Original Article

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Risk Factors and Surgical Site Infection in Patients with Surgical Antibiotic Prophylaxis in the Indian Population: A Prospective Cohort Study

Karthik Sankar, Pharm. D.[1], Deepika Anbalagan, Pharm. D.[1], Balaswetha Baskaran, Pharm. D.[1], Vysali Segaran, Pharm. D.[1], Yogitha Prabakar, Pharm. D.[1], Sridhar Raghu, Pharm. D.[1], Vidhya Krishna, M.D.[2], Venkatesan Singaram, Ph.D.[3], Xavier Santhiyagu, Ph.D.[4], Muhasaparur Ganesan Rajanandh, M. Pharm., Ph.D.[5]

[1]Department of Pharmacy Practice, Sri Ramachandra Faculty of Pharmacy, Sri Ramachandra Institute of Higher Education and Research, Porur, Chennai 600116, India.

[2]Department of Pediatrics, Post-doctoral fellow in Infectious Diseases, Sri Ramachandra Medical College and Research Institute, Porur, Chennai 600116, India.

[3]Department of Engineering and Technology, Sri Ramachandra Faculty of Engineering and Technology, Porur, Chennai 600116, India.

[4]Department of Statistics, Loyola College, Chennai, Tamilnadu 600034, India.

[5]Department of Pharmacy Practice, SRM College of Pharmacy, SRM Institute of Science and Technology, Kattankulathur, 603203, Tamil Nadu, India.

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Abstract:

Objective: To assess the risk factors and Surgical Site Infections (SSI) in patients with surgical antibiotic prophylaxis (SAP) within the Indian population.

Material and Methods: A prospective cohort study, consisting of 1,362 patients, with the age of 18 and above; admitted for various surgical procedures, and prescribed with SAP were included. In order to determine the significance of categorical data, the chi-square test, and Multiple binary logistic regression via the backward wald method was used to identify the risk factors. Various risk factors and their association to SSI were assessed, with a probability value of ≤0.05 being considered as a significant level.

Contact: Muhasaparur Ganesan Rajanandh, M. Pharm., Ph.D.
Department of Pharmacy Practice, SRM College of Pharmacy,
SRM Institute of Science and Technology, Kattankulathur, 603203, Tamil Nadu, India.
E-mail: mgrpharm@gmail.com

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Result: In total, 171 SSI were observed; with an incidence of 12.6% [95% CI=11.1-16.6] among all study patients (1,362). Cefotaxime was the most prescribed SAP in this study. In total 59.6% had gram-positive organisms and 40.4% had gram-negative organisms. Type of surgery, female gender, smoking and alcohol, diabetes with hypertension, microbial growth, American Society of Anesthesiologists (ASA) score (class III), hospital guidelines, and pre-operative hospital stays (>7 days) were the significant risk factors (p-value<0.05) associated with SSI. There was no significant association with drain use, nor redosing (p-value>0.05).

Conclusion: This study emphasizes the significant risk factors; such as age, female gender, types of surgery, ASA score, nonadherence to hospital guidelines, monomicrobial and polymicrobial growth and poor compliance to SAP being associated with SSI in surgical patients. These risk factors allow a better understanding related to SSI, which may have therapeutic implications.

Keywords: antibiotic prophylaxis, deep wound, superficial wound, surgical site infection

Introduction

Surgical Site Infection (SSI) is a type of nosocomial infection, which occurs at or near a surgical incision/wound after a surgical procedure. SSI was the most surveyed and most frequent healthcare-associated infection in low and middle income countries (LMICs); affecting up to one-third of patients whom underwent surgery. Additionally, SSI related deaths account for more than one-third of postoperative mortalities worldwide[1,2].

The incidences of SSI in developed countries, such as in the United State of America (USA) (1.9%), France (1.0%) and Italy (2.6%) are lower than in developing countries, such as Turkey (4.1%), China (4.5%) and India (5.0%). India, being a LMIC, has expectedly high rates of SSI, with many studies conducted in India on the prevalence of SSI, having had a proven rate of SSI ranging between 4% and 30%[3].

