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Effectiveness Of Preoperative Antibiotic Prophylaxis Timing in Reducing Surgical Site Infections: A Prospective Observational Study

Dr. Sanjeev R Navalyal[1], Dr. Praveen Kumar K H[2], Dr. Prafullachandra Hoogar[3], Dr. Lata K Mankani[*4]

[1] Associate Professor, Department of General Surgery, KLE Jagadguru Gangadhar Mahaswamigalu Moorusavirmath Medical College and Hospital, Hubli, KLE Academy of Higher Education and Research, Deemed to be University, Belagavi, Karnataka, India – 590010

[2] Assistant Professor, Department of General Surgery, KLE Jagadguru Gangadhar Mahaswamigalu Moorusavirmath Medical College and Hospital, Hubli, KLE Academy of Higher Education and Research, Deemed to be University, Belagavi, Karnataka, India – 590010

[3] Assistant Professor, Department of General Surgery, KLE Jagadguru Gangadhar Mahaswamigalu Moorusavirmath Medical College and Hospital, Hubli, KLE Academy of Higher Education and Research, Deemed to be University, Belagavi, Karnataka, India – 590010

[*4]Dr. Lata K Mankani, Assistant Professor, Department of Obstetrics & Gynecology, KLE Jagadguru Gangadhar Mahaswamigalu Moorusavirmath Medical College and Hospital, Hubli, KLE Academy of Higher Education and Research, Deemed to be University, Belagavi, Karnataka, India – 590010

***Corresponding Author:**
Dr. Lata K Mankani

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ABSTRACT

Background: Surgical site infections (SSIs) remain a significant cause of postoperative morbidity, increased healthcare costs, and prolonged hospital stays despite advances in surgical techniques and antimicrobial therapy. The timing of preoperative antibiotic prophylaxis administration has been identified as a critical factor in SSI prevention, yet optimal timing parameters remain debated. This study aimed to evaluate the effectiveness of different preoperative antibiotic prophylaxis timing intervals in reducing SSIs across various surgical procedures.

Methods: A prospective observational study was conducted at a tertiary care teaching hospital from January 2023 to December 2023. We enrolled 450 patients undergoing clean and clean-contaminated surgeries who received prophylactic antibiotics. Patients were categorized into three groups based on antibiotic administration timing: Group A (120-60 minutes before incision), Group B (60-30 minutes before incision), and Group C (30-0 minutes before incision). Patient demographics, comorbidities, surgical characteristics, timing of antibiotic administration, and development of SSI within 30 days post-surgery were recorded. Statistical analysis was performed using chi-square tests and multivariate logistic regression to identify significant associations.

Results: The overall SSI rate was 7.6% (34/450 patients). SSI rates by timing group were: Group A (120-60 minutes) 12.1%, Group B (60-30 minutes) 4.2%, and Group C (30-0 minutes) 6.8%. Multivariate analysis revealed that antibiotic administration 60-30 minutes before incision was associated with significantly lower SSI rates compared to other timing intervals (adjusted OR 0.38, 95% CI 0.21-0.67, p=0.001). Additional independent risk factors for SSI included diabetes mellitus, prolonged operative time (>2 hours), emergency surgeries, and higher ASA scores.

Conclusion: This study demonstrates that optimal timing of preoperative antibiotic prophylaxis is 60-30 minutes before surgical incision. Implementation of standardized protocols emphasizing this timing window could significantly reduce SSI rates. Hospital antimicrobial stewardship programs should focus on this timing parameter as a key quality improvement measure.

Keywords: *Surgical site infection, antibiotic prophylaxis, timing, prospective study*

1. INTRODUCTION

Surgical site infections (SSIs) represent one of the most prevalent healthcare-associated infections globally, imposing substantial burdens on healthcare systems, patients, and society [1,2]. Despite significant advances in infection control practices, surgical techniques, and antimicrobial therapy, SSIs continue to affect approximately 11% of surgical patients worldwide, with rates up to 20% in some low and middle-income countries [3]. The Centers for Disease Control and Prevention (CDC) has established that SSIs account for approximately 20% of all healthcare-associated infections, making them the third most common nosocomial infection [4].

The economic impact of SSIs is substantial, with an estimated annual cost exceeding $3.5 billion in the United States alone [5]. Each SSI is associated with approximately 7-11 additional days of hospitalization and increases the risk of readmission by fivefold [6]. Furthermore, patients who develop SSIs have a 2-11 times higher risk of mortality compared to those without infections [7]. These statistics underscore the critical importance of effective preventive strategies in reducing the incidence of SSIs.

The pathophysiology of SSIs involves complex interactions between host factors, microbial characteristics, and perioperative circumstances. The risk of SSI begins at the moment of surgical incision when skin flora, exogenous microbes from the environment, or endogenous bacteria from manipulated organs can contaminate the surgical site [8]. This contamination can lead to infection when the bacterial load exceeds the host's defense mechanisms, facilitated by factors such as tissue damage, foreign materials, and impaired local blood supply [9].

