

# Appropriateness and Cost of Prophylaxis Stress Ulcer For Inpatient in the Internal Medicine Department in a Government Hospital : A Cross-Sectional Study

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## ABSTRACT

Guidelines from ASHP (1999) prohibit acid-suppressing therapy for stress ulcer prophylaxis (SUP) in patients who are not critically ill. The use of stress ulcer prophylaxis is not recommended in non-ICU patients with < 2 risk factors. Inappropriate use of stress ulcer prophylaxis can increase costs for patients. This study aims to determine the evaluation of the use and the cost of stress ulcer prophylaxis.

This research was a non-experimental observational study with a cross-sectional approach. Data collection was carried out retrospectively using the consecutive sampling method with a random sampling technique on the medical records of inpatients in the internal medicine ward of Government Hospital from January to December 2020, totaling 340 samples.

The results showed that Proton Pump Inhibitors (PPIs) were the most widely used acid-suppressing drugs, namely 45.8%. Furthermore, the H2 Receptor Antagonist (H2RA) was 42.6%, the sucralfate group was 7.4%, and the antacid group was 4.2%. Out of 340 patients, 57 patients, or 16.8%, were in the right indication based on the guidelines and 283 patients, or 83.2%, were under the wrong indication for stress ulcer prophylaxis. Using stress ulcer prophylaxis with the right indication so that the therapy could save treatment costs by Rp. 19.933.582.

There was a high prevalence of inappropriate Stress ulcer prophylaxis prescription among inpatients in the internal medicine department, if these drugs are given with the appropriate indications could save more on the cost of prophylaxis. An effective intervention strategy should be developed by the clinician pharmacists to reduce inappropriate SUP drugs.

**Keywords:** *acid suppression therapy, inappropriate indication, stress ulcer, stress ulcer prophylaxis*

## 1. INTRODUCTION

The use of stress ulcer prophylaxis is generally given to critically ill patients and treated in the intensive care unit (ICU). Appropriate use of Stress Ulcer Prophylaxis (SUP) is defined when proton pump inhibitors (PPIs) and H2-receptor antagonists (H2RA) are administered to patients with at least one risk factor (coagulopathy, mechanical ventilation  $\geq$  48 hours, and gastrointestinal bleeding or ulceration within a year) prior to hospitalization) or with some minor risk factors (sepsis, multiple organ failure, liver failure, renal insufficiency,

inpatient ICU  $\geq$  7 days, hypotension or shock, organ transplant, multiple trauma, burns of more than 25-30% of body surface area, major surgery, hidden gastrointestinal bleeding  $\geq$  6 days, and use of anticoagulants, corticosteroids, or nonsteroidal anti-inflammatory drugs (NSAIDs) [1].

The American Society of Health-System (ASHP) in 1999 published guidelines for the use of Stress Ulcer Prophylaxis (SUP) in medical, surgical, respiratory and pediatric patients in the ICU [2]. Research related to

inappropriate prescribing of acid-suppressing therapy due to a low-risk factor for bleeding in the use of stress ulcer prophylaxis based on the Stress Ulcer-related Gastrointestinal Bleeding (SURGIB) criteria was developed by [3] of 88.5% and an estimated cost savings of inpatient medication hospitalization of \$114,622 (approximately IDR 1,396,095,960) in the 253 studied patients [4].

Long-term use of acid-suppressing therapy is of particular concern as complications (Clostridium difficile, namely, diarrhea, osteoporosis, and pneumonia) are associated, particularly when proton pump inhibitors are used for long durations at high doses. Research from [5], [6] stated that the incidence of Clostridium difficile infection increased 3 times from prolonged use of stress ulcer prophylaxis.

If the stress ulcer prophylaxis is not used based on the indications of the disease in the patient, it will lead to unexpected side effects such as diarrhea due to Clostridium-difficile and the incidence of pneumonia and increased unnecessary costs. Therefore, by evaluating the use of stress ulcer prophylaxis, it can be an evaluation for health workers in providing therapy to patients and obtaining optimal therapeutic effectiveness.