Based on the National Nosocomial Infections Surveillance System (NNIS), SSIs are the third most frequently reported nosocomial infections; accounting for 14-16% of all the nosocomial infections in India. The most common causative organisms isolated were: *Staphylococcus aureus*, *Escherichia coli*, *Proteus mirabilis* and *Pseudomonas aeruginosa* and Methicillin-resistant *staphylococcus aureus* (MRSA)[4,5].

Surgical antibiotic prophylaxis (SAP) refers to the prevention of infections and their complications by prescribing an effective antimicrobial agent prior to exposure to contamination during surgery.

Environments, surgeons, and patients are all known risk factors for SSI, so it is possible to intervene against some of these factors. (e.g. conditions in the operating room). Whereas other elements; such as advanced age and diabetes mellitus are inherent patient risks which cannot be modified. Bacteria may still enter the wound despite effective decontamination and antisepsis from the operating room environment, instruments, surgical staff, or patient skin. Notably, SSIs rarely result from bacterial contamination from distant blood-borne seeding of the wound site during the postoperative period, as they typically result from intraoperative contamination. The integrity of host defense is a factor to take into account, as acquired host response impairment is objectively related to higher rates of SSI; as in the case of chronic illnesses, malnutrition, hyperglycemia, and conditions linked to prolonged corticosteroid intake as well as other infection at locations[6-8].

The three risk index, according to the NNIS, are documented by the American Society of Anesthesiologists (ASA) index, which classifies patients according to their clinical conditions into one of four categories (I, II, III, IV). Wound classification represents the classification of a surgical wound by a surgical team, in terms of the potential presence of microorganisms and length of operation, i.e. duration of surgery[9].

Systemic antibiotics given as prophylaxis before the surgery can reduce the incidence of SSI significantly[10], as the administration of prophylactic antibiotics, before or after 120 minutes of incision, have been found to be associated with an increased risk of SSI[11].

The selection and application of SAP should be conducted according to medical characteristics including: the type of surgical incision, the possibility of infection, the type of potential pathogens and the prophylactic effect of antibiotics[12,13].

According to the USA Institute of Health Improvement: SSI, the SAP should be given within 60 minutes prior to incision and to be discontinued within 24 hours (48 hours for cardiac patients)[14]. There is significant evidence that prolonged SAP postoperatively has no benefit in reducing SSI after surgery when compared to a single dose. The shortest, effective duration of antimicrobial administration for preventing SSI is not known; however, evidence is mounting that postoperative antimicrobial administration is not necessary for most procedures[15].

SSI raises mortality and morbidity rates, increased costs due to prolonged hospitalization, requires additional diagnostic tests and therapeutic antibiotic treatment and rarely, additional surgery[16]. Thus the objective of this present study was to examine the various influencing risk factors of SSI in surgical patients receiving SAP within Indian population.

Material and Methods

Study design: inclusion and exclusion criteria

A prospective cohort study was conducted in the department of general surgery, in a tertiary care teaching hospital; from 2018 to 2021. The study population was aged 18 years and above, of all genders, having been admitted for various surgeries and prescribed with SAP. Patients willing to give informed consent were included in the study. Patient's demographic information, medical status, medication history, prescribing practices of SAP; according to hospital guidelines, comorbid condition, duration of surgery and hospital stay, type of surgery, ASA score, types of wound class, pre and post-operative SAP, redosing, drains used, polymicrobial and monomicrobial growth were assessed for SSI. Bacterial strain cultures isolated from fluids from intra-abdominal infections, incisions, abscesses, fistulas, blood, urine and sputum were observed in the hospitalized patients. Additionally, susceptibility to SAP was also assessed by diffusion and standard micro dilution methods. Identification and susceptibility testing was performed using the Vitek 2 system (Biomerieux Vitek 2 Compact) in a microbiological laboratory.