Surgical antibiotic prophylaxis (SAP) has been established as one of the most effective measures for preventing SSIs. The primary objective of SAP is to achieve adequate tissue concentrations of appropriate antibiotics at the time of incision and throughout the procedure to prevent bacterial colonization and subsequent infection [10]. The effectiveness of SAP depends on several factors, including the choice of antibiotic, dosage, route of administration, and critically, the timing of administration.

The importance of appropriate timing of preoperative antibiotic prophylaxis has been recognized for decades, dating back to experimental studies by Burke in 1961, which demonstrated that antibiotics were most effective when tissue concentrations were adequate at the time of bacterial contamination [11]. This principle has formed the foundation for current recommendations regarding the timing of SAP. However, despite general consensus on the importance of timing, the optimal window for antibiotic administration before surgical incision remains a subject of debate.

Current guidelines from major organizations such as the American Society of Health-System Pharmacists (ASHP), the Infectious Diseases Society of America (IDSA), the Surgical Infection Society (SIS), and the World Health Organization (WHO) recommend administering prophylactic antibiotics within 60 minutes before surgical incision [12,13]. However, these recommendations are based on limited and sometimes conflicting evidence, with variations in the precise timing window suggested.

A landmark study by Classen et al. demonstrated that antibiotics administered within 2 hours before incision were associated with the lowest SSI rates [14]. However, a systematic review and meta-analysis by de Jonge et al. examining data from 54,552 patients across 14 studies found that within the 120-minute window before incision, no clear differential effects could be identified between different timing intervals, challenging the widely accepted recommendation of administration within 60 minutes before incision [15].

The TAPAS (Timing of Preoperative Antibiotic Prophylaxis and Surgical Site Infection) observational cohort study by de Jonge et al. specifically examined the 60-minute window before incision, dividing it into 60-30 minutes and 30-0 minutes intervals [16]. This study found no conclusive evidence of a difference in SSI risk between these narrower intervals, further complicating the determination of optimal timing.

Pharmacokinetic considerations suggest that different antibiotics may have different optimal timing windows. For instance, antibiotics with shorter half-lives or those requiring longer infusion times, such as vancomycin and fluoroquinolones, may necessitate different administration schedules compared to cephalosporins [17]. Furthermore, patient factors such as body mass index, comorbidities, and the type of surgical procedure may influence the optimal timing of antibiotic prophylaxis.

The 2017 CDC guidelines for the prevention of SSIs specifically address the timing of antibiotic prophylaxis, recommending administration within 120 minutes before incision, while considering the pharmacokinetics of the specific antibiotic used [4]. This represents a shift from the previously strict 60-minute window, acknowledging that certain antibiotics, particularly vancomycin and fluoroquinolones, require longer infusion times to minimize toxicity and should therefore be started earlier.

Recent advancements in understanding the role of antibiotic pharmacodynamics in SSI prevention have also highlighted the importance of maintaining adequate antibiotic concentrations throughout the surgical procedure. Studies have shown that redosing during lengthy procedures or in cases of significant blood loss is crucial for maintaining effective antibiotic levels [18]. Current guidelines recommend redosing at intervals of one to two times the half-life of the antibiotic if the procedure duration exceeds this timeframe [12].

In the context of antimicrobial stewardship and the global challenge of antimicrobial resistance, optimizing antibiotic prophylaxis practices, including timing, is essential. By ensuring that antibiotics are administered at the most effective time, healthcare providers can maximize the protective benefits while minimizing unnecessary antibiotic use [19]. This approach aligns with the broader goals of antimicrobial stewardship: to improve patient outcomes while reducing the development of antibiotic resistance.

The discrepancies in the existing literature highlight the need for further research to clarify the optimal timing of preoperative antibiotic prophylaxis across different surgical settings. Most previous studies have been retrospective or have focused on specific surgical procedures, limiting their generalizability. Additionally, many studies have not adequately controlled for potential confounding factors that may influence SSI risk, such as patient characteristics, surgical complexity, and perioperative care practices.

In India, where the burden of SSIs is estimated to be higher than in high-income countries, with reported rates ranging from 5% to 24% across different surgical disciplines, understanding the optimal timing of antibiotic prophylaxis is particularly crucial [20]. Despite this, there is a paucity of prospective studies from Indian healthcare settings examining the relationship between the timing of antibiotic prophylaxis and SSI outcomes.

The present study aims to address this knowledge gap by prospectively evaluating the effectiveness of different preoperative antibiotic prophylaxis timing intervals in reducing SSIs across various surgical procedures in an Indian tertiary care setting. By focusing on the specific timing windows of 120-60 minutes, 60-30 minutes, and 30-0 minutes before incision, this study seeks to provide evidence-based guidance for optimizing antibiotic prophylaxis practices and ultimately reducing the burden of SSIs in surgical patients.

2. AIMS AND OBJECTIVES

Primary Aim: To evaluate the effectiveness of different preoperative antibiotic prophylaxis timing intervals in reducing the incidence of surgical site infections in patients undergoing clean and clean-contaminated surgeries.

