48 (82.6)	0.009188
Absent	133	85 (63.9)	
Admission			
ICU/semi-ICU	7	2(28.6)	0.005218
Indoor	153	114(74.5)	
Outdoor	31	17 (54.8)	
Woundclass [#]			
Clean	126	76 (60.3)	0.001524
Cleancontaminated	53	47 (88.7)	
Contaminated	7	6(85.7)	
Dirty	5	4(80.0)	
Surgery			
Biliarysurgery	82	43 (52.4)	0.0001
Cholecystectomy	51		
Choledocholithotomy	11		
Choledochalcystexcision	6		
Liverresection,orootherbileducts/GB-relatedoperation	14		
GI surgery	109	90 (82.6)	

Appendicectomy	68		
Hepaticojejunostomy	12		
Gastrectomy	11		
Gastrojejunostomy	9		
Truncalvagotomy	9		
Type of urgency			
Emergency	52	44 (84.6)	0.005886
Elective	139	89 (64.0)	
Laboratory results			
Total cases tested		191	
Total cases with positive isolation		133 (69.6)	
Single isolate	130		
Double isolate	3		
Total number of isolates, n(%)		136	
Gram negative	82 (60.3)		
Gram positive	54 (39.7)		

*Cardiovascular disease 16 (10.9%), hypertension 42 (28.6%), diabetes mellitus 39 (26.5%), HIV/AIDS 4 (2.7%), other infections 14 (9.5%), bronchial asthma

16 (10.9%), multiple comorbidities 7 (4.8%), and others 9 (6.1%). #The majority of the procedures had no clean wounds, mainly contaminated (34%) and clean-contaminated (30%). GI=Gastrointestinal, ICU=Intensive care unit

Compromise in the degree of aseptic methods and lengthy hospital stays, such as in severe emergency situations, are predicted in life-saving operations and emergency treatments.¹⁷ and ¹⁸ Going back to a couple earlier pieces, we observed a substantially greater isolation rate ($P = 0.005218$) in filthy and contaminated wounds compared to clean wounds in our research [Table 1]. This finding is likely due to the increased bacterial burden in infected wounds.^[17]

Table 2: Isolated microbes from surgical-site infection lesions

<u>Name of the microbe</u>	<u>Frequency (%)</u>
<i>S. aureus</i>	44 (33.1)
<i>K. pneumonia</i>	37 (27.9)
<i>P. aeruginosa</i>	24 (18)
<i>Citrobacter</i> sp.	5 (3.8)
<i>E. coli</i>	5 (3.8)
<i>Staphylococcus</i> sp. (other than <i>S. aureus</i>)	4 (3.0)
<i>Enterococci</i>	3 (2.3)
<i>Acinetobacter</i> sp.	3 (2.3)
<i>Enterobacter</i> sp.	3 (2.3)
<i>Proteus</i> sp.	2 (1.5)

Mixedinfection(type1)	2(1.5)
Mixedinfection(type2)	1(0.8)
Anaerobes	0
Type1= <i>S.aureus</i> and <i>E.coli</i> ; Type2= <i>S.aureus</i> and <i>Klebsiella</i> . <i>S.aureus</i> = <i>Staphylococcus aureus</i> , <i>K.pneumonia</i> = <i>Kl</i> <i>ebsiellapneumonia</i> , <i>P.aeruginosa</i> = <i>Pseudomonasaeruginosa</i> , <i>E.coli</i> = <i>Es</i> <i>cherichiacoli</i>	

Consistent with the prior research, 136 isolates were found; 130 of them were single isolates, while 3 instances had two.[14] It is common practice to connect monomicrobial isolates with sterile surgical procedures and polymicrobial isolates with unclean or filthy wounds.[17] Consistent with other research, the majority of our isolates were Gram-negative (60.3%). The year 19 The Gram-negative bacteria's tendency to colonize inanimate surfaces and settings in hospitals, their antibiotic resistance, and the ease with which they may be contaminated from the digestive system after surgery are the reasons for their prevalence. Consistent with several other studies, *Klebsiella* species ranked second overall (27.9% vs. 33.1% in Table 2), behind *S. aureus*.(6, 17) *Klebsiella* is a frequent fomite and airborne pollutant in operating rooms and hospitals, which may explain why it is so prevalent there. Seven and twelve *Pseudomonas* seems to be the most common kind of bacteria in certain research. Geographical location, season, variations in aseptic practices, resistance patterns, and surgical procedures are some of the possible causes of this variance in dominating species. Gram-negative gut flora might be a sign of SSI if the internal organs, particularly the lower gastrointestinal tract (gut), are examined. In most cases, foreign bacteria or skin colonizers will be the most common in sterile treatments.[17]

Ten isolates of methicillin-resistant *Staphylococcus* were found during antibiotic susceptibility testing, accounting for 19.6% of the total. **Table 3**. This percentage was previously determined to be 44% in a Mumbai-based research and 30.3% in an Indian one. referenced in [18,19] Macrolide resistance was found in about 31.9% of *S. aureus* strains (MIC 8 μ g/mL or above), with 3 (6.4% of the total) isolates exhibiting very high levels of resistance (MIC 64 μ g/mL) as shown in Table 3. Similarly, a resistant strain was found in 21.3% of *S. aureus* isolates.

