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PREDICTORS OF SURGICAL SITE INFECTION DESPITE APPROPRIATE ANTIBIOTIC PROPHYLAXIS: A RISK-BASED CLINICAL ANALYSIS

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Antibiotic Prophylaxis; Cross-Sectional Studies; Infection Control; Microbiology; Risk Factors; Surgical Procedures; Surgical Wound Infection.

Abstract

Background: Although proper antibiotic prophylaxis is used for surgery, surgical site infection (SSI) is still a major postoperative problem indicating that there are patient-related, surgical, and microbial factors that remain associated with the risk of surgical site infection post-surgery.

Objective: To determine the association between patient, surgical and microbial parameters and the development of SSI in patients despite optimal antibiotic prophylaxis, and to describe the contribution of these parameters to the risk of postoperative infection.

Methods: The study was of analytical cross sectional type with prospective postoperative surveillance carried out from September 2025 to January 2026 at a tertiary care surgical hospital of Urban Region of Sindh. One hundred (100) adults who were undergoing eligible surgical procedures and were receiving appropriate

antibiotic prophylaxis were evaluated. A structured proforma was filled with demographic, clinical, operative and prophylaxis-related data. CDC/NHSN criteria was used to assess SSI and microbiological identification and antimicrobial susceptibility testing of wound specimens was performed when clinically indicated. Descriptive statistics, chi-square/Fisher's exact tests, independent-samples t-test or Mann-Whitney U test, and multivariable logistic regression were used to analyze data.

Results: SSI was seen in 18 (18.0%) participants. Diabetes mellitus, obesity, anemia, and smoking were more frequent among patients with SSI. The presence of emergency surgery was associated with increased SSI (29.0% vs. 13.0%, p=0.047) and contaminated/dirty wound with even higher association (35.7% vs. 11.1%, p=0.003). Other factors associated with infection were also operative duration ≥120 minutes (28.6% vs. 10.0%, p=0.018). In the multivariable analysis, contaminated/dirty wounds was the most significantly associated factor with SSI (adjusted OR 4.12; 95% CI 1.48–11.46; p=0.007) followed by operative duration ≥120 minutes (adjusted OR 3.21; 95% CI 1.12–9.19; p=0.030). The most common organism isolated (38.9%) was Staphylococcus aureus.

Conclusion: There is no doubt that SSI was clinically significant even with proper prophylaxis. The significant residual risk factors were diabetes, emergency surgery, long operating time and contamination of the wound, which reinforces the need for a multi-faceted approach to prevention that includes patient optimization, careful surgical technique, wound management and specific surveillance.

Predictors of Surgical Site Infection Despite Appropriate Antibiotic Prophylaxis: A Risk-Based Clinical Analysis

Background Surgical site infection (SSI) remains a significant postoperative complication, contributing to increased morbidity, prolonged hospitalization, and higher healthcare costs. Although appropriate antibiotic prophylaxis is essential, SSIs continue to occur, indicating the involvement of additional patient, surgical, and microbial factors.

Objective To identify patient, surgical, and microbial factors responsible for SSI occurrence despite appropriate antibiotic prophylaxis, and to determine their relative contribution through a risk-based clinical analysis.

