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## Evaluation of antimicrobial stewardship implementation in elective surgery in dr Cipto Mangunkusumo General Hospital using Gyssens Method

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### Abstract

**Introduction.** Nowadays, surgical site infections (SSI) remain the most common complication of surgical procedures. In prevention, prophylactic antibiotics are the first option, which leads to the high use of antibiotics. However, antibiotic administration should be based on strategies such as stewardship. Thus, the study aimed to assess the situation using Gyssens' method.

**Method.** A retrospective cohort study analyzed the antibiotic administration of most major elective surgeries, including thyroidectomy, mastectomy, and cholecystectomy, proceeded in Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia, from January to July 2023. Indication, type, dosage, timing, interval, duration, and route of administration were the variables of interest.

**Results.** Of 191 subjects who underwent the most common elective surgery procedures, 30 used combination antibiotics. Gyssens category 0 consists of 165 subjects (86.5%), and 11 subjects (5.8%) were classified as category IIA, indicating inappropriate dose (inadequate, insufficient). Inaccuracies were identified as mistimed administration (5.8%), less effective antibiotic selection (3.1%), incorrect dosage (2.6%), and inappropriate timing (2.1%). The association of Gyssens categories with SSIs showed a p-value of > 0.05 with an odds ratio of 1, indicating that both appropriate and inappropriate antibiotics of the Gyssens category showed no impact on SSIs or non-SSIs.

**Conclusion.** The adherence to antimicrobial stewardship in the most common elective surgery in the Department of Surgery, dr. Cipto Mangunkusumo General Hospital was 86.4 and subjected to improvement.

**Keywords:** surgical site infections, elective surgery, antibiotic, antibiotic resistance, Gyssens method

### Introduction

Surgical site infections (SSI) are complications found postoperatively, significantly higher in emergency settings than elective. This is related to better preoperative care in elective surgery. Some known factors led to SSI, including the procedure, degree of contamination, transfusion, operating theater, and personnel. However, using antibiotics is the first option most surgeons have considered.

Nevertheless, despite the toxicity, the high use of antibiotics, particularly broad-spectrum antibiotics, is responsible for increasing the multidrug resistance organism (MDRO). A study conducted in Surabaya, Indonesia, identified 54% of 3275 *E. coli* carriers resistant to commonly used antibiotics in Indonesia.<sup>4</sup> A study in Palembang, Indonesia, identified 490 out of 552 (88.7%) patients diagnosed with MDRO, mostly gram-negative bacteria resistant to imipenem cefazolin and tigecycline.<sup>5</sup> Inappropriate use of antibiotics then poses a challenge in addressing antibiotic resistance worldwide.<sup>1,2</sup>

Antimicrobial stewardship refers to implementing a fully responsible prescription of antibiotics that focuses on patient safety regarding the prevention of antimicrobial toxicity and antibiotic resistance. These two mentioned preventive measures were the core program of antimicrobial stewardship.

A simple method mostly used worldwide to evaluate appropriateness – qualitatively – in antibiotic prescription proposed by Gyssens. In recent years, this kind of evaluation has periodically proceeded in Dr. Cipto Mangunkusumo General Hospital (CMGH), Jakarta. However, the evaluation proceeded to take representative samples randomly. This study aimed to find how far the adherence to stewardship programs is in most elective procedures.

### Method

A retrospective cohort study enrolled patients who underwent elective surgery at Dr. Cipto Mangunkusumo General Hospital (CMGH), a tertiary hospital in Jakarta, Indonesia. Those who underwent major surgery, including thyroidectomy, mastectomy, and cholecystectomy, which are the most common elective procedures between January and July 2023, were included. Complicated procedures beyond thyroidectomy, mastectomy, and cholecystectomy, tracheal or oesophageal complications in thyroidectomy, and biliary tract complications of cholecystectomy were excluded.

Indication, type, dosage, timing, interval, duration of administration, and route of antibiotics were the variables of interest analyzed using the Gyssens flowchart. The subject characteristics, including age, gender, body mass index (BMI), diagnosis, operative procedure, duration of operation, length of hospital stay, and mortality status were recorded and presented descriptively. Data distribution was analyzed using Kolmogorov Smirnov. Numerical data were presented in median and interquartile range (IQR) and analyzed using—Fisher test. Multivariate analysis was analyzed using logistic regression.

The ethics committee of the Faculty of Medicine, Universitas Indonesia, approved the study on 8<sup>th</sup> January 2024 with the Ref. No. 23–11–1947.

### Results

One hundred ninety-one subjects underwent elective surgery between January and July 2023 and enrolled in the study. Of these subjects, the median age was 48 (13–83) years. The median duration of surgical procedures proceeded was 225 (50–795) minutes. The length of stays pre- and postoperatively is presented in Table 1.