Specific Objectives:

1. To determine the incidence of surgical site infections among patients receiving preoperative antibiotic prophylaxis at different time intervals before surgical incision (120-60 minutes, 60-30 minutes, and 30-0 minutes).
2. To identify the optimal timing window for preoperative antibiotic prophylaxis that is associated with the lowest rate of surgical site infections.
3. To analyze patient-related and procedure-related risk factors that may influence the relationship between antibiotic timing and surgical site infection development.
4. To evaluate compliance with current institutional guidelines for preoperative antibiotic prophylaxis timing and identify barriers to adherence.
5. To assess the microbial profile of surgical site infections and antibiotic susceptibility patterns when infections occur despite prophylaxis.

3. MATERIALS AND METHODS

Study Design and Setting

This prospective observational study was conducted in the Department of General Surgery at KAHER's Jagadguru Gangadhar Mahaswamigalu Moorusaviramath Medical College, Hubballi, India, from January 1, 2023, to December 31, 2023.

Study Population

Consecutive adult patients (≥18 years) undergoing elective or emergency clean and clean-contaminated surgeries in the Department of General Surgery were eligible for inclusion. Surgical procedures were classified according to the CDC wound classification system [4].

Inclusion Criteria:

1. Patients aged 18 years and above
2. Patients undergoing clean or clean-contaminated surgeries
3. Patients receiving preoperative antibiotic prophylaxis
4. Patients willing to provide informed consent and complete the 30-day follow-up period

Exclusion Criteria:

1. Patients with active infection at the time of surgery
2. Patients who had received antibiotics within 72 hours before surgery for reasons other than surgical prophylaxis
3. Patients undergoing contaminated or dirty surgeries
4. Immunocompromised patients (HIV, active malignancy on chemotherapy, transplant recipients on immunosuppressants)
5. Patients with documented allergy to the standard prophylactic antibiotics
6. Pregnant women

Sample Size Calculation

Based on previous studies [15,16] reporting an overall SSI rate of approximately 10% and an expected reduction to 5% with optimal antibiotic timing, a sample size of 434 patients was calculated to be necessary to detect this difference with 80% power and a significance level of 0.05. Accounting for a 5% dropout rate, the final sample size was determined to be 450 patients.

Data Collection

Trained research assistants collected data using a standardized case report form. The following information was recorded:

1. **Patient characteristics**: Age, gender, body mass index (BMI), smoking status, comorbidities (diabetes mellitus, hypertension, chronic obstructive pulmonary disease, coronary artery disease, chronic kidney disease), American Society of Anesthesiologists (ASA) physical status score
2. **Surgical details**: Type of surgery, surgical approach (open/laparoscopic), duration of surgery, wound class (clean/clean-contaminated), emergency or elective status, use of drains, intraoperative blood loss, body temperature
3. **Antibiotic prophylaxis details**: Type of antibiotic, dose, timing of administration relative to surgical incision, repeat doses if applicable
4. **Outcome measures**: Development of SSI within 30 days of surgery, type of SSI (superficial, deep, or organ/space), day of diagnosis, microbiological profile (when cultures were obtained), antibiotic susceptibility patterns

Study Protocol

Patients were enrolled preoperatively after obtaining informed consent. Standard institutional protocol for preoperative antibiotic prophylaxis was followed, which recommended administration of the first dose of prophylactic antibiotics within 60 minutes before surgical incision. The actual timing of antibiotic administration was precisely documented by the anesthesia team.

The timing of antibiotic administration was categorized into three groups:

- **Group A**: 120-60 minutes before incision
- **Group B**: 60-30 minutes before incision
- **Group C**: 30-0 minutes before incision

The choice of antibiotic was based on institutional guidelines:

- For clean surgeries: Cefazolin 1-2g IV
- For clean-contaminated surgeries: Cefazolin 1-2g IV + Metronidazole 500mg IV
- For patients with β-lactam allergy: Clindamycin 600-900mg IV

Intraoperative redosing was administered if the duration of surgery exceeded two half-lives of the antibiotic or if blood loss exceeded 1500 ml. Postoperative antibiotics were continued only if clinically indicated and not as routine prophylaxis.

Follow-up and SSI Surveillance

All patients were followed for 30 days postoperatively to monitor for the development of SSI. Follow-up assessments were conducted:

1. Daily during hospitalization
2. At the time of discharge
3. At scheduled postoperative visits (7, 14, and 30 days after surgery)

4. Additional visits if patients developed signs or symptoms of infection

Patients who did not return for scheduled follow-up visits were contacted by telephone to assess their wound status and were requested to visit the outpatient department if any concerns were identified.

SSI Definition and Classification

SSIs were defined and classified according to the CDC/National Healthcare Safety Network (NHSN) criteria [4]:

1. **Superficial incisional SSI**: Infection involving only the skin and subcutaneous tissue of the incision, occurring within 30 days after surgery, with at least one of the following:
    - Purulent drainage from the superficial incision
    - Organisms isolated from an aseptically obtained culture
    - At least one of the following signs or symptoms: pain or tenderness, localized swelling, redness, or heat
    - Diagnosis of superficial incisional SSI by the surgeon or attending physician
2. **Deep incisional SSI**: Infection involving deep soft tissues (e.g., fascial and muscle layers) of the incision, occurring within 30 days after surgery, with at least one of the following:
    - Purulent drainage from the deep incision
    - Deep incision that spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms: fever (>38°C), localized pain, or tenderness
    - An abscess or other evidence of infection involving the deep incision found on direct examination, during reoperation, or by histopathologic or radiologic examination
    - Diagnosis of deep incisional SSI by the surgeon or attending physician
3. **Organ/space SSI**: Infection involving any part of the anatomy (e.g., organs or spaces) other than the incision, opened or manipulated during surgery, occurring within 30 days after surgery, with at least one of the following:
    - Purulent drainage from a drain placed into the organ/space
    - Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space
    - An abscess or other evidence of infection involving the organ/space found on direct examination, during reoperation, or by histopathologic or radiologic examination
    - Diagnosis of an organ/space SSI by a surgeon or attending physician

Microbiological Assessment

When SSI was suspected, wound swabs or tissue samples were collected for culture and sensitivity testing before initiating antibiotic therapy. All samples were processed in the institutional microbiology laboratory according to standard protocols. Antibiotic susceptibility testing was performed using the Kirby-Bauer disk diffusion method following Clinical and Laboratory Standards Institute (CLSI) guidelines.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics software (version 26.0). Descriptive statistics were presented as frequencies and percentages for categorical variables and as means ± standard deviations or medians with interquartile ranges for continuous variables, depending on the distribution of data.

The primary outcome measure was the incidence of SSI within 30 days of surgery. The chi-square test or Fisher's exact test was used to compare the incidence of SSI among the three timing groups and to assess the association between categorical variables and SSI. The Student's t-test or Mann-Whitney U test was used to compare continuous variables between patients with and without SSI.

Univariate logistic regression analysis was performed to identify potential risk factors for SSI. Variables with a p-value < 0.1 in the univariate analysis were included in a multivariate logistic regression model to identify independent risk factors for SSI. Results were presented as odds ratios (ORs) with 95% confidence intervals (CIs). A p-value < 0.05 was considered statistically significant.

4. RESULTS

Patient Characteristics

A total of 483 patients were initially assessed for eligibility, of whom 450 were included in the final analysis. Thirty-three patients were excluded: 15 had received antibiotics within 72 hours before surgery, 10 had active infection at the time of

surgery, 5 were immunocompromised, and 3 withdrew consent.

The mean age of the study population was 48.6 ± 15.8 years, with a male-to-female ratio of 1.3:1 (254 males, 196 females). The demographic and clinical characteristics of the patients are presented in Table 1. The most common comorbidity was diabetes mellitus (22.2%), followed by hypertension (18.7%) and obesity (BMI ≥ 30 kg/m²) (14.2%).

Table 1: Demographic and Clinical Characteristics of the Study Population

Characteristic	Total (n=450)	No SSI (n=416)	SSI (n=34)	P-value
Age (years)				0.042*
Mean ± SD	48.6 ± 15.8	47.9 ± 15.6	56.4 ± 16.2	
Gender				0.682
Male	254 (56.4%)	236 (56.7%)	18 (52.9%)	
Female	196 (43.6%)	180 (43.3%)	16 (47.1%)	
BMI (kg/m²)				0.025*
<18.5	42 (9.3%)	40 (9.6%)	2 (5.9%)	
18.5-24.9	182 (40.4%)	172 (41.3%)	10 (29.4%)	
25-29.9	162 (36.0%)	151 (36.3%)	11 (32.4%)	
≥30	64 (14.2%)	53 (12.7%)	11 (32.4%)	
Comorbidities				
Diabetes mellitus	100 (22.2%)	85 (20.4%)	15 (44.1%)	0.001*
Hypertension	84 (18.7%)	75 (18.0%)	9 (26.5%)	0.219
COPD	36 (8.0%)	32 (7.7%)	4 (11.8%)	0.399
Coronary artery disease	32 (7.1%)	29 (7.0%)	3 (8.8%)	0.682
Chronic kidney disease	22 (4.9%)	19 (4.6%)	3 (8.8%)	0.273
Smoking status				0.048*
Current smoker	94 (20.9%)	82 (19.7%)	12 (35.3%)	
Ex-smoker	68 (15.1%)	63 (15.1%)	5 (14.7%)	
Never smoker	288 (64.0%)	271 (65.1%)	17 (50.0%)	
ASA score				0.004*
I	196 (43.6%)	189 (45.4%)	7 (20.6%)	
II	186 (41.3%)	169 (40.6%)	17 (50.0%)	
III	62 (13.8%)	54 (13.0%)	8 (23.5%)	
IV	6 (1.3%)	4 (1.0%)	2 (5.9%)	

*Statistically significant ($p<0.05$) COPD: Chronic Obstructive Pulmonary Disease ASA: American Society of

Anesthesiologists

Surgical Characteristics

The distribution of surgical procedures and their characteristics are summarized in Table 2. The most common surgical procedures were cholecystectomy (18.2%), hernia repair (16.9%), and appendectomy (14.7%). The majority of surgeries were elective (76.7%) and clean-contaminated (58.2%). The mean duration of surgery was 95.3 ± 42.6 minutes.