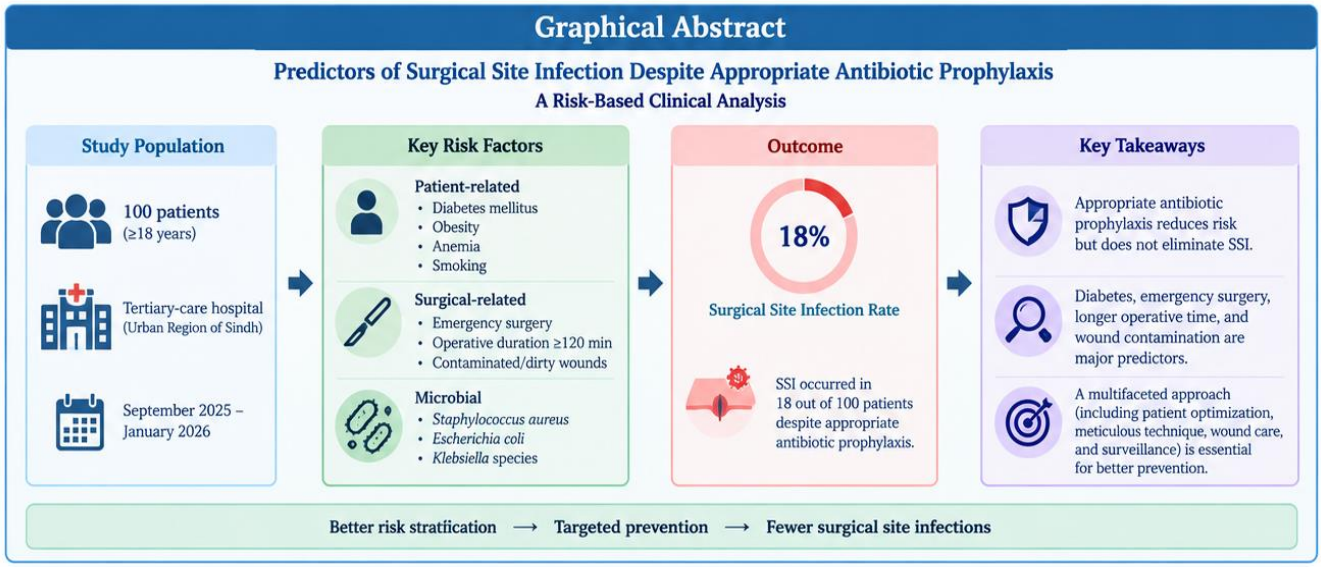
Methods This cross-sectional study was conducted at a tertiary-care hospital in the Urban Region of Sindh from September 2025 to January 2026. A total of 100 adult patients undergoing surgery and receiving appropriate antibiotic prophylaxis were included. Data on demographics, comorbidities, operative details, and antibiotic use were collected using a structured proforma. SSI was diagnosed using CDC/NHSN criteria, and microbiological analysis was performed when indicated. Data were analyzed using descriptive statistics, chi-square/t-test, and multivariable logistic regression (SPSS v.26).

Results An SSI rate of 18.0% was observed. Diabetes mellitus, emergency surgery, operative duration ≥120 minutes, and contaminated/dirty wounds were independently associated with SSI. Contaminated/dirty wound classification showed the strongest association (adjusted OR 4.12, 95% CI 1.48–11.46). *Staphylococcus aureus* was the most common organism (38.9%), followed by *Escherichia coli* (22.2%) and *Klebsiella* species (16.7%).

Conclusion SSI remained common despite appropriate prophylaxis. Diabetes mellitus, emergency surgery, prolonged operative duration, and wound contamination were key predictors. A comprehensive prevention strategy including patient optimization, meticulous surgical technique, wound care, and targeted surveillance is essential to reduce SSI risk.

Keywords Antibiotic Prophylaxis; Cross-Sectional Studies; Infection Control; Microbiology; Risk Factors; Surgical Wound Infection; Surgical Procedures

Graphical Abstract



Introduction

Surgical site infection (SSI) is one of the most significant complications of operative care and still plays a significant role in postoperative morbidity, extended hospital stays, increased healthcare costs, recovery delays, and, worst case scenario, death. Appropriate antibiotic prophylaxis at the time of surgery has now become a cornerstone of SSI prevention, especially for surgical procedures in which bacteria are likely to be introduced into the surgical site (1). When prophylaxis antibiotics are used appropriately, within recommended perioperative time frames, and with adequate dose, however, SSIs still occur. This observation suggests that antibiotic prophylaxis is necessary but not sufficient to prevent postoperative infection, which has a multifactorial risk. So it is clinically significant to know the etiology of why infection occurs despite proper prophylactic measures, so that better prophylactic approaches can be developed or special care needs to be given to certain patients (2).