There was one isolate with a very high level of resistance to ciprofloxacin, with a MIC of 32 μ g/mL, out of the range of 8 μ g/mL. It was shown that neither vancomycin nor linezolid were resistant. Nevertheless, according to Table 3, three of the isolates had linezolid MIC values that were 4 μ g/mL, which is the highest limit of sensitivity, suggesting that the resistance mechanism may have evolved. With an upper limit of sensitivity of 4 μ g/mL and a vancomycin MIC below 1 μ g/mL, all three of the enterococci isolates (n = 3) were found to be free of VRE. For phenotypic confirmatory testing, 32 (58.2%) of the 55 Enterobacteriaceae isolates tested positive for pure ESBL production; all of these strains were inhibited by combination discs of ceftazidime/cefotaxime and clavulanate, with a zone diameter difference (compared to ceftazidime/cefotaxime without clavulanate) greater than 5 mm.[9] Resistance to beta-lactams, including 3rd-generation cephalosporin and several other medicines, is one type of multidrug

resistance that is associated with ESBL formation. Approximately 10 Enterobacteriaceae isolates (18.2%) were found to produce both metalloenzymes and lactamases. Prior research has also shown this increased resistance in SSI-associated *Klebsiella* and *Escherichia* bacteria. According to Table 3, three of the isolates tested positive for carbapenemase in MHT (one each for *Klebsiella*, *E. coli*, and *Citrobacter* sp.) [17]. These same isolates also showed a very high MIC value of meropenem. Among *Klebsiella* isolates, 5.5% were found to be carbapenem-resistant in a Saudi Arabian investigation, but 67% of *Klebsiella* associated with SSIs were resistant to this antibiotic in another study. Both [18,20] The percentage of Enterobacteriaceae isolates resistant to ciprofloxacin was about 56.4%, whereas the percentage resistant to amikacin was 27.1%. Prior research has also shown similar results, particularly for *Klebsiella*. [17] Eight (33.3%) of the twenty-four *Pseudomonas aeruginosa* isolates had a ciprofloxacin minimum inhibitory concentration (MIC) of 4 μ g/mL, three (12.5%) had a MIC of 8 μ g/mL, which is twice the resistance breakpoint, and twelve (50%) had a ceftazidime MIC ranging from 32 to 64 μ g/mL, with a resistant breakpoint of 32 μ g/mL. Three different *Acinetobacter* sp. isolates showed resistance to ciprofloxacin, amikacin, ceftazidime, and cefotaxime, with minimum inhibitory concentrations (MICs) ranging from 8 μ g/mL to 64-128 μ g/mL, respectively. *Pseudomonas aeruginosa* (67%) and multidrug-resistant *Acinetobacter* sp. (70% carbapenem-resistant) were also detected in high frequency in the SSI cases studied by El-Kholy et al. [20]

In summary

It is concerning that carbapenem resistance has emerged in SSI patients, with a minimum inhibitory concentration (MIC) three times greater than the CLSI threshold for resistant levels. There is an immediate need to address the high prevalence of ESBL and resistant *Pseudomonas* in the SSI patients at our hospital. Although 19.1% (9/47) of MRSA may be trending toward an increasing level, the MRSA level was not very high when compared to Western research.

Table 3: Salient points in antimicrobial sensitivity testing results

Agent/group	Phenotype/species	Resistance in	n(%)	Comment
<i>Enterobacteriaceae</i> <i>e</i> (n=55)	ESBL producer (pure)	<i>Klebsiella</i> sp.	32	MIC (Epsilon test) confirmed the result
		<i>E. coli</i>	(58.2)	
		<i>Citrobacter</i>	24	
		<i>Enterobacter</i>	3	
		<i>Proteus</i>	2	
			2	
	Mixed beta-lactamase		1	8(14.6)
		<i>Klebsiella</i> sp.	6	
		<i>E. coli</i>	1	
	Carbapenemase	<i>Enterobacter</i> sp.	1	3(5.5)

