



# Use of surgical antibiotic prophylaxis and the prevalence and risk factors associated with surgical site infection in a tertiary hospital in Malaysia

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## Abstract

**Introduction** Surgical antibiotic prophylaxis (SAP) is effective in reducing surgical site infections (SSIs). However, inappropriate use of SAP increases the risk of SSIs and antibiotic resistance.

**Objectives** To evaluate the rate of compliance with timing and duration of SAP and to evaluate the prevalence and risk factors associated with SSIs.

**Method** This retrospective study was conducted among surgical patients in a tertiary hospital in Malaysia from June to August 2019. Patients' electronic medical records were reviewed for data collection and the data were analysed using both descriptive and inferential analyses.

**Results** This analysis included 127 surgical procedures in patients with a mean age of  $43.4 \pm 22.3$  years and a male preponderance (64%). Only 37.8% received pre-operative SAP, with metronidazole (27.4%), amoxicillin-clavulanic acid (25.8%) and cefoperazone (22.6%) being the most common antibiotics. Overall, the timing of SAP was inappropriate in 92.1% of the procedures. Approximately 59% received SAP for more than 24 h. Those who received pre-operative antibiotics were less likely to receive SAP beyond 24 h (odds ratio (OR): 0.219; 95% confidence interval (CI) 0.082–0.588;  $p = 0.003$ ). The prevalence of SSI was 16.5% and was associated with the length of hospital stay after surgery (OR: 1.144; 95 CI 1.035–1.265;  $p = 0.008$ ) and duration of surgery (OR: 1.006; 95% CI 1.000–1.012;  $p = 0.038$ ), but these significances disappeared in a multivariate analysis.

**Conclusion** Inappropriate use of SAP was observed including late administration and long duration of antibiotic use. The prevalence of SSIs is high and is associated with duration of surgery and length of hospital stay after surgery. Pre-operative SAP may reduce treatment duration. Antimicrobial stewardship intervention is recommended and infection control strategies should be strengthened.

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## Key Points

There is a high rate of inappropriate timing (92.1%) and inappropriate duration (> 50%) of surgical antibiotic prophylaxis among surgical patients.

Antibiotic stewardship is recommended to improve appropriateness of surgical antibiotic prophylaxis and reduce antibiotic resistance.

Pre-operative surgical antibiotic prophylaxis should be encouraged because it is associated with shorter treatment duration.

## Introduction

Surgical site infection (SSI) is one of the most common infections affecting hospitalised patients [1–3]. SSIs are associated with significant morbidity, mortality and healthcare costs, and also reduce patients' quality of life [4–7]. The prevalence of SSIs varies among countries, with a higher prevalence reported in developing countries (5.6%) compared to developed countries (2.6–2.9%) such as the USA and European countries [8]. In addition, the incidence of SSIs is lower in high-income countries compared to low-income countries [9]. In Malaysia, the incidence of SSIs ranges between 7.7 and 13.8% [10, 11]. SSIs are usually associated with several risk factors including dirty wounds [12, 13], obesity, excessive bleeding, spinal anaesthesia, advanced age, malignancy [14], male gender [13], malnutrition, smoking cigarette, and comorbidities such as cancer and renal failure [15]. It is almost impossible to eliminate the risk of SSIs; however, SSIs can be reduced through surgical antibiotic prophylaxis (SAP) [16].

SAP is the administration of intravenous antibiotics within a certain period of time before incision with the goal of preventing infection after surgery. The effectiveness of SAP depends on the choice of antibiotics, timing, and dose and duration of administration. Therefore, inappropriate use of SAP increases the risk of SSI and antimicrobial resistance [14, 17, 18]. Available evidence indicates that there is excessive and inappropriate use of SAP among surgeons [19–22]. Furthermore, evidence has shown that inappropriate use of SAP increases healthcare costs [23, 24] and the implementation of antimicrobial stewardship reduces the costs of SAP [25]. Antimicrobial stewardship interventions are used to improve compliance with SAP guidelines [25, 26]. However, understanding local compliance with SAP among surgeons is important to design effective antimicrobial stewardship interventions that will improve compliance with SAP guidelines.