Surgical procedures

Among various surgical procedures (SPs), this study included 8 types of SPs, according to the International Classification of Diseases, Ninth Revision (ICD-9) criteria. Bench marking was performed against the United states Centers for Disease Control-National Healthcare Safety Network (U.S. CDC-NHSN). The 8 SPs were: abdominal hysterectomy (HYST); abdominal aortic aneurysm repair (AAA); appendix surgery (APPY), bile duct, liver or pancreatic surgery (BILI); colon surgery (COLO), thyroid surgery (THYR), gastric surgery (GAST) and gallbladder surgery (CHOL).

Risk categories

The risk of each SPs, following the NNIS System risk index, applies a range from zero to three points for the absence or presence of the following three composite variables including:

1. Wound classification, as either contaminated or dirty
2. An ASA preoperative assessment score of 3, 4, or 5

3. Duration of the operation exceeding the 75th percentile of operation time

Statistical analysis

To characterize the data using descriptive statistics, n (%) was used for categorical variables and the mean (S.D.), and median (IQR) were used for continuous variables. A Multiple binary logistic regression model with a backward elimination method was used to find the risk factors for the SSI. To find the significant difference between the bi-variate samples in independent groups, the unpaired sample t-test was used. To find the significance in categorical data chi-square test was used. In all the above statistical tools a p-value≤0.05 was considered as a significant level.

Ethics approval

The study protocol was approved by the Institutional Ethics Committee (CSP/18/SEP/73/249).

Results

Patient population and characteristics

After obtaining ethics approval a total of 1,496 patients were enrolled in the study; however, from this 106 patients withdrew their consent and 28 did not turn up; leaving 1,362 patients to complete the study. The rate of SSI identified in the study was 12.6%. The results showed that the female population had higher SSI rates than that of their male counterparts (57.9% Vs. 40.3%). There were no patients in this study who were classified under the dirty wound class.

Patient demographics as well as clinical and surgical characteristics of the patients having undergone various surgeries and the significant risk factors associated with SSI in this study are depicted in (Table 1). The multivariate binary logistic regression via the backward Wald method confirmed that multiple-dose postoperative prophylaxis, duration, age nor duration of surgery were not significantly associated with the rates of SSI. Of the potential patient and procedure-related risk factors, female gender, ASA score III, Adherence to hospital guidelines, diabetes mellitus (DM) & hypertension (HTN) and pre-operative hospital stays >7 days were both independently and significantly associated with SSI (Table 2).

The duration of operation median (IQR) was found to be 143 (95.25) minutes. The 75th percentile NNIS T value (Minutes) and risk of SSI occurrence among various surgical procedures in the study patients are shown in (Table 3).

Microbial resistance towards various SAP among SSI patients

In total, 59.6% had Gram-positive organism and 40.4% had Gram-negative organism. The various organisms isolated from this study and their resistant towards SAP included: 33.9% *S. aureus* isolates with 8.1% being found to be resistant to Cloxacillin, 21.0% of *E. faecalis* isolates, 6.4% resistant towards Ampicillin, Ciprofloxacin, 19.8% of *E. coli* isolates, 12.2% were resistant to 3rd generation Cephalosporin, 11.1% of Coagulase-negative *Staphylococcus* isolates, 2.3% were resistant to Cloxacillin, 6.4% of *K. pneumoniae* isolates, 1.7% showed resistant to 3rd generation Cephalosporin, 5.2% of *P. aeruginosa* isolates 1.1% had resistance towards cefotaxime and 2.3% of Methicillin-resistant staphylococcus aureus (MRSA) isolates 1.1% showed resistance to Vancomycin, Linezolid and Cotrimoxazole.

Monomicrobial and Poly microbial growth towards various wound classes in SSI patients

Both monomicrobial and polymicrobial growth as well as risk of SSI, classified by wound class, are depicted in (Table 4).