	positive(MHT test)	<i>Klebsiella</i> sp.	1	Meropenem MIC is 16 µg/uL (3-fold higher than the resistant level, i.e., 4 µg/mL)
		<i>E. coli</i>	1	Meropenem MIC is 8 µg/uL (i.e., 2-fold higher than the resistant level, i.e., 4 µg/mL)
		<i>Citrobacter</i> sp.	1	Meropenem MIC is 8 µg/uL (i.e., 2-fold higher than the resistant level, i.e., 4 µg/mL)
Non-Enterobacteriaceae Gram negatives	<i>Pseudomonas</i> ssp. (n=24)	Quinolone-resistant pseudomonas	11 (45.8)	Ciprofloxacin MIC >8 µg/mL in 3 isolates (double the resistance limit, i.e., 4 µg/mL)
		3rd-generation cephalosporin-resistant pseudomonas	12 (50.0)	Ceftazidime MIC = 32–64 µg/mL
		Meropenem-resistant pseudomonas	2 (8.3)	Meropenem MIC 8 µg/mL in one isolate (equal to resistance limit)
		<i>Acinetobacter</i> sp. (n=3)	3 (100)	Resistant to amikacin, beta-lactams, and quinolones
Gram-positive cocci	<i>S. aureus</i> (n=47)	<i>S. aureus</i> resistant to penicillin	47 (100)	10 Upenicillin G discussed
		MRSA	9 (19.1)	Confirmed in oxacillin agar media
		Macrolide-resistant <i>S. aureus</i> (MIC >8 µg/mL)	15 (31.9)	In three isolates, MIC for erythromycin was 64 µg/mL
		Quinolone-resistant <i>S. aureus</i> (>4 µg/mL)	11 (23.4)	In one isolate, MIC was 32 µg/mL
		Vancomycin-resistant/intermediate <i>S. aureus</i> (VRSA/VISA)	0	MIC value of all strains was below 2 µg/mL
		Linezolid-resistant <i>S. aureus</i>	0	Three isolates had MIC = 4 µg/mL (upper limit for sensitive strain), while all other isolates had MIC below 0.5 µg/mL
		<i>Staphylococcus</i> sp. other than <i>S.</i>	1	

	<i>aureus</i> showing MRS (30μg disc screening followed by oxacillin agar testing)	
<i>Enterococcus</i> sp. (n=3)	Vancomycin-resistant <i>enterococci</i>	0

When we say "Escherichia coli" or "Staphylococcus aureus," we mean just that. The following abbreviations are used: MHT stands for "Modified Hodge test," VRSA for "Vancomycin-resistant Staphylococcus aureus," VISA for "Vancomycin intermediate Staphylococcus aureus," MRSA for "Methicillin-resistant Staphylococcus aureus," ESBL for "Extended-spectrum beta-lactamase producer," and MRS for "Methicillin-resistant Staphylococcus." The results of our study highlight the critical need of taking immediate action to prevent antibiotic resistance. This includes being wise with antibiotic use, providing optimal surgical prophylaxis, practicing antibiotic stewardship, and establishing an efficient infection control program, particularly for surgical patients.

References

1. This sentence is a citation for a study by Allegranzi et al. (2002). Systematic study and meta-analysis of the burden of endemic healthcare-associated infections in developing nations. Published in the Lancet in 2011, volume 377, pages 228–41.
2. Casey AL, Petrosillo N, Hudson PM, Mitchell SA, and Crosby C. 3. Badia JM. A comprehensive analysis spanning six European nations examining the effects of surgical site infections on healthcare expenditures and patient outcomes. Public Health Viruses 2017;96:1–15.
3. Umscheid CA, Mitchell MD, Doshi JA, Agarwal R, Williams K, Brennan PJ. Trying to predict the amount of avoidable healthcare-associated infections, together with the accompanying expenditures and fatality rates. Epidemic Prevention Journal of Hospital Epidemiology 2011; 32: 101–14%.
4. Health-Related Infections and Antimicrobial Utilization in European Acute Care Hospitals: A Point Prevalence Survey (ECDC) Version 3.1.2 of the ECDC PPS Validation Protocol was used in 2021. Downloadable at: <https://www.ecdc.europa.eu/en/publications-data/point-prevalence-survey-healthcare-associated-infections-and-antimicrobial-use-4.pdf>. Access was last made on July 10, 2021..
5. Myatra SN, Dwivedy A, Bagasrawala I, Rosenthal VD, Chakravarthy M, Singh S, et al. The International Nosocomial Infection Control Consortium assessed the prevalence of surgical site infections in six Indian cities (INICC). International Journal of Health 2015;7:354–9.
6. The authors: Allegranzi B, Zayed B, Bischoff P, Kubilay NZ, de Jonge S, de Vries F, and others. A worldwide evidence-based viewpoint on the new World Health Organization guidelines

for preventing surgical site infections during and after surgery. The article was published in 2016 in the Lancet Infect Dis journal and covered pages 288 to 303.

7. Yu H., Gaffney M., Emons MF, Mardekian J., Girgenti D., and Campbell RS. Problems with clinical outcomes and the use of resources linked to Staphylococcus aureus infections, whether methicillin-resistant or methicillin-sensitive, after elective surgery. Surgery: Infectious Diseases (Larchmt) 2015;16:543-52.

8. Institute for Clinical and Laboratory Standards. Anaerobic Specimen Detection Principles and Procedures; Implemented Guidelines. File M56-A of the CLSI. Clinical and Laboratory Standard Institute; 2014. 10. Wayne, PA-based organization. Standards for Clinical and Laboratory Medicine (CLI)