Table 2: Surgical Characteristics and Antibiotic Prophylaxis Details

Characteristic	Total (n=450)	No SSI (n=416)	SSI (n=34)	P-value
Type of surgery				0.092
Cholecystectomy	82 (18.2%)	78 (18.8%)	4 (11.8%)	
Hernia repair	76 (16.9%)	73 (17.5%)	3 (8.8%)	
Appendectomy	66 (14.7%)	62 (14.9%)	4 (11.8%)	
Thyroidectomy	42 (9.3%)	40 (9.6%)	2 (5.9%)	
Breast surgery	38 (8.4%)	36 (8.7%)	2 (5.9%)	
Colorectal surgery	36 (8.0%)	29 (7.0%)	7 (20.6%)	
Gastroduodenal surgery	30 (6.7%)	26 (6.3%)	4 (11.8%)	
Small bowel surgery	28 (6.2%)	24 (5.8%)	4 (11.8%)	
Splenectomy	12 (2.7%)	11 (2.6%)	1 (2.9%)	
Others	40 (8.9%)	37 (8.9%)	3 (8.8%)	
Surgical approach				0.013*
Open	254 (56.4%)	228 (54.8%)	26 (76.5%)	
Laparoscopic	196 (43.6%)	188 (45.2%)	8 (23.5%)	
Wound classification				0.040*
Clean	188 (41.8%)	179 (43.0%)	9 (26.5%)	
Clean-contaminated	262 (58.2%)	237 (57.0%)	25 (73.5%)	
Surgery status				0.002*
Elective	345 (76.7%)	326 (78.4%)	19 (55.9%)	
Emergency	105 (23.3%)	90 (21.6%)	15 (44.1%)	
Duration of surgery (minutes)				0.001*
Mean ± SD	95.3 ± 42.6	93.1 ± 40.8	120.6 ± 55.2	
<60	128 (28.4%)	123 (29.6%)	5 (14.7%)	
60-120	214 (47.6%)	202 (48.6%)	12 (35.3%)	
>120	108 (24.0%)	91 (21.9%)	17 (50.0%)	

Characteristic	Total (n=450)	No SSI (n=416)	SSI (n=34)	P-value
Use of drains	186 (41.3%)	166 (39.9%)	20 (58.8%)	0.032*
Intraoperative blood loss (mL)				0.004*
<200	310 (68.9%)	294 (70.7%)	16 (47.1%)	
200-500	98 (21.8%)	86 (20.7%)	12 (35.3%)	
>500	42 (9.3%)	36 (8.7%)	6 (17.6%)	
Intraoperative hypothermia (<36°C)	74 (16.4%)	65 (15.6%)	9 (26.5%)	0.102

*Statistically significant (p<0.05)

Antibiotic Prophylaxis Details

All patients received preoperative antibiotic prophylaxis according to institutional protocol. Cefazolin was the most commonly used antibiotic (68.9%), followed by the combination of cefazolin and metronidazole (25.8%). Clindamycin was used in 24 patients (5.3%) with documented β-lactam allergy. The distribution of patients according to the timing of antibiotic administration is presented in Table 3.

Table 3: Antibiotic Prophylaxis Details and Timing Groups

Characteristic	Total (n=450)	No SSI (n=416)	SSI (n=34)	P-value
Type of antibiotic				0.731
Cefazolin	310 (68.9%)	288 (69.2%)	22 (64.7%)	
Cefazolin + Metronidazole	116 (25.8%)	106 (25.5%)	10 (29.4%)	
Clindamycin	24 (5.3%)	22 (5.3%)	2 (5.9%)	
Timing of antibiotic administration				0.003*
Group A (120-60 minutes before incision)	132 (29.3%)	116 (27.9%)	16 (47.1%)	
Group B (60-30 minutes before incision)	192 (42.7%)	184 (44.2%)	8 (23.5%)	
Group C (30-0 minutes before incision)	126 (28.0%)	116 (27.9%)	10 (29.4%)	
Intraoperative redosing required	72 (16.0%)	62 (14.9%)	10 (29.4%)	0.027*
Duration of postoperative antibiotics				<0.001*
None (single dose)	214 (47.6%)	208 (50.0%)	6 (17.6%)	
24 hours	172 (38.2%)	158 (38.0%)	14 (41.2%)	
>24 hours	64 (14.2%)	50 (12.0%)	14 (41.2%)	

*Statistically significant (p<0.05)

Incidence and Characteristics of SSI

The overall incidence of SSI was 7.6% (34/450 patients). The SSI rates according to the timing of antibiotic administration were: Group A (120-60 minutes) 12.1% (16/132), Group B (60-30 minutes) 4.2% (8/192), and Group C (30-0 minutes) 7.9% (10/126). The difference in SSI rates between the three groups was statistically significant (p=0.003).

Among the 34 patients who developed SSI, 21 (61.8%) had superficial incisional SSI, 9 (26.5%) had deep incisional SSI,

and 4 (11.8%) had organ/space SSI. The median time to SSI diagnosis was 7 days (range: 3-18 days). Wound cultures were obtained from all patients with SSI, and pathogens were identified in 28 cases (82.4%). The most common organisms isolated were Staphylococcus aureus (42.9%), Escherichia coli (25.0%), and Pseudomonas aeruginosa (14.3%).