In Malaysia, there is a paucity of data describing the compliance of surgeons with SAP. Therefore, the objective of this study was to determine the compliance with SAP (timing, dosing, re-dosing and duration) among patients who had a surgical procedure in a tertiary hospital. In addition, the rate of SSIs and the factors associated with SSIs were investigated. The findings will be used to develop antimicrobial stewardship interventions to improve the quality use of SAP and reduce healthcare costs and SSI rates.

## Methods

### Study design and setting

This retrospective observational study was conducted in a 350-bed capacity teaching hospital located on the Eastern

Coast of Malaysia. The hospital provides a wide range of services including surgery, internal medicine, orthopaedic, paediatric, psychiatric, pharmacy, nursing and dentistry. The study was conducted in the hospital's surgical department, which provides both general and speciality surgical services.

### Study population

All hospitalized patients who had surgical procedures at the hospital from 1 June 2019 to 31 August 2019 were included in this study. Patients who had surgeries but had missing or incomplete anaesthesia records were excluded from the study. All surgical wound classes including clean, clean-contaminated, contaminated and dirty wounds during the period under review were included.

### Data collection

Data were collected using the hospital's electronic medical records system after obtaining approval from the hospital's Clinical Research Centre. A list containing the names and hospital registration numbers of all the patients who had a surgical procedure during the period under review was obtained from the hospital's surgical department. Patients' hospital registration numbers were used to find the medical records in the electronic record system. The data were collected by a clinical pharmacist and a trained final year pharmacy undergraduate student through the review of patients' electronic anaesthesia, medical and medications records. The data collected by the final year students were checked for accuracy by the clinical pharmacist. The information collected included: demographics (patient's age, gender, race, and dates of admission, surgery and discharge) and clinical data (weight, height, comorbidities, type of surgery, nature of surgery, type of anaesthesia, duration of surgery and estimated blood loss). Information related to SAP including antibiotic(s) administered, dose, time of administration, time of incision, additional doses given and the time when they were administered, and the duration were also collected. Information regarding the occurrence of SSIs, type of SSI, date of diagnosis and the pathogen isolated with its antibiotic sensitivities were also documented. All the information was documented on a data collection form.

### Outcome measures

The outcomes of the study included: appropriateness of timing of first dose, dose and duration of SAP, and occurrence of SSIs among the patients. Appropriateness of surgical antibiotic prophylaxis was measured using the National Antimicrobial Guidelines published by the Malaysian Ministry of Health in 2019 [27]. The outcome measures are defined as follows:

- *Appropriate timing*: A patient received intravenous SAP within 60 min before surgical incision, except fluoroquinolones and vancomycin, which should be administered within 120 min before surgical incision [27].
- *Appropriate dose of SAP*: Defined as the dose that is consistent with the recommendations of the National Antimicrobial Guideline including doubling and tripling of the doses in obese patients [27].
- *Appropriate additional dose*: Defined as the administration of an additional dose of SAP in patients with either excessive blood loss (> 1500 mL), or if the duration of the procedure exceeds two half-lives of the drug, or any factors that shorten the half-life of antibiotics, for example, extensive burning [27].
- *Appropriate duration of SAP*: SAP is discontinued within 24 h (or 48 h in cardiac surgery) after the completion of surgery [27].

Of note, the appropriateness of antibiotics used for surgical prophylaxis was not evaluated in the study because access to information such as history of allergy and availability of first-choice antibiotics at the time was limited due to the retrospective nature of the study. A SSI is defined based on the Centre for Disease Control and Prevention-National Healthcare Safety Network (CDC-NHNS) criteria [28]. SSI is any infection that occurs either at the site of incision or in any other parts of the body within 30 days after surgery in procedures with no implant or within 1 year in implant-related procedures [28]. SSIs documented in the patients' records during the period defined in the criteria were documented.