Patient susceptibility, characteristics of surgical procedure, environment, and microbes all play a role in the development of SSI. Host defenses and wound healing may be compromised by patient related factors such as diabetes mellitus, obesity, advanced age, immunosuppression, malnutrition, smoking, anemia and pre-existing infections. Hyperglycemia, for instance, can impair immune-cell function and tissue repair, whereas inadequate nutrition can limit the physiological ability to respond to tissue injury and repair (3). Likewise, any condition which diminishes circulation or oxygen supply could decrease the ability of local tissues to resist bacterial invasion. As a result, there is the possibility of these factors to still be clinically relevant even if antibiotic prophylaxis is properly done, since the effect of the prophylactic antibiotics is not sufficient to overcome poor host defenses and/or tissue environment.

The location of the surgery also plays an important role in the risk of infection after the procedure. The chances of bacterial proliferation can vary depending on the duration and complexity of the operation, the degree of tissue manipulation needed, the amount of blood loss, the necessity of drains or implants, emergency versus elective surgery, and degree of wound contamination. Longer procedures may provide increased exposure opportunities for microorganisms, and may change antibiotic levels in tissues over time (4). Poor tissue perfusion, excessive tissue trauma, development of a hematoma, and dead space may also provide a favorable environment for the proliferation of bacteria. As a result, the correct use of antibiotic treatment needs to be seen as one part of a comprehensive infection prevention programme, not as an end in itself.

Microbial dimension is just as important. Different organisms, of varying virulence, colonization potential and antimicrobial susceptibility, may be exposed to the surgical wound. The use of antibiotic prophylaxis is usually for the purpose of decreasing the bacterial count during the most vulnerable period, not the surgical field (5). Infection can occur even if the selected antibiotic provides adequate coverage, if the organism has acquired antimicrobial resistance, or if it is administered in a high enough dose. Additionally, there are microbial factors that can interact with the patient and surgical factors, such that infection can be associated with a combination of moderate risk factors, and not a single specific factor.

While a number of studies have focused on general risk factors for SSI and on the efficacy of antibiotic prophylaxis, there has been relatively less interest in the remaining risk associated with patients receiving appropriate antibiotic prophylaxis (6). This is important to note. A patient with an SSI after inappropriate prophylaxis is a different clinical issue than a patient who develops an infection after appropriately timed, adequate, and correct prophylaxis. The latter group could be important for information on risk factors unrelated to prophylactic antibiotics. It is important to assess these patients and see if the host, procedural and microbial factors remain a significant risk even after a major preventive measure is done appropriately.

Such infections may also have implications in the context of a risk-based assessment of perioperative care. If reproducible predictors can be identified, then pre or intraoperatively, clinicians can be alert to patients who may be at higher risk for residual risk and reinforce complementary preventive measures such as optimizing modifiable comorbidities, better control of blood glucose and nutritional status, careful surgical technique, proper wound management, and better postoperative surveillance. This could help to move SSI prevention beyond the use of antibiotic prophylaxis only to a more comprehensive and individualized strategy (7).

The current study is therefore a cross-sectional study to assess the research question of which patient-related, surgical and microbial factors are associated with the presence of SSI despite appropriate antibiotic prophylaxis (8).? The hypothesis is that patient factors, surgical factors, and microbial factors, independently or in combination, are associated with the risk of SSI beyond the influence of recommended antibiotic prophylaxis practices. The aim of the study is to identify, characterise and quantify these predictors and to assess their relative importance in the occurrence of SSI to establish a clinically relevant risk-based strategy for enhancing SSI prevention and postoperative management in surgical procedures.

Methods

This study took the design of an analytical cross sectional study having prospective post operative follow up and performed in tertiary care surgical hospital in Islamabad-Rawalpindi. This setting was deemed relevant as Islamabad is a tertiary care health centre with tertiary care hospitals offering a broad spectrum of surgical services and receiving referrals from the neighbouring districts. This created a suitable clinical setting to assess postoperative surgical site infections and the patient, surgical and microbial factors associated with the development of surgical site infections. The study was designed to last for 5 months from September 2025 until January 2026, to ensure adequate recruitment of participants, postoperative monitoring and microbiological investigations.