Table 1 Baseline demographics, clinical and surgical characteristics of study patients

Variables	Patients without SSI (n=1191) n (%)	Patients with SSI (n=171) n (%)	p-value
Age (in years)			
Mean±S.D.	49.09±14.30	54.30±15.18	0.09
Gender			
Male	647 (90.36)	69 (9.64)	0.03
Female	520 (84.00)	99 (16.00)	
Transgender	24 (88.89)	3 (11.11)	
Wound class			
Clean	744 (87.63)	105 (12.37)	0.12
Clean-contaminated	429 (87.20)	63 (12.80)	0.23
Contaminated	18 (85.71)	3 (14.29)	0.01
Dirty	0 (0.00)	-	-
Personal habits/abuse			
Smoker and alcohol	384 (90.35)	41 (9.65)	0.02
Alcohol	261 (91.90)	23 (8.10)	0.56
Smoking	217 (77.22)	64 (22.78)	0.19
Others	329 (88.44)	43 (11.56)	0.21
Medical conditions			
DM & HTN	343 (86.18)	55 (13.82)	0.02
Obesity	183 (97.56)	26 (12.44)	0.14
DM	150 (83.80)	29 (16.20)	0.12
Anaemia	96 (85.71)	16 (14.29)	0.03
HTN	113 (86.26)	18 (13.74)	0.50
Hypothyroidism	62 (89.86)	7 (10.14)	0.80
Hyperkalaemia	31 (79.49)	8 (20.51)	0.60
No co morbidity	213 (94.66)	12 (5.33)	0.31
Types of surgery			
Elective	860 (88.30)	114 (11.70)	0.02
Emergency	331 (85.31)	57 (14.69)	<0.01
ASA score			
Class I	367 (87.17)	54 (12.83)	0.05
Class II	280 (93.65)	19 (6.35)	
Class III	504 (83.72)	98 (16.28)	
Class IV	40 (100)	0 (0.00)	
Pre-operative hospital stays (days)			
0-1	356 (94.68)	20 (5.32)	
2-7	314 (87.47)	45 (12.53)	0.24
>7	521 (83.09)	106 (1.69)	
Drain used			
Yes	475 (79.97)	119 (20.03)	0.12
No	716 (93.23)	52 (6.77)	
Duration of surgery (minutes)			
30	780 (96.18)	31 (3.82)	
30-60	287 (121.25)	61 (17.53)	0.12
>60	124 (61.08)	79 (38.91)	
SAP redosing intervals			
Yes	519 (88.27)	69 (11.73)	0.21
No	672 (86.82)	102 (13.18)	

ASA=American Society of Anesthesiologists, DM=diabetes mellitus, HTN=hypertension, SAP=surgical antibiotic prophylaxis, SSI=surgical site infection
Pearson's chi-square was used to find influencing risk factors for SSI (except for age, mean±S.D was used).
p-value=significant at 0.01<p-value<0.05.

Table 2 Multivariate binary logistic regression analysis of risk factors for SSI in various surgical patients

Variable	RR (95% CI)	p-value[a]
SAP		
Duration of prophylaxis		
Single dose[b]	Reference	
Multiple postoperative doses for <24 hours	1.9 (1.2–7.0)	0.26
Multiple postoperative doses for >24 hours	1.1 (0.7–6.2)	0.69
Timing of administration of prophylaxis		
>60 minute before incision	1.8 (1.6–3.4)	0.75
31–60 minute before incision	1.2 (0.6–2.6)	1.42
1–30 minute before incision	Reference	
During or after incision	2.5 (1.2–6.8)	0.25
Patient- and procedure-related variables		
Age (years)	1.1 (0.9–1.2)	0.19
Medical condition		
DM & HTN	2.3 (1.1–4.0)	0.05
Anaemia	0.5 (0.2–1.0)	0.32
Female sex	1.4 (0.8–3.4)	0.04
ASA score		
I	Reference	
II	1.5 (0.6–3.8)	0.08
III	2.8 (0.8–6.2)	0.02
Adherence to hospital guidelines	1.2 (1.7–2.5)	<0.01
Pre-operative hospital stays (days)	Reference	
0–1		
2–7	3.8 (1.8–6.2)	0.12
>7	5.1 (3.1–8.8)	0.04

ASA=American Society of Anaesthesiologists, RR=relative risk, CI=confidence interval, SAP=surgical antibiotic prophylaxis, DM=diabetes mellitus, HTN=hypertension
[a]Multivariate binary logistic regression via the backward Wald method was used to find influencing risk factors, [b]Zero postoperative doses p-value=significant at 0.01<p-value<0.05.