Table 4: Characteristics of Surgical Site Infections

Characteristic	Number (%)
SSI Incidence by Timing Group	
Group A (120-60 minutes before incision)	16/132 (12.1%)
Group B (60-30 minutes before incision)	8/192 (4.2%)
Group C (30-0 minutes before incision)	10/126 (7.9%)
Type of SSI	
Superficial incisional	21 (61.8%)
Deep incisional	9 (26.5%)
Organ/space	4 (11.8%)
Time to SSI diagnosis (days)	
Median (range)	7 (3-18)
≤7 days	19 (55.9%)
8-14 days	12 (35.3%)
15-30 days	3 (8.8%)
Microbiology (n=28 positive cultures)	
Staphylococcus aureus	12 (42.9%)
Methicillin-sensitive	8 (28.6%)
Methicillin-resistant	4 (14.3%)
Escherichia coli	7 (25.0%)
Pseudomonas aeruginosa	4 (14.3%)
Klebsiella species	3 (10.7%)
Enterococcus species	2 (7.1%)
Treatment Required	
Antibiotics only	20 (58.8%)
Wound drainage/debridement	11 (32.4%)
Reoperation	3 (8.8%)
Additional hospital stay due to SSI (days)	

Characteristic	Number (%)
Mean ± SD	8.2 ± 4.6

Risk Factors for SSI

Univariate analysis identified several potential risk factors for SSI, including advanced age, obesity, diabetes mellitus, smoking, higher ASA score, open surgical approach, clean-contaminated wounds, emergency surgery, longer duration of surgery, use of drains, higher intraoperative blood loss, and timing of antibiotic prophylaxis (Table 5).

Variables with a p-value < 0.1 in the univariate analysis were included in the multivariate logistic regression model. After adjusting for confounding factors, the following variables remained independent risk factors for SSI:

1. Diabetes mellitus (adjusted OR 2.67, 95% CI 1.21-5.87, p=0.015)
2. ASA score III-IV (adjusted OR 2.35, 95% CI 1.03-5.36, p=0.042)
3. Emergency surgery (adjusted OR 2.18, 95% CI 1.04-4.58, p=0.039)
4. Duration of surgery >120 minutes (adjusted OR 2.94, 95% CI 1.34-6.45, p=0.007)
5. Antibiotic administration timing (reference: Group B [60-30 minutes])
    - Group A [120-60 minutes]: adjusted OR 2.87, 95% CI 1.19-6.92, p=0.019
    - Group C [30-0 minutes]: adjusted OR 1.82, 95% CI 0.70-4.72, p=0.217

Table 5: Univariate and Multivariate Analysis of Risk Factors for SSI

Risk Factor	Univariate Analysis	Multivariate Analysis
	OR (95% CI)	OR (95% CI)
Age ≥65 years	1.95 (0.94-4.06)*	1.47 (0.65-3.33)
Gender (Male vs. Female)	0.86 (0.43-1.73)	-
BMI ≥30 kg/m²	3.29 (1.53-7.07)*	1.86 (0.79-4.36)
Diabetes mellitus	3.07 (1.49-6.32)*	2.67 (1.21-5.87)*
Current smoker	2.22 (1.05-4.68)*	1.78 (0.78-4.05)
ASA score III-IV	2.71 (1.28-5.74)*	2.35 (1.03-5.36)*
Open surgical approach	2.67 (1.19-6.00)*	1.62 (0.66-3.97)
Clean-contaminated wound	2.10 (0.96-4.60)*	1.53 (0.65-3.59)
Emergency surgery	2.86 (1.41-5.81)*	2.18 (1.04-4.58)*
Duration of surgery >120 minutes	3.56 (1.77-7.17)*	2.94 (1.34-6.45)*
Use of drains	2.15 (1.06-4.35)*	1.40 (0.62-3.17)
Blood loss >500 mL	2.25 (0.88-5.75)*	1.33 (0.46-3.83)
Intraoperative hypothermia	1.95 (0.87-4.37)*	1.52 (0.62-3.70)
Timing of antibiotic prophylaxis		
Group B (60-30 min) [Reference]	1.00	1.00
Group A (120-60 min)	3.17 (1.32-7.62)*	2.87 (1.19-6.92)*

Risk Factor	Univariate Analysis	Multivariate Analysis
Group C (30-0 min)	1.98 (0.77-5.13)	1.82 (0.70-4.72)

*Statistically significant ($p<0.05$ for multivariate analysis, $p<0.1$ for univariate analysis) OR: Odds Ratio, CI: Confidence Interval

5. DISCUSSION

This prospective observational study evaluated the impact of preoperative antibiotic prophylaxis timing on the incidence of SSI in patients undergoing clean and clean-contaminated surgeries. Our findings demonstrate that the timing of antibiotic administration significantly influences SSI rates, with the 60-30 minutes interval before surgical incision being associated with the lowest risk of infection.

The overall SSI rate in our study was 7.6%, which is comparable to the reported rates of 5-10% in similar studies from other tertiary care centers in India [20]. However, this rate is higher than the 2-5% reported in high-income countries [4], highlighting the need for enhanced infection prevention strategies in resource-limited settings. The majority of SSIs (61.8%) were superficial incisional, which is consistent with previous studies [15,16].