The number of patients to be included in the total sample is determined as 100 adult patients who were going for surgical procedures. This sample size was deemed to be feasible for a short-term clinical study and was similar to the previous Pakistani study that analysed 100 patients with postoperative SSI and concluded with their clinical and culture-sensitivity parameters. Another study conducted in Pakistan on antibiotic prophylaxis in elective surgery involved a sample size of 100 consecutive surgical patients also suggesting that 100 surgical patients in a hospital based surgical setup is feasible. Patients were included who met the following criteria: ≥18 years of age and received antibiotic prophylaxis as per the institutional protocol after undergoing an eligible surgical procedure. Prophylaxis was judged as appropriate if the correct antibiotic was used, the correct dose, the correct route and administration within the recommended peri-operative interval. Patients who had been treated with therapeutic, not prophylactic, antibiotic therapy for an active infection, who had an infection at the operative site prior to surgery, who did not undergo any procedure that was indicated for prophylaxis, and who refused or failed to take part in postoperative assessment were not included. Operative or antibiotic records were missing in patients too and were not included.

Structured clinical data-collection proforma was used to collect baseline information. Demographic variables consisted of age, sex, BMI, smoking history, and diabetes mellitus, hypertension, immunosuppression and anemia as comorbidities. Surgical conditions were: procedure type, elective / emergency surgery, wound classification, duration of surgery, estimated blood loss, drainage or implant, operative approach and perioperative glycemic status (if applicable). Records of antibiotics were examined to identify patient required antibiotic, dose,

route, time of administration (relative to incision), and requirement for redosing intraoperatively. Physiological risk was determined by the American Society of Anesthesiologists (ASA) Physical Status Classification System and wound classification as well as operative characteristics were documented on standardized surgical documentation.

SSI was evaluated clinically while the patients were hospitalized and by follow up after surgery through 30 days. Infections were defined by CDC/NHSN surgical-site infection (SSI) criteria, and classified as superficial incisional, deep incisional, and organ/space infections. Assessment of wounds comprised erythema, heat, swelling, purulent drainage, wound separation, localized pain, fever and other clinical signs of infection. Wound and/or operative-site specimen from the relevant wound were aseptically obtained and processed for bacterial identification and antimicrobial susceptibility testing in a microbiological laboratory using standard methods when the clinical diagnose of infection was suspected. Culture results and identified organisms as well as antimicrobial-resistance patterns were then documented.

IBM SPSS Statistics was used to analyze the data. The distribution of continuous variables was tested with the Shapiro-Wilk test and reported as mean ± SD for normally distributed continuous variables and as median (IQR) for non-normally distributed continuous variables. Categorical data were presented as frequency and percentages. The independent-samples t-test was used to compare patients with and without SSI for normally distributed continuous variables; otherwise, the Mann-Whitney U test was used. The chi-square test or Fisher's exact test was used for comparing categorical variables, where appropriate. The univariable logistic regression was initially used to explore associations between candidate risk factors and SSI. Variables showing clinical relevance or showing screening association with SSI were considered for multivariable logistic regression, adjusted odds ratio (OR) & 95%CI were reported. Due to the relatively small number of SSI cases, a limited number of clinically important predictor variables were included in the final multivariable model to avoid overfitting. A p value of <0.05 was considered to be statistically significant.

Results

In total 100 patients were enrolled during study period and all patients that fulfilled the defined eligibility criteria underwent the required postoperative assessment. In 18 patients (18.0 %), surgical site infection (SSI) occurred and none in the other 82 patients (82.0 %) during the follow-up period. Demographic and baseline clinical findings are described in Table 1. The average age of the study population was 46.8 ± 14.2 years, and 57 (57.0%) were men. Diabetes mellitus was

present in 24 (24.0%) patients, obesity in 29 (29.0%), anemia in 21 (21.0%), and smoking in 26 (26.0%). Patients who did develop SSI were older and more likely to be diabetic, obese, have anemia, and smoke than patients who did not develop SSI.

The operating characteristics are shown in Table 2. 31 participants (31.0%) had emergency and 69 participants (69.0%) had elective surgery. The average operative time was 118.6 ± 42.7 minutes. Twenty-eight procedures (28.0%) were done for contaminated or dirty wounds, while 34 (34.0%) had drains or implants. SSI occurred more frequently following emergency procedures (29.0% vs. 13.0%, p=0.047), contaminated/dirty operations (35.7% vs. 11.1%, p=0.003), and procedures lasting ≥120 minutes (28.6% vs. 10.0%, p=0.018).