Table 3 Risk index and SSI rates in patients having undergone various surgical procedures

Surgical procedure code	Surgical procedure	No. of procedures (N=1,362)	Surgical duration 75th percentile (Minutes)	Risk index category	SSI n=171 n (%)
AAA	Abdominal aortic aneurysm repair	393	177	1, 2	48 (12.21)
APPY	Appendix surgery	281	84	2	42 (14.95)
BILI	Bile duct, liver or pancreatic surgery	242	302	2	51 (21.07)
COLO	Colon surgery	154	220	0, 1	9 (9.09)
GAST	Gastric surgery	53	124	0, 1	4 (7.55)
PRST	Prostate surgery	139	162	1	2 (1.44)
THYR	Thyroid surgery	74	120	1, 2	9 (12.16)
HYST	Abdominal hysterectomy	26	112	1	1 (3.85)

values are presented as n (%), unless defined otherwise
SSI=surgical site infection

Table 4 Polymicrobial and Monomicrobial infections and SSI among various wound classes

Microorganism growth	n (%)	Wound class SSI (n=171) n (%)			p-value
		Clean n=105 (%)	Clean-contaminated n=63 (%)	Contaminated n=3 (%)	
Monomicrobial	103 (60.23)	68 (66.02)	34 (33.01)	1 (0.97)	0.01
Polymicrobial	68 (39.77)	37 (54.41)	29 (42.65)	2 (2.94)	0.01

SSI=surgical site infection
values are presented as n (%), unless defined otherwise, Pearson's chi-square method was used to find the influencing risk factors for SSI.
p-value=significant at 0.01<p-value<0.05.

Discussion

The various risk factors and SSI in patients with SAP in the Indian population were studied, and the results were compared with the available literature's. The rate of SSI identified in this study was 12.6%, which falls within the expected range of the SSI rate in India; ranging from 1.6% to 38%[16]. Although 12.6% is considered low for an low-and middle-income countries (LMIC), it is higher compared to many high-income countries, wherein, SSI rates typically range from 0.9-5.2%[17,18]. Among LMICs a lower rate of SSI has been reported in South America and South East Asia[19,20].

Some investigators have speculated that older age increases the prevalence of co-morbid conditions, severity of acute illnesses, and a decreased host response to bacterial invasion all of which appear to contribute to an increased risk of SSI; however, no such associations were observed in this current study[21,22]. One study has demonstrated that gonadal hormones differently modulate cutaneous wound healing, with androgen contributing to stress-induced impairment of the healing; whereas, oestrogen did not. Few researchers have reported male patients as having a higher risk of SSI than females[23,24], in contrast, this study reported a higher SSI risk among female patients. According to the available literature, patients with DM and HTN often have macrovascular and microvascular diseases and, consequently, peripheral pulses may be present despite local tissue hypoxia in the microcirculation of the foot. This hypoxia results in decreased blood flow to the surgical site, which subsequently decreases a patient's ability to mount an immune response toward off infection. Similarly, smoking and alcohol can decrease the oxygen levels, distorting a patient's immune system and can delay healing. Additionally, it reduces the level of tumour necrosis factor and produces changes in the inflammatory macrophage responses to interferon-γ; therefore, increasing the risk of infection at the wound site. These risk factors have been strongly associated with SSI in this study[25,26]. Multiple researchers reported wound class, duration of surgery, transfusions, length of preoperative hospital stay, polytrauma patients and obesity, have been associated with SSI. These factors have been observed from specific surgeries like orthopaedics and cardiac surgeries; however, such significant risk factor associations were not observed in this study[27,28]. Although duration of surgical procedures is a highly reliable indicator for difficult procedures and underlying conditions, and in addition to longer surgeries, obesity and preoperative stay have shown a statistical association with SSI[27,29], such associations were not observed in this study.