## 2. MATERIALS AND METHODS

### 2.1. Research design and Participant

The study was conducted by taking medical record data of inpatients at the Government Hospital and the costs of using stress ulcer prophylaxis from January 2020 to December 2020. Patient characteristics and therapy data were obtained from medical record data, while therapy costs were obtained from the hospital's finance department. The sample in this study was all inpatients in the internal medicine ward who used stress ulcer prophylaxis and met the inclusion criteria at the Government Hospital Yogyakarta for January 2020 - December 2020. The inclusion criteria were that patients hospitalized in the internal medicine ward were given stress ulcer prophylaxis during treatment with data, and the medical records were complete and legible. The exclusion criteria were (1) Patients who entered experienced bleeding in the gastrointestinal tract which was marked by the occurrence of hematemesis, melena, and blackish red NG fluid, (2) Patients with a diagnosis of gastrointestinal disorders, (3) a history of peptic ulcers or gastrointestinal bleeding within 1 year prior to admission.

### 2.2. Sample Size Calculation

Calculation of the sample was conducted using the proportion estimation formula by taking the following assumptions: the proportion of appropriate use of stress ulcer prophylaxis = 0.5, a margin of error = 5%, and a 95% confidence interval [7].

$$n = \frac{Z_{\alpha/2}^2 P(1 - P)}{d^2}$$

$$n = \frac{(1,96)^2 0,5(1 - 0,5)}{(0,05^2)} = 384$$

The correction formula is used if the population is less than 10,000 (total patient population in 1 year (N) = 3000), which can represent the study sample. The corrected number of samples is as follows:

$$n = \frac{N \times n}{N + n} = \frac{3000 \times 384}{3000 + 384} = 340$$

340 samples were selected with a random sampling technique.

### 2.3. Research Instrument

The research instruments included medical records of patients hospitalized in the internal medicine ward of Government Hospital in 2020 and Guidelines for the American Journal of Health-System Pharmacy (ASHP) 1999; Stress Ulcer Prophylaxis Clinical Guidelines, Stanford Hospital and Clinics 2015 as a therapeutic reference.

Sample recording was adjusted according to the inclusion criteria such as gender, patient age, length of hospitalization, drug name, drug class, drug dose, rules of use, and duration of drug use.

### 2.4. Criteria Establishment

Based on published evidence-based guidelines and previous literature for the clinical practices of SUP, we established the criteria to evaluate the appropriateness of SUP medication. SUP medication was judged to be appropriate if inpatient in internal medicine department had one major or at least two minor risk factors (ASHP 1999; Stress Ulcer Prophylaxis Clinical Guidelines, Stanford Hospital and Clinics 2015) in Table 1.

**Table 1.** Risk Factor for Stress Ulcer

**The Presence of one major risk factor from the following:**

- 1 Respiratory failure: mechanical ventilation >48 h
- 2 Coagulopathy: platelet count <50,000/mm<sup>3</sup> ( $50 \times 10^9$  /L), international normalized ratio >1.5, or partial thromboplastin time >2.0 times the control value

**The presence of at least two minor risk factors of the following:**

- 1 Head injury with a Glasgow Coma Score of  $\leq 10$  or an inability to obey simple commands
- 2 Thermal injury involving >35% of the body surface area
- 3 Partial hepatectomy
- 4 Hepatic or renal transplantation
- 5 Multiple traumas with the Injury Severity Score of  $\geq 16$
- 6 Acute renal failure or hepatic failure
- 7 Traumatic brain injury or spinal cord injury
- 8 Insufficiency Renal
- 9 Sepsis
- 10 Occult or overt bleeding for  $\geq 6$  days
- 11 Length of stay > 7 days
- 12 Corticosteroid therapy (>250 mg/d hydrocortisone or equivalent daily)
- 13 Using antiplatelet

## 2.5 Outcome Measurements

Our primary outcome variable was the appropriateness evaluation of SUP prescribing patterns for inpatients in Internal medicine Department and Cost of using stress ulcer prophylaxis both the total cost and average cost per patient of appropriate and inappropriate indicated prophylactic use

## 2.6. Statistical analysis

Data analysis in this study was in the form of descriptive analysis to describe the characteristics of patients based on gender, age, length of hospitalization and risk factors, to determine the profile of stress ulcer prophylaxis used by inpatients in the internal medicine ward of Government Hospital based on the class of drugs used, to determine the accuracy and inaccuracy of the indications for the use of stress ulcer prophylaxis for inpatients in the internal medicine ward, as well as identifying the costs calculated by multiplying the total number of appropriate and inappropriate therapeutic doses given during hospitalization with the price of the drug used.