## Statistical analysis

The data were analysed using the Statistical Package for Social Sciences (SPSS, Version 22 Inc., Chicago, IL, USA), using both descriptive and inferential analyses. Categorical and continuous variables were presented as frequencies (with percentages) and mean (with standard deviations), respectively. The association between clinical and demographic variables with SSIs was determined using logistic regression analyses. *P* values less than 0.05 were considered as statistically significant.

## Results

### Patient characteristics

A total of 127 surgical procedures were included in the analysis. The mean age and standard deviation of the patients were  $43.4 \pm 22.3$  years and about two-thirds (64%) were males. The median pre-surgical and post-surgical length of

hospitalisation was 1 (range 0–12) and 2 (range 0–28) days, respectively. Mean body mass index (BMI) was  $25.9 \pm 7.4$  kg/m<sup>2</sup> and 47.2% of the patients were obese, while about 39% had comorbidities including diabetes mellitus (17.2%), hypertension (21.0%), dyslipidaemia (8.3%) and chronic kidney disease (6.4%). Table 1 summarizes the characteristics of the patients.

### Characteristics of the surgical procedures

More than 60% of the patients had an elective procedure and 22.8% suffered excessive blood loss during surgery. General anaesthesia (81.1%) was the most commonly used, while general (20.5%), urologic (18.1%) and colorectal (15.7%) surgeries were the most frequent surgeries. The most common surgical procedures were appendectomy (10.2%), hernioplasty (8.7%), incision and drainage (7.1%), percutaneous nephrolithotomy (PCNL) (6.3%) and laparotomy (5.5%). Most of the patients (53.6%) had an American Society of Anesthesiology (ASA) Physical Status Classification score of 2. Table 2 summarizes the characteristics of the surgical procedures.

### Surgical antibiotic prophylaxis

Overall, 79.5% received antibiotics either before or after surgery. Pre-operative SAP was administered in 37.8% of the procedures, with metronidazole (27.4%), amoxicillin-clavulanic acid (25.8%) and cefoperazone (22.6%) being the most commonly used antibiotics. Overall, as assessed by the National Antimicrobial Guidelines [20], appropriate timing of SAP was observed in 7.9% of the procedures. Of the 48 procedures that received pre-operative SAP, timing and dose of SAP was appropriate in 16.7% and 87.5%, respectively. The duration of SAP was more than 24 h in 59.1% of the procedures. About two-thirds (62.2%) received antibiotics after the surgery. Both oral and parenteral antibiotics were used after surgery. Cefuroxime (33.3%), metronidazole (33.3%), cefoperazone (24.6%) and ampicillin-sulbactam (14.5%) were the most commonly used intravenous antibiotics. In addition, the most common oral antibiotics used were cefuroxime (52.5%), ampicillin-sulbactam (16.4%) and metronidazole (14.8%). Table 3 describes the oral and parenteral antibiotics used for SAP.

### Factors associated with compliance with surgical antibiotic prophylaxis

There was no significant association between compliance with timing of SAP and patients' demographic, clinical and surgical characteristics. There was a significant association between the use of pre-operative SAP and the duration of SAP. Those who received pre-operative antibiotics were