Various surgeries; such as BILI, with a risk index of 2 had 21.07% of SSI, APPY had 14.95% of SSI, AAA had 12.21% of SSI and THYR had 12.16% of SSI. This study identified that a risk index of 2 was associated with a higher SSI rate than of 0, 1. A similar result from Sachin M. Patel et al reported that the rate of SSI increased with the increase in the risk index[30].

Pre-operative hospital stays are associated with a greater incidence of SSI; however, this link is obscured mostly by infections or concurrent conditions[5]. In this study the variable length of preoperative stay and occurrence of SSI had no statistical correlation, though a similar finding was observed from Mujagic et al[31]; contrarily, few studies have emphasized that preoperative stays have been linked to SSI[32,33]. Patients that received pre-operative SAP treatment have had a lower incidence of SSI; which is a well-known fact[34]. However, a study conducted by Shahane et al provided strong support to our findings, in that they reported a marginal increase of SSI with preoperative SAP[35]. In contrast to previous studies, a non-significant association between the use of a drain during surgery and an increased risk of SSI was observed in many studies[16,36].

SSIs have occurred more frequently during emergency surgeries (14.69%) than during elective surgeries (11.7%), which is consistent with a few studies that concluded emergency surgeries to be 2.6 times more likely to result in SSIs than elective surgeries[37]. However in contrast, Shahane V et al. found that elective surgeries were more prone to SSI (7.9%) than emergency surgeries (2.7%)[35].

Intraoperative redosing of antibiotics has been shown to be important for longer operating procedures[19]. This study did not find any significant association between redoing SAP and SSI. However, a prior study from Zanetti et al represented a significant association, with a 16% reduction in the overall risk of SSI attributable to redosing SAP[38].

From infected surgical incision sites, this study isolated multiple strains of bacteria; among them *S. aureus* was the most frequent organism (33.9%), isolated from SSI patients; followed by *E. faecalis*, *E. coli*, *K. Pneumonia*, coagulase-negative *Staphylococcus*, *P. aeruginosa* and MRSA: a similar observation has been reported by Ling et al[20]. In this present study: *S. Aureus*, *E. faecalis*, *E. coli*, *K. Pneumonia*, coagulase-negative *Staphylococcus*, *P. aeruginosa* and MRSA, showed resistance to cloxacillin, 3rd generation cephalosporin, ampicillin, ciprofloxacin and vancomycin. This is concordant with other findings from Peter et al[39].

A significant association between monomicrobial (p-value<0.001) and polymicrobial infections and SSI was found in this study. This could be due to the misuse of antibiotics without culture report or nonadherence with hospital guidelines. This finding was in tandem with the study conducted by Negi et al[40].

Limitations

This study has a few limitations in that there was an exclusion of patient charts for those whom were below 18 years, and it was restricted to general surgery. Additionally, there was a lack of detailed information concerning the type of surgical procedure, individual surgeons, type of operating room and ventilation.

Other limitations of this study, were that it was conducted at a single center and data on the intra-operative temperature of patients, personal hygiene and dirty surgeries were not collected nor analysed in this study.

Conclusion

The prescribing procedure of SAP was not adequate, as most of the SAP were not given according to the microbial culture sensitivity report; thus, escalating the risk of SSI in pre and post-operative cases. Multiple postoperative dosing did not contribute to a reduction of the incidence of SSI. This study unveils the various influencing risk factors; such as age, female gender, types of surgery, ASA score, nonadherence to hospital guidelines, and monomicrobial and polymicrobial growth that have been associated with SSI. It is, therefore, necessary to make efforts to ensure safer surgical procedures, with a minimal degree of wound contamination and adherence to well-designed hospital policies; based on standard guidelines. These aspects enable us a gain a better understanding of SSI, which may have therapeutic implications.

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Conflict of interest

There are no conflicts of interest to declare.

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