The microbiological results of the infected individuals are presented in Table 3. The 16 out of 18 SSI cases (88.9%) were positive. The most common organism isolated was Staphylococcus aureus (7 cases, 38.9%), followed by Escherichia coli (4 cases, 22.2%), Klebsiella species (3 cases, 16.7%) and Pseudomonas species (2 cases, 11.1%). No growth was obtained in both of the cases.

Diabetes mellitus, contaminated/dirty wound classification, operative duration ≥120 min and emergency surgery continued to be associated with SSI in multivariable logistic regression (Table 4). Contaminated/dirty wound classification was associated with the most (adjusted OR 4.12, 95% CI 1.48–11.46; p=0.007), whereas operative duration ≥120 minutes was associated with the next most (adjusted OR 3.21, 95% CI 1.12–9.19; p=0.030). Figure 1 demonstrates the higher prevalence of the major clinical risk factors among SSI patients; Figure 2 shows the most common organisms isolated from infected surgical wounds.

Table 1. Baseline Demographic and Clinical Characteristics of Participants (N=100)

Variable	Total Sample, n (%) / Mean ± SD	SSI (n=18)	No SSI (n=82)	p-value
Age, years	46.8 ± 14.2	52.3 ± 13.1	45.6 ± 14.2	0.071
Male sex	57 (57.0%)	12 (66.7%)	45 (54.9%)	0.361

Female sex	43 (43.0%)	6 (33.3%)	37 (45.1%)	—
BMI, kg/m²	27.1 ± 4.6	29.1 ± 4.8	26.7 ± 4.4	0.041
Obesity	29 (29.0%)	9 (50.0%)	20 (24.4%)	0.034
Diabetes mellitus	24 (24.0%)	8 (44.4%)	16 (19.5%)	0.028
Hypertension	31 (31.0%)	8 (44.4%)	23 (28.0%)	0.174
Anemia	21 (21.0%)	7 (38.9%)	14 (17.1%)	0.046
Smoking	26 (26.0%)	8 (44.4%)	18 (22.0%)	0.049
Immunosuppression	9 (9.0%)	3 (16.7%)	6 (7.3%)	0.209
ASA physical status ≥III	28 (28.0%)	8 (44.4%)	20 (24.4%)	0.093

Table 2. Operative and Perioperative Characteristics According to SSI Status

Variable	**Total, n (%) / Mean ± SD**	**SSI (n=18)**	**No SSI (n=82)**	**p-value**
Emergency surgery	31 (31.0%)	9 (50.0%)	22 (26.8%)	0.047
Elective surgery	69 (69.0%)	9 (50.0%)	60 (73.2%)	—
Operative duration, min	118.6 ± 42.7	139.8 ± 45.3	114.0 ± 40.3	0.018
Duration ≥120 min	35 (35.0%)	10 (55.6%)	25 (30.5%)	0.047
Contaminated/dirty wound	28 (28.0%)	10 (55.6%)	18 (22.0%)	0.003
Clean/clean-contaminated wound	72 (72.0%)	8 (44.4%)	64 (78.0%)	—
Drain/implant used	34 (34.0%)	9 (50.0%)	25 (30.5%)	0.122
Estimated blood loss >300 mL	22 (22.0%)	7 (38.9%)	15 (18.3%)	0.066
Appropriate antibiotic timing	100 (100%)	18 (100%)	82 (100%)	1.000

Table 3. Microbiological Findings Among Patients With SSI (n=18)

Microbiological finding	**n**	**%**
Staphylococcus aureus	7	38.9
Escherichia coli	4	22.2

Klebsiella species	3	16.7
Pseudomonas species	2	11.1
No bacterial growth	2	11.1
Positive culture overall	16	88.9