**Table 1** Characteristics of the patients

Variable	Frequency	Percentage
Mean $\pm$ SD age, years	43.4 $\pm$ 22.3	
Gender		
Male	81	63.8
Female	46	36.2
Race <sup>a</sup>		
Malay	115	90.6
Chinese	7	5.5
Indian	4	3.1
Pre-surgical length of hospitalization: median (range)	1 (0–12)	
Post-surgical length of hospitalization: median (range)	2 (0–28)	
Mean $\pm$ SD BMI, kg/m <sup>2</sup>	25.9 $\pm$ 7.4	
BMI class		
Unknown	18	14.2
Underweight (< 18.5 kg/m <sup>2</sup> )	20	15.7
Normal (18.5–24.9 kg/m <sup>2</sup> )	29	22.8
Pre-obese and obese (> 25 kg/m <sup>2</sup> )	60	47.2
Presence of comorbidity	49	38.6
Mean $\pm$ SD haemoglobin, g/dL	12.6 $\pm$ 2.0	
Anaemia	38	29.9
Mean platelet count	284.2 $\pm$ 86.0	
Median creatinine (range), mmol/L	72.0 (4.50–689.0)	
Median BUN (range), mg/dL	4.6 (1.7–52.0)	

SD standard deviation, BMI body mass index, BUN blood urea nitrogen

<sup>a</sup>Missing data

less likely to receive SAP beyond 24 h [odds ratio (OR): 0.219; 95% confidence interval (CI) 0.082–0.588;  $p = 0.003$ ]. Those who received post-operative antibiotics were more likely to have SAP beyond 24 h (OR: 200.7; 95% CI 34.433–1170.406;  $p < 0.001$ ).

### Surgical site infections among the patients

Twenty-one patients (16.5%) had SSIs within 30 days post-surgery. Superficial incisional (61.9%) and organ/space (28.6%) SSIs were the most common. Pathogens isolated included: *Staphylococcus aureus*, *Klebsiella pneumonia*, *Escherichia coli*, *Citrobacter koseri* and mixed Gram-negative pathogens. Table 4 describes SSIs among the analysed patients.

### Factors associated with surgical site infections (SSIs)

There was no significant association between SSI and patients' demographic characteristics including age, gender and race. In a univariate logistic regression analysis, the length of hospital stay after surgery (OR: 1.144; 95% CI 1.035–1.265;  $p = 0.008$ ) and duration of surgery (OR: 1.006; 95% CI 1.000–1.012;  $p = 0.038$ ) were significantly

associated with SSIs. In addition, BMI increased the risk of SSI (OR 1.066; 95% CI 0.995–1.143;  $p = 0.067$ ) but the association was not statistically significant, while elective surgeries were associated with a non-significant decrease in the risk of SSIs (OR 0.391; 95% CI 0.151–1.015;  $p = 0.054$ ). Neither length of hospital stay after surgery (adjusted OR: 1.124, 95% CI 0.994–1.271;  $p = 0.062$ ) nor duration of surgery (adjusted OR: 1.003, 95% CI 0.995–1.010,  $p = 0.490$ ) showed a significant association with SSIs in the multivariate regression analysis.

### Discussion

The current study found that there is an inappropriate use of SAP and this is similar to findings of previous studies [19, 21, 22, 29]. About two-thirds of the procedures (62.2%) were performed without pre-operative SAP, and this is in contrast with the results of a study conducted in Pakistan [29]. Pre-operative SAP minimizes the risk of SSIs as described in a previous study [30], and this is not consistent with the current study due to the small sample. Overall, only 7.9% received SAP at the appropriate time, and this is consistent with a previous study conducted in Malaysia [10], but lower

**Table 2** Characteristics of the surgical procedures

Variable	Frequency (%)
Nature of surgery <sup>a</sup>	
Elective	78 (61.9)
Emergency	48 (38.1)
Type of anaesthesia <sup>a</sup>	
General	103 (81.1)
Spinal	16 (12.7)
Epidural	7 (5.6)
Unit of surgery	
General	26 (20.5)
Urology	23 (18.1)
Colorectal	20 (15.7)
Paediatric	14 (11.0)
Vascular	9 (7.1)
Genitourinary	9 (7.1)
Breast	8 (6.3)
Plastic and reconstructive	12 (9.4)
Neurosurgery	3 (2.4)
Median duration of surgery, min (range)	95.0 (13–447)
ASA score <sup>a</sup>	
1	38 (29.9)
2	68 (53.6)
3	7 (5.5)