The most significant finding of our study was the marked difference in SSI rates according to the timing of antibiotic prophylaxis. Patients who received antibiotics 60-30 minutes before incision (Group B) had the lowest SSI rate (4.2%), compared to those who received antibiotics 120-60 minutes before incision (Group A, 12.1%) or 30-0 minutes before incision (Group C, 7.9%). After adjusting for potential confounding factors, antibiotic administration 120-60 minutes before incision was associated with nearly three times higher odds of SSI compared to administration 60-30 minutes before incision (adjusted OR 2.87, 95% CI 1.19-6.92, p=0.019).

These findings align with the pharmacokinetic principles of antibiotic prophylaxis, which emphasize the importance of achieving adequate tissue concentrations at the time of incision [10,11]. When antibiotics are administered too early (120-60 minutes before incision), tissue concentrations may begin to decline before the surgical procedure commences, particularly for antibiotics with shorter half-lives such as cefazolin (half-life of 1.2-2.2 hours) [10]. Conversely, administration very close to incision (30-0 minutes) may not allow sufficient time for the antibiotic to distribute to the tissues adequately. The 60-30 minute window appears to represent the optimal balance, ensuring maximal tissue concentrations at the time of bacterial contamination.

Our results contrast with those of the systematic review and meta-analysis by de Jonge et al. [15], which found no significant difference in SSI risk when comparing administration within 120-60 minutes versus 60-0 minutes before incision. However, that meta-analysis did not specifically examine the narrower 60-30 minute window. Our findings are more in line with a recent pharmacokinetic study by Sattar et al. [17], which proposed that the ideal time to administer cefazolin is approximately 40 minutes before incision based on pharmacological profiles.

The TAPAS observational cohort study by de Jonge et al. [16] compared the 60-30 minute and 30-0 minute intervals and found no conclusive evidence of a difference in SSI risk. In contrast, our study demonstrated a trend toward higher SSI risk in the 30-0 minute group compared to the 60-30 minute group, although this difference did not reach statistical significance in the multivariate analysis (adjusted OR 1.82, 95% CI 0.70-4.72, p=0.217). This discrepancy might be attributed to differences in patient populations, surgical procedures, or antibiotic regimens.

In addition to antibiotic timing, our study identified several independent risk factors for SSI, consistent with previous research. Diabetes mellitus was associated with a 2.67-fold increased risk of SSI, likely due to impaired wound healing, vascular insufficiency, and altered immune function in diabetic patients [7,8]. Higher ASA scores (III-IV) reflecting poorer physiological status were also associated with increased SSI risk (adjusted OR 2.35), as were emergency surgeries (adjusted OR 2.18) and prolonged operative time >120 minutes (adjusted OR 2.94).

The microbiology of SSIs in our study showed a predominance of Staphylococcus aureus (42.9%), followed by gram-negative organisms such as Escherichia coli (25.0%) and Pseudomonas aeruginosa (14.3%). This is consistent with the expected microbial profile in clean and clean-contaminated surgeries, where skin flora and enteric organisms are the most common pathogens [8]. Notably, 33.3% of Staphylococcus aureus isolates were methicillin-resistant, highlighting the growing challenge of antimicrobial resistance in surgical infections.

Our study has several strengths. First, its prospective design allowed for accurate documentation of antibiotic timing and standardized assessment of outcomes. Second, the inclusion of various surgical procedures enhances the generalizability of our findings. Third, the 30-day follow-up period ensured comprehensive capture of SSIs, including those occurring after discharge. Fourth, the multivariate analysis controlled for potential confounding factors, providing a more accurate assessment of the independent effect of antibiotic timing.

However, several limitations should be acknowledged. First, as an observational study, it cannot establish causality

definitively. Second, despite multivariate adjustment, residual confounding by unmeasured variables cannot be excluded. Third, the study was conducted at a single center, potentially limiting the generalizability of the findings to other settings with different patient populations or surgical practices. Fourth, we did not measure serum or tissue antibiotic concentrations, which would have provided direct evidence of the pharmacokinetic principles underlying our findings.

The clinical implications of our study are significant. Our findings support a more specific recommendation for the timing of preoperative antibiotic prophylaxis, favoring administration 60-30 minutes before surgical incision for cephalosporins. This narrower window provides more precise guidance compared to the broader "within 60 minutes" recommendation in current guidelines [12,13]. Implementation of standardized protocols emphasizing this optimal timing window could significantly reduce SSI rates and associated morbidity, mortality, and healthcare costs.

Future research should focus on several areas. First, randomized controlled trials comparing different timing intervals would provide stronger evidence. Second, pharmacokinetic studies measuring tissue antibiotic concentrations at different time points would help elucidate the underlying mechanisms. Third, studies examining the optimal timing for specific antibiotics, particularly those with different pharmacokinetic profiles, would help refine recommendations further. Fourth, implementation research evaluating strategies to improve compliance with optimal timing would translate these findings into clinical practice.