Table 1. Subjects baseline characteristics

Baseline Characteristics	Median (Q1–Q3)
Age (years)	48 (13–83)
Operative duration (minutes)	225 (50–793)
Preoperative hospital stays (days)	2 (1–25)
Postoperative hospital stays (days)	2 (1–12)

When focused on antibiotic use, 30 subjects were treated with combination antibiotics. We found 165 subjects (86.4%) were classified as appropriate (category 0) and were classified as inappropriate: 1) 11 subjects (5.8%) were of category IIA (inappropriate dose), with most

Table 2. Antibiotic use for prophylactic measures

Category	Σ (n)	Percent (%)	SSI* (%)
0	165	86.4	–
I	4	2.1	–
IIA	11	5.8	1 (100)
IIB	5	2.6	–
IIC	–	–	–
IIIA	–	–	–
IIIB	–	–	–
IVA	6	3.1	–
IVB	–	–	–
IVC	–	–	–
IVD	–	–	–
V	–	–	–
Total	191	100	1

\*SSI: surgical site infections

Thyroidectomy using the open method places the highest frequency (51.7% of the female subjects). The second place was per laparoscopic and per laparotomy cholecystectomy (53.7% of male patients as the primary population in the laparoscopic method and 4.9% in the laparotomy method). The least frequent elective surgeries were simple mastectomy (2.4%) and laparotomy cholecystectomy (2.4%).

Inappropriate uses were recorded in subjects who underwent mastectomy, thyroidectomy, and cholecystectomy related to timing intervals. There were instances of antibiotics not being repeated after three hours of surgery. Two subjects (6.9%) underwent modified radical

Table 3. Description of antibiotic use

Operation		Gyssens					Total
		0	I	IIA	IIB	IVA	
Mastectomy	Simple n(%)	4 (100)	0 (0)	0 (0)	0 (0)	0 (0)	4 (100)
	Modified Radical n(%)	23 (92)	0 (0)	0 (0)	2 (8)	0 (0)	25 (100)
Thyroidectomy	Open n(%)	73 (94.8)	2 (2.6)	0 (0)	2 (2.6)	0 (0)	77 (100)
	TOETSA n(%)	5 (83.3)	0 (0)	0 (0)	1 (16.7)	0 (0)	6 (100)
Cholecystectomy	Laparotomy n(%)	5 (83.3)	0 (0)	1 (16.7%)	0 (0)	0 (0)	6 (100)
	Laparoscopy n(%)	55 (75.3)	2 (2.7)	10 (13.7)	0 (0)	6 (8.2)	73 (100)
Total		165 (86.4)	4 (2.1)	11 (5.8)	5 (2.6)	6 (3.1)	191 (100)

Further analyses were focused on the association between antibiotic use and outcomes. This study recorded no mortality; thus, no survival analyses were conducted. The association of Gyssens categories and SSIs was analyzed using binary logistic multivariate analysis, with Gyssens categories as the independent variable (more than two categories) and SSIs as the dependent variable. The Hosmer and Lemeshow test yielded a p-value of 0.000, indicating that the independent variables were not equivalent and that a comparison with the dependent variable could not proceed. Subsequently, data recoding was performed, with Gyssens categories as the independent variable categorized into appropriate (Gyssens 0) and inappropriate (Gyssens 0–VI) usage, compared to the dependent variable SSIs, including SSIs and non–SSIs. This data was then analyzed using a bivariate test of two proportions. Since some data were zero and the data were less than 20%

subjects receiving inadequate dosages (insufficient); 2) 6 subjects (3.1%) were of category IVA (another effective antibiotic available) with the majority of these subjects having undergone biliary surgery and were treated with doripenem, ampicillin-sulbactam, and cefazolin; 3) Other subjects of category I, consisting of 3a) four subjects (2.1%). Prophylactic antibiotics were given at the time of incision, and 3b) of category IIB five subjects (2.6%). Timely repeated antibiotic administration intervals are not being met. SSI was recorded in one subject following cholecystectomy surgery.

mastectomy surgeries, and three subjects (3.6%) underwent thyroidectomy. Additionally, prophylactic antibiotics were given at incision (0 minutes preoperatively) in one subject (1.2%). Five subjects who underwent cholecystectomy were treated with therapeutic measures due to infection with elevated leukocyte and C-reactive protein levels. All subjects who received therapeutic antibiotics were classified as Gyssens category 0. Among subjects given prophylactic antibiotics, two subjects (2.5%) were given just before incision. There were 11 subjects (14%) who received inappropriate doses and six subjects (7.6%) who could have been administered more effective antibiotics.

of the entire table, the chi-square test assumption was not met. Therefore, the Fisher's exact test was used.