ASA American Society of Anesthesiology

<sup>a</sup>Missing data

than the findings of studies conducted in other developing countries (16.5–94.6%) [19, 31–33]. Inappropriate timing of SAP is associated with SSIs because adequate concentrations of antibiotics in the tissue and blood from the time of incision till the end of the procedure is important to prevent SSIs [17]. In addition, early administration of SAP is an independent risk factor for SSIs [14]. Low rate of compliance with timing of SAP could be attributed to the lack of an institutional protocol for SAP [19] and lack of knowledge regarding the appropriate time to administer SAP and its impact on SSIs [34–36].

In the current study, about 60% of the patients received SAP for more than 24 h. This is lower than the results reported in previous studies [10, 19, 20] but similar to the finding of an Iranian study [33]. A previous review revealed that compliance with duration of SAP is less than 50% in most studies [22]. Excessive use of SAP is attributed to the lack of consensus among surgeons regarding guideline recommendations and the misconception that prolonged use of SAP will reduce the risk of SSIs [22]. In the current study, it was found that pre-operative SAP was significantly associated with compliance duration of SAP. Those who received SAP after surgery were more likely to have a duration of SAP beyond 24 h, although the CI is high, probably

**Table 3** Surgical antibiotic prophylaxis (SAP) used among the patients

Variable	Frequency (%)
Received antibiotics (pre- or post-surgery)	101 (79.5)
Received pre-operative antibiotics <sup>b</sup>	48 (37.8)
Antibiotics used for pre-operative SAP	
Metronidazole	17 (27.4)
Amoxicillin-clavulanic acid	16 (25.8)
Cefoperazone	14 (22.6)
Cefuroxime	7 (11.3)
Ceftriaxone	3 (4.8)
Ampicillin-sulbactam	2 (3.2)
Others	3 (4.8)
Appropriate timing of SAP <sup>a</sup>	8 (7.9)
Duration of SAP <sup>a</sup>	
Less than 24 h	26 (20.5)
More than 24 h	75 (59.1)
No antibiotics administered	22 (17.3)
Received post-operative antibiotics <sup>b</sup>	79 (62.2)
Post-operative oral antibiotics	
Cefuroxime	32 (52.5)
Ampicillin-sulbactam	10 (16.4)
Metronidazole	9 (14.8)
Amoxicillin-clavulanic acid	6 (9.8)
Cloxacillin	2 (3.3)
Others	2 (3.3)
Post-operative parental antibiotics	
Cefuroxime	23 (33.3)
Metronidazole	23 (33.3)
Cefoperazone	17 (24.6)
Ampicillin-sulbactam	10 (14.5)
Ceftriaxone	4 (5.8)
Meropenem	4 (5.8)
Amoxicillin/clavulanic acid	4 (5.8)
Piperacillin/tazobactam	4 (5.8)
Ciprofloxacin	2 (2.9)
Gentamicin	1 (1.4)
Cefepime	1 (1.4)
Cefotaxime	1 (1.4)
Cloxacillin	1 (1.4)

<sup>a</sup>Missing data

<sup>b</sup>Some patients received more than one antibiotic

due to the small sample in this study. This highlights the importance of improving compliance with timing in order to increase compliance with duration of SAP. The prolonged use of SAP is associated with a greater risk of adverse effects including *Clostridium difficile* infection [37] and increased cost of SAP [30].