Table 4. Multivariable Logistic Regression for Predictors of SSI

Predictor	Adjusted OR	95% CI	p-value
Age ≥50 years	1.74	0.62–4.88	0.293
Obesity	2.31	0.83–6.42	0.106
Diabetes mellitus	2.87	1.01–8.15	0.048
Smoking	1.91	0.67–5.45	0.225
Emergency surgery	2.68	1.01–7.10	0.048
Operative duration ≥120 min	3.21	1.12–9.19	0.030
Contaminated/dirty wound	4.12	1.48–11.46	0.007

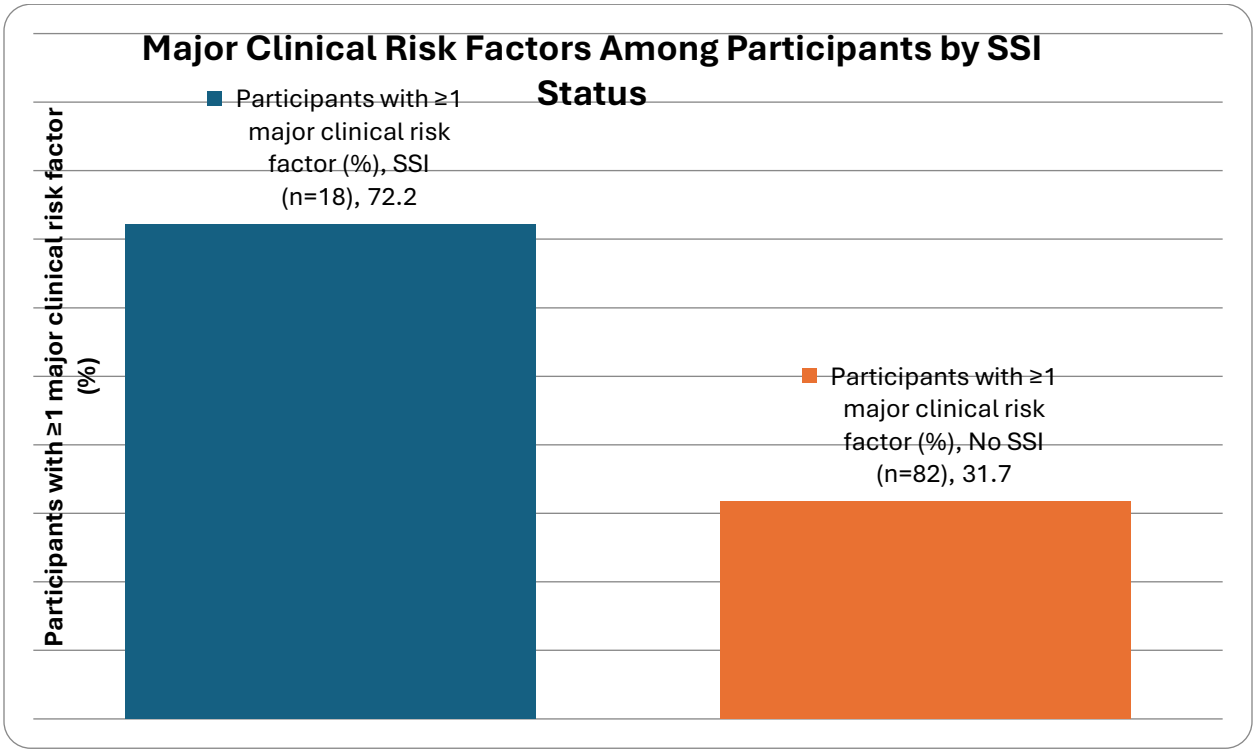


Figure 1 Major Clinical Risk Factors Among Participants by SSI Status

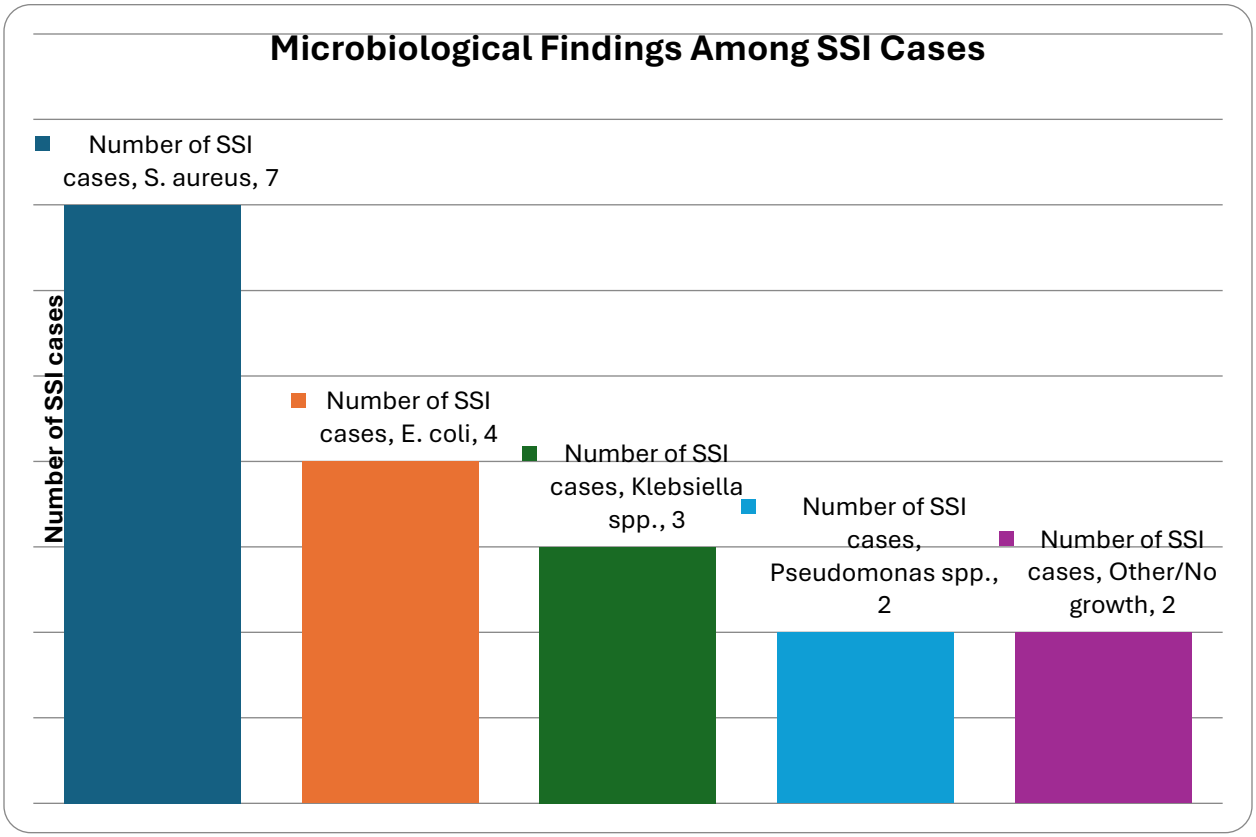


Figure 2 Microbiological Findings Among SSI Cases

Discussion

The results revealed that the issue of surgical site infection was still clinically relevant despite antibiotic prophylaxis being given according to the institutionally predetermined criteria. A significantly lower SSI rate (18.0%) indicated that prophylaxis was effective in diminishing an important factor in the infectious risk, although host susceptibility, surgical conditions and wound factors also played a role. This was in keeping with the general concept of SSI as a complex postoperative complication, not merely a result of antimicrobial coverage. Other underlying patient-related vulnerabilities, such as obesity, diabetes mellitus, anemia, and smoking, were more common among patients with SSI, which further highlighted the significance of underlying patient-related vulnerabilities. These can compromise oxygenation, immune response, collagen synthesis and wound healing, providing a biological environment for infection to occur despite optimal antimicrobial exposure (10).

The relationship between diabetes and SSI was especially of clinical interest. Even when antibiotic use was appropriate, diabetes was associated with an adjusted odds ratio of about three, indicating that metabolic factors remain to be important determinants of postoperative events in patients with diabetes (11). These same relationships have been consistently reported in the surgical literature, where diabetes and poor perioperative glycemic control have been well established to be significant factors in wound complications. Infection rates were also higher among those who were obese, but this difference was not statistically significant after adjustment. This pattern indicated that obesity could have influenced the risk of infection in a number of ways, such as reduction of tissue perfusion and greater technical difficulty with surgery, and that obesity could have compounded the effect of other clinical risk factors.