## 3. RESULT AND DISCUSSION

Based on the data obtained from 340 samples in Table 1, there are more male patients (55%) than female patients (45%). Patient characteristics by gender are dominated by males, with a higher prevalence of male smokers (62.9%). Based on Riskesdas 2018 data,

regularly consuming coffee could increase the risk of stress ulcers. Coffee containing caffeine can stimulate the hormone gastrin, which stimulates and accelerates the production of stomach acid, resulting in gastric ulceration. In addition, regularly drinking coffee can increase the risk of 3.57 times experiencing gastritis. If it is left untreated, it will worsen and that the stomach acid can cause ulcers [8].

Inpatients in the internal medicine ward who receive stress ulcer prophylaxis are given at > 65 years old who have entered the elderly. The increasing age can experience a decrease in gastric mucosal function, reduced secretory function, and loss of nutritional factors in the gastric mucosa so that the stomach is prone to bleeding. [9]. Age does not affect the incidence of stress ulcers as it is not included as a risk factor for gastrointestinal bleeding. However, several studies revealed that older age becomes one factor in the administration of excessive gastric acid-suppressing drugs [10].

Furthermore, the maximum length of hospitalization was  $\leq 7$  days with a percentage of 93.24% and > 7 days with a percentage of 6.76%. A study [10] explained that patients who required longer hospitalization and more medical services could unconsciously encourage doctors to provide stress ulcer prophylaxis, preventing more gastrointestinal bleeding complications. Elderly patients and a longer hospitalization were shown to be major predictors of overuse of stress ulcer prophylaxis. In addition, [11] have similarly identified factors contributing to the overuse of stress ulcer prophylaxis. They revealed that the length of hospitalization is one of the factors in which stress ulcer prophylaxis is frequently used.

In this study, the major risk factor was the incidence of coagulopathy (12.35%), in which most of the patients were dengue fever patients. Therefore, according to [12], it is necessary to give anti-ulcer to prevent stress ulcers. Meanwhile, the minor risk factor is the use of antiplatelets (10.59%) which can inhibit the production of prostaglandins by the gastric mucosa associated with gastric epithelial damage [13]. A study conducted by [14] revealed that there were 52 patients receiving antiplatelets, where the use of antiplatelets had a significant effect on the incidence of bleeding.

The profile of stress ulcer prophylaxis in inpatients in the internal medicine ward at the Government Hospital in 2020 was mostly the Proton Pump Inhibitor (PPI) group of 45.8%. Acid suppressive therapy (AST), including proton pump inhibitors and H<sub>2</sub> receptor

antagonists (H2RA) as stress ulcer prophylaxis, is one of the most common medical practices in inpatients [4].

The PPI drug is stronger in increasing gastric pH than H2RA and maintains gastric pH between 3.5 – 5.0, which can minimize the risk of gastric mucosal injury. Of the four meta-analyses comparing PPIs with H2RAs, three suggested that PPIs are superior to H2RAs [15].

Evaluation of the use of stress ulcer prophylaxis revealed that patients prescribed acid-suppressing drugs were 40 patients or 11.76%. 1 indication had a major risk factor, 17 patients or 5% had at least 2 or more indications of a minor risk factor as stress ulcers prophylaxis, and 283 patients or 83.24% received acid-suppressing drugs without appropriate indications.

In recent years, the practice of stress ulcer prophylaxis has become commonplace in patients with general treatment and few or no supporting evidence [16]. Inappropriate use of indications for stress ulcer prophylaxis can increase the incidence of unexpected drug reactions, drug interactions, problems in polypharmacy and unnecessary drug costs [17].

A cost analysis was performed to assess the economic impact of stress ulcer prophylaxis during the therapy without incorrect indications. The calculation of the cost of prophylaxis is based on the total oral administration or injection of acid-suppressing drugs given during hospitalization by looking at the smallest unit of drug price from the hospital.

The biggest expenditure on stress ulcer prophylaxis was the inappropriate of giving the drug, which was Rp. 19.933.582. It indicated that the hospital could save on that cost if the drug is not used Rp. 19,933,582. Moreover, there were limitations in identifying the patient's direct costs, so the calculation of this cost is only from the drug's price.

Researchers have not been able to explain the factors that influence the high prevalence of inappropriate prescribing but there is a similar study that observed about the factors that influence the inappropriate prescribing of prophylactic stress ulcers, a study state that the reasons why clinicians prescribed SUP inappropriately were multifactorial. First, the fear of development of stress ulcer syndrome in non-ICU patients who were not on SUP therapy, Second, Due to the tense relationship between doctors and patients in China, doctors had to prescribe SUP therapy for low-risk inpatients so as to protect themselves from litigation,

third, the incidence of an adverse reaction related to Acid suppression medicines has not been high, and for this reason, doctors have believed PPIs to be safe [20].