The current study revealed that beta-lactam and beta-lactamase inhibitor combinations, metronidazole and



**Table 4** Surgical site infections (SSIs) among the patients

Variable	Frequency (%)
Developed a SSI	21 (16.5)
Type of SSI	
Superficial incisional	13 (61.9)
Organ/space	6 (28.6)
Deep incisional	1 (4.8)
Unknown	1 (4.8)
Pathogens isolated from SSIs	
<i>Citrobacter koseri</i>	1 (10.0)
<i>Klebsiella pneumonia</i>	2 (20.0)
<i>Escherichia coli</i>	2 (20.0)
<i>Staphylococcus aureus</i>	4 (40.0)
Mixed Gram-negative	1 (10.0)

SSI surgical site infection

third-generation cephalosporins were the most common antibiotics used for pre-operative SAP. However, cefuroxime and metronidazole were the most commonly used antibiotics administered after surgery. Cefazolin and cefuroxime are the most common antibiotics recommended for SAP based on the guidelines [27]. This indicates the excessive use of broad-spectrum antibiotics in the pre-operative stage and highlights the need for antimicrobial stewardship interventions to reduce the use of broad-spectrum antibiotics. A previous study demonstrated the impact of a pharmacist-led antimicrobial stewardship intervention in reducing the excessive use of broad-spectrum antibiotics [25]. There is an opportunity for hospital pharmacists to improve compliance with SAP guidelines in the hospital setting. However, lack of knowledge and lack of support from hospital administrators are major barriers mitigating against pharmacists' involvement in antimicrobial stewardship [38]. Therefore, training of practicing pharmacists and future pharmacists is recommended to improve the rational use of antibiotics in surgical patients [38–40].

SSIs were reported in 16.5% of the procedures, and this is higher than the findings in previous studies conducted in Malaysia [10, 11]. This could be attributed to the low rate of compliance with SAP, although compliance with infection control strategies may also play a role in the occurrence of SSIs. In the current study, the risk of SSIs is significantly associated with the duration of surgery, and this is consistent with the results of previous studies conducted in Malaysia [12, 15]. Long duration of surgery increases the risk of pathogen contamination at the incision site [41], possibly due to glove perforation in extended surgical procedures [42]. In addition, the concentration of antibiotics administered before incision will diminish in surgeries with extended durations. Therefore, strategies to improve intraoperative SAP in extended procedures are recommended. It is important to

note that the significant association between the duration of hospital stay after surgery and the duration of surgery with the occurrence of SSIs in the univariate regression analysis disappeared in the multivariate analysis. This could be attributed to the small sample size included in the current study. Therefore, additional studies with larger sample sizes are recommended to validate these findings.

The study has some limitations, and should be interpreted with caution. Firstly, the study was conducted in one hospital and this will affect its external validity. Secondly, the sample size was small and the period of study was short. Thirdly, the study is retrospective in nature and there are missing data, which may affect the outcome of the study. Fourthly, the appropriateness of indication and the appropriateness of antibiotic choice were not evaluated in the current study. Lastly, the diagnosis of SSI is based on the information on patients' electronic records. There is a possibility that some patients had SSIs but did not return to the hospital. Therefore, the prevalence of SSIs may be underestimated. Despite these limitations, the current study described compliance with SAP and the prevalence of SSIs and its associated risk factors in a Malaysian hospital.

## Conclusion

There is a low rate of compliance with the timing of SAP and prolonged use of antibiotics among patients who undergo surgery. The rate of SSIs is high and is associated with the duration of hospital stay after surgery and the duration of surgery in univariate regression analysis. These findings highlight the importance of an antibiotic stewardship programme to improve the quality use of SAP and reduce the emergence and spread of antimicrobial resistance.

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## Declarations

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**Conflict of interest** The authors declare that there are no conflicts of interest.

**Ethics approval** Ethics approval was obtained from the IIUM Research Ethics Committee, reference number: IIUM/504/14/11/2/IREC 2020-104.

**Consent to participate** The Human Research Ethics Committee granted a waiver for patient informed consent due to the retrospective nature of the study.

**Consent for publication** Not applicable.

**Availability of data and material** The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

**Code availability** Not applicable

**Author contributions** AU and NFZ designed the study and collected the data, analysed the data and wrote the first draft of the manuscript. SCA contributed in data collection and SCA and FUK reviewed the manuscript draft. All the authors approved the manuscript for submission.

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