6. CONCLUSION

This prospective observational study demonstrates that the optimal timing of preoperative antibiotic prophylaxis is 60-30 minutes before surgical incision, associated with significantly lower SSI rates compared to administration 120-60 minutes before incision. Other independent risk factors for SSI include diabetes mellitus, higher ASA scores, emergency surgery, and prolonged operative time. These findings suggest that current guidelines recommending administration "within 60 minutes" before incision should be refined to emphasize the 60-30 minute window for optimal effectiveness.

Implementation of standardized protocols emphasizing this optimal timing window could significantly reduce SSI rates and associated morbidity, mortality, and healthcare costs. Hospital antimicrobial stewardship programs should focus on this timing parameter as a key quality improvement measure. Future research should validate these findings through randomized controlled trials and pharmacokinetic studies, as well as explore optimal timing for specific antibiotics with different pharmacokinetic profiles.

REFERENCES

[1] Magill SS, Edwards JR, Bamberg W, Beldavs ZG, Dumyati G, Kainer MA, et al. Multistate point-prevalence survey of health care-associated infections. N Engl J Med. 2014;370(13):1198-208.

[2] Anderson DJ, Podgorny K, Berríos-Torres SI, Bratzler DW, Dellinger EP, Greene L, et al. Strategies to prevent surgical site infections in acute care hospitals: 2014 Update. Infect Control Hosp Epidemiol. 2014;35(6):605-27.

[3] World Health Organization. Global guidelines for the prevention of surgical site infection. 2nd ed. Geneva: World Health Organization; 2018.

[4] Berrios-Torres SI, Umscheid CA, Bratzler DW, Leas B, Stone EC, Kelz RR, et al. Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection, 2017. JAMA Surg. 2017;152(8):784-91.

[5] de Lissovoy G, Fraeman K, Hutchins V, Murphy D, Song D, Vaughn BB. Surgical site infection: incidence and impact on hospital utilization and treatment costs. Am J Infect Control. 2009;37(5):387-97.

[6] Ban KA, Minei JP, Laronga C, Harbrecht BG, Jensen EH, Fry DE, et al. American College of Surgeons and Surgical Infection Society: Surgical Site Infection Guidelines, 2016 Update. J Am Coll Surg. 2017;224(1):59-74.

[7] Owens CD, Stoessel K. Surgical site infections: epidemiology, microbiology and prevention. J Hosp Infect. 2008;70 Suppl 2:3-10.

[8] Reichman DE, Greenberg JA. Reducing surgical site infections: a review. Rev Obstet Gynecol. 2009;2(4):212-21.

[9] Cheng H, Chen BP, Soleas IM, Ferko NC, Cameron CG, Hinoul P. Prolonged operative duration increases risk of surgical site infections: a systematic review. Surg Infect. 2017;18(6):722-35.

[10] Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health Syst Pharm. 2013;70(3):195-283.

[11] Burke JF. The effective period of preventive antibiotic action in experimental incisions and dermal lesions. Surgery. 1961;50:161-8.

[12] Bratzler DW, Houck PM; Surgical Infection Prevention Guidelines Writers Workgroup. Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project. Clin Infect Dis. 2004;38(12):1706-15.

[13] World Health Organization. Summary of a systematic review on optimal timing for preoperative surgical antibiotic prophylaxis. In: Global Guidelines for the Prevention of Surgical Site Infection. Geneva: World Health Organization; 2018.

[14] Classen DC, Evans RS, Pestotnik SL, Horn SD, Menlove RL, Burke JP. The timing of prophylactic administration of antibiotics and the risk of surgical-wound infection. N Engl J Med. 1992;326(5):281-6.

[15] de Jonge SW, Gans SL, Atema JJ, Solomkin JS, Dellinger PE, Boermeester MA. Timing of preoperative antibiotic prophylaxis in 54,552 patients and the risk of surgical site infection: A systematic review and meta-analysis. Medicine (Baltimore). 2017;96(29):e6903.

[16] de Jonge SW, Boldingh QJJ, Koch AH, Daniels L, de Vries EN, Spijkerman IJB, et al. Timing of Preoperative Antibiotic Prophylaxis and Surgical Site Infection: TAPAS, An Observational Cohort Study. Ann Surg. 2021;274(4):e308-e314.

[17] Sattar R, Marshall R, Wong KY, Scott LJ, Robinson A, Ahmed A, et al. The Ideal Time to Administer Pre-operative Antibiotics: Current and Future Practices. Cureus. 2021;13(8):e17501.

[18] Thampi N, Guzman-Cottrill J, Bartlett AH, Berg W, Cantey JB, Kitt E, et al. SHEA/IDSA/APIC Practice Recommendation: Strategies to prevent surgical site infections in acute-care hospitals: 2022 Update. Infect Control Hosp Epidemiol. 2023;44(5):793-839.

[19] Heinz J, Walshaw J, Kwan JY, Long J, Carradice D, Totty J, et al. PRESS survey: PREvention of surgical site infection—a global pan-specialty survey of practice protocol. Front Surg. 2023;10:1251444.

[20] Sharma G, Sharma S, Thakur K, Gupta A, Kalsi D, Jaswal KK. Surgical site infection in a tertiary care center in North India: A prospective study. Indian J Med Microbiol. 2019;37(3):383-8.