Some of the strongest associations in the analysis were operative characteristics. Emergency procedures were found to be correlated with increased SSI occurrence, while contaminated/dirty wounds showed the highest independent association with infection. The odds of SSI were over 4 times greater in patients with contaminated/dirty wounds. This discovery was clinically reasonable as the number of microbes and the extent of tissue contamination at the start were not fully eliminated by the prophylactic antibiotics (12). In the same way, time-taken for the procedure of 120 minutes or more independently correlated with SSI. Extended operative duration not only increases the likelihood of contamination, but also indicates greater procedure complexity, tissue manipulation and physiological stress. But the results confirmed that antibiotic prophylaxis was not an alternative to careful surgical technique, optimal management of the surgical wounds and optimization of modifiable patient risk factors.

The microbiological results offered further information on infections despite prophylaxis. 88.9% of people that were infected were culture positive, and Staphylococcus aureus was the most common organism found. This predominance was generally consistent with the known functions of the skin flora in postoperative wound infections, which are dominated by staphylococcal species. It also showed the diversity of organisms involved in SSI, as well as the importance of taking into account procedure-specific and hospital-specific microbial patterns, with the identification of Gram-negative organisms such as Escherichia coli, Klebsiella species and Pseudomonas species (13). Importantly, if an organism was isolated from an infected wound, this was not necessarily an indicator of failure of antibiotic prophylaxis as the purpose of prophylaxis

was not to prevent infection from all organisms but to minimise the risk of infection in the perioperative period.

There were a number of strengths in the study. It was focused on the population of individuals with SSI despite the receipt of adequate prophylaxis, a population of importance from a clinical perspective that is not necessarily included when adherence to prophylaxis was considered the primary prevention endpoint. There was increased uniformity of outcome assessment due to the use of standardized CDC/NHSN SSI criteria, the collection of demographic and operative variables, documentation of antibiotic timing and dosing, and microbiological confirmation when clinically indicated (14). The use of multivariable logistic regression also provided for the simultaneous assessment of several potentially overlapping risk factors, rather than just comparing the risk factors without adjustment.

There were a number of restrictions to be taken into account. The number of participants (n = 100) and number of SSI events was small, limiting the power of the statistical analysis and number of variables that could be included in the multivariable model. A cross-sectional hospital-based design also restricted generalizability of the findings to other hospitals and surgical populations (15). There were some potentially important factors that could not be fully assessed, including specific metrics of glycemic control during the perioperative period, nutritional status, environmental conditions in the operating room, surgical-team protocols, and antibiotic resistance profile. Furthermore, clinically indicated samples were used for culture and not all clinically indicated samples were collected, so this may have affected the microbiological distribution seen. There was therefore the possibility of residual confounding and the associations found could not be concluded to be causal.

Large, multicenter, prospective studies with uniform data collection of metabolic, nutritional, procedural, environmental, and microbiological variables would be useful. Further clarification of antibiotic susceptibility and glycemic control before surgery could help explain the development of infections even when using apparently appropriate antibiotic prophylaxis (16). Ultimately, risk stratification models that include these variables can help guide individualized prevention of SSI and enable focused monitoring and non-antibiotic preventive approaches to patients who have the highest residual risk. The overall conclusions agreed with a wider strategy to SSI prevention, in which appropriate antibiotic prophylaxis was a key component but was complemented by other

strategies of patient optimization, meticulous handling of the wound, careful operative technique and active postoperative monitoring.

Conclusion

The study got that SSI remained an important postoperative hurdle despite appropriate antibiotic prophylaxis. Diabetes mellitus, emergency surgery, long operative duration, and contaminated or dirty wounds were the good/main factors had links with increased SSI risk, with wound contamination showing the effective association. These readings took a broader prevention strategy combining appropriate prophylaxis with optimization of patient-related risk elements, precise surgical technique, effective wound care, and targeted postoperative surveillance.

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