One Study reported that several adverse effects (specified in C. difficile infections, respiratory infections, hypomagnesemia, adverse skeletal muscle effects, psychiatric symptoms) after reducing inappropriate proton pump inhibitor use for stress ulcer prophylaxis decreased significantly (35% control group versus 8% intervention group) [19].

Associated with those factors, researcher indicated that more information was required for clinicians about rationality and efficiency of their prescribing practices. Effective intervention strategies should be executed by clinical pharmacists to reduce improper SUP medication.

The American Society Health-System Pharmacist guidelines 1999 and Guideline from Stanford hospital can be implemented in clinical practice to prevent unnecessary acid-suppressing therapy in patients due to the low risk of stress ulcer bleeding. Computerized ordering systems can reduce unnecessary use of acid suppression therapy, lower patient prescribing costs, and limit side effects [17].

## 4. FIGURES AND TABLES

**Table 1.** Patients Characteristics

Parameter	Number of Patients (n, %)
<b>Gender</b>	
Female	153 (45)
Male	187 (55)
<b>Age</b>	
05-11 years old	4 (1,2)
12-16 years old	9 (2,6)
17-25 years old	28 (8,2)
26-35 years old	28 (8,2)
36-45 years old	42 (12,4)
46-55 years old	74 (21,8)
56-65 years old	57 (19,7)
> 65 years old	88 (25,9)
<b>Length of Hospitalization (days)</b>	
≤ 7	317 (93,24)
> 7	23 (6,76)
<b>Risk Factors:</b>	
Coagulopathy	40 (12.35)
Antiplatelet Use	38 (10.59)

Corticosteroid Use	29 (8.53)
CHF	26 (7.94)
Kidney Insufficiency	13 (3.82)
Sepsis	12 (3.53)
Head injury	3 (0.88)

**Table 2.** Profile of the Use of Stress Ulcer Prophylaxis

Agent	Type	Number	%
Proton Pump Inhibitor (PPI)	Lansoprazol	66	14,0%
	Inj	36	7,6%
	Lansoprazol	84	17,6%
	Cap		
	Pantoprazol		
	Inj		
	Esomeprazol	4	0,8%
	Inj	2	0,4%
	Esomeprazol		
	Tab		
	Omeprazol Inj	3	6%
	Omeprazol	21	4,4%
	Tab		
H2-Receptor Antagonis (H2RA)	Ranitidin Inj	187	39,6%
	Ranitidin Tab	14	3,0%
Sukralfat	Sukralfat Syr	18	3,8%
	Sukralfat Tab	17	3,6%
Antasida	Antasida Syr	4	0,8%
	Antasida Tab	16	3,4%
<b>TOTAL</b>		<b>472</b>	<b>100%</b>

**Table 3.** The Use of Stress Ulcer Prophylaxis

Stress Ulcer Prophylaxis	n, %
Correct indication	
<b>1 major risk factor</b>	40 (11.76)
<b>≥ 2 minor risk factors</b>	17 (5)
Incorrect indication	283 (83.24)
<b>TOTAL</b>	<b>340</b>

**Table 4.** Drug Expenses for the Use of Stress Ulcer Prophylaxis

Indication	Number of Patients	Total Drug Cost	Average Cost
<b>Appropriate</b>	57	Rp 6.240.384	Rp 109.480

Inappropriate	283	Rp 19.933.582	Rp 70.436
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#### 4. CONCLUSION

Based on the result of this study, the profile of the use of stress ulcer prophylactic drugs in patients hospitalized in the internal medicine ward at Government Hospital in 2020 included the Proton Pump Inhibitor (PPI) of 45.8%, the Histamine-2 Receptor Antagonist of 42.6%, sucralfate of 7,4%, and the antacid of 4.2%. The use of stress ulcer prophylaxis in the patients described 57 patients or 16.8% with correct indications and 283 patients or 83.2% with incorrect indications. Expenditure on the use of stress ulcer prophylaxis drugs in a correct indication was Rp 6.240.384 with an average of Rp 109.480 for 57 patients and Rp 19.933.582 for an incorrect indication with an average of Rp 70,436 for 283 patients

#### ETHIC STATEMENT

This study has conducted an ethical review. It has been declared ethical by The Ethical Committee Hospital Government from Yogyakarta with the letter Number 1804126.

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