Table 4. Association between Gyssens category and surgical site infection

Gyssens	SSI		Total	p <sup>f</sup> value	OR (CI 95%)
	No	Yes			
Appropriate use n(%)	165 (100)	0 (0)	165 (100)	0.136	1.04 (0.96–1.12)
Inappropriate use n(%)	25 (96.2)	1 (3.8)	26 (100)		
Total n(%)	190 (99.5)	1 (0.5)	191 (100)		

The Gyssens categories and SSIs showed a p-value>0.05 with an odds ratio of 1, indicating that both appropriate and inappropriate Gyssens categories did not have an impact on the occurrence of SSIs or non–SSIs.

## Discussion

Of subjects' characteristics, age is referred to as a substantial factor that may affect antibiotic use. Some studies support the hypothesis that age is one of the risk factors affecting antibiotic use. By the principle of antibiotic use, healthcare providers must adhere to an accurate dose of antibiotics. Dose adjustments are necessary based on the age group and BMI of each patient. If the total dose per kilogram of body weight in children exceeds the adult dose, then the adult dose should be administered. These facts refer to the basics of evaluating the appropriateness.

The study recorded that the length of stays denoted an equal median value of two days preoperatively and postoperatively, with the longest preoperative and postoperative lengths of stays of 25 days and 12 days, respectively. It may explain why, in the study, only a subject facing SSI. A study by Syaiful et al. at CMGH (2012 to 2017) showed that subjects between 25 and 65 years who were hospitalized for longer durations had a higher risk of experiencing SSI.<sup>3</sup>

The study shows that 86.4% of antibiotic use was appropriate, indicating adherence to antimicrobial stewardship programs. The remaining (13.6%) were categorized as inappropriateness. The inappropriateness includes inappropriate dosing intervals (5.8%), selection of less effective antibiotics (3.1%), inappropriate doses (2.6%), and administration at inappropriate times (2.1%). Though inappropriateness is relatively low, continuous improvement should be made regarding the knowledge gap. However, the study showed better than the study findings of Rokhani et al. in 2020 at Dr. H. Slamet Martodirdjo Pamekasan Regional General Hospital focused on prophylactic antibiotics evaluated using Gyssens' method, which found appropriateness of 79.7% and inappropriateness of 20.3%.<sup>4</sup>

The study also showed no association of Gyssens classification with the incidence of surgical site infection. This finding may be associated with a low incidence of SSI in the study. Among the eleven subjects classified as Gyssens IIA, only a subject experienced a surgical site infection. In comparison, some centers in Southeast America denoted that out of 532,694 elective surgical procedures, 3,988 were followed by complex SSI (prevalence rate of 0.7 infections per 100 procedures). Meanwhile, data in Indonesia showed the prevalence of SSI at 2–18%. This study categorized 165 subjects (86.4%) as 0, indicating that antibiotic usage in patients undergoing elective surgical procedures at CMGH is appropriate. However, inappropriate dosing also needs to be noted about drug utilization as it is still quite common and leads to the emergence of SSI.

The study findings are similar to those of Rana et al.<sup>5</sup> which showed that inappropriate dosing and antibiotic prophylaxis regimens may increase the incidence of SSIs by 13.04%. For preoperative and intraoperative antibiotic prophylaxis, it is important to choose antibiotics with the narrowest antibacterial spectrum to reduce the emergence of antibiotic resistance. The antibiotics administered should also be active against the most likely organisms to contaminate for that type of surgery; first-generation cephalosporins are excellent agents for skin and soft tissue infections due to their susceptibility to *Streptococcus pyogenes* and *S. aureus* that are methicillin-resistant. The use of single-dose cefazolin

before surgery is currently the preferred prophylactic regimen used by most hospitals.<sup>14</sup> According to antibiotic usage guidelines, prophylactic antibiotics should be administered less than 30 minutes before incision, ideally during induction. The administration of prophylactic antibiotics should be precise to ensure optimal serum or tissue levels at the time of incision.<sup>4,5</sup>

The appropriateness of antibiotics of 86.4% indicates the efficacy in preventing SSI. Further, the study findings show that SSI associated with the inappropriateness in dosing intervals (namely, repeated prophylactic administration) remains encountered. However, further studies are needed regarding other influencing factors of SSI in these subjects. On the other hand, the study findings indicate an insignificant association between the appropriateness of antibiotics and the occurrence of SSI. An odds ratio of 1 indicates that the occurrence of SSI is more influenced by other factors, which is not the focus of this study. This is the limitation of this study. With the power of study >80%, the authors are convinced to recommend improving antimicrobial stewardship implementation in the center.

## Conclusion

The adherence to antimicrobial stewardship in the most common elective surgery in the Department of Surgery, dr. Cipto Mangunkusumo General Hospital was 86.4 and subjected to improvement.

## Disclosure

The authors declare no conflict of interest.

## Role of authors

Conceptualization YM RPU, Data curation RPU YM, Formal analysis RPU YM, Funding acquisition RPU, Investigation RPU, Methodology RPU YM, Project administration RPU, Resources RPU, Software RPU, Supervision YM, Validation RPU YM, Visualization RPU, Writing original draft preparation RPU YM, Writing review and editing RPU YM.

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