

# Prescription Pattern and Appropriateness of Stress Induce Ulcer Prophylaxis in Dessie Referral Hospital, North East Ethiopia; Cross-Sectional Study

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## Abstract

**Background:** Stress-related mucosal damage includes the spectrum of pathology attributed to the acute, erosive, inflammatory insult to the upper gastrointestinal tract associated with critical illness. This study assessed prescription pattern and appropriateness of Stress Induce Ulcer Prophylaxis (SIUP) in Dessie Referral Hospital, North East Ethiopia.

**Methodology:** An institutional-based cross-sectional study design used to assess prescription pattern and appropriateness of SIUP of 107 patients from May 1 to June 22, 2018. Simple random sampling technique was used to select the study participants. Statistical package for social sciences version 20 was used to compute descriptive and inferential statistics.

**Results:** The response rate of the study was 93.15%. Of 100 patients, 82 had been received SIUP and only 50 (50%) fulfilled the prescription criteria. One-third (33%) of participants had more than three morbidities. The number of morbidities ranged from 1-5 with a mean  $2.11 \pm 0.99$ . On average,  $4.56 \pm 1.54$  (1 to 9) number of drugs per patient was prescribed. From 50 patients who fulfill prescription criteria's, 36 (72%) were based on major and 14 (28%) were based on minor criteria. Eighteen patients didn't receive SIUP while they fulfilled the criteria. Omeprazole 12 (24%) and cimetidine 38 (76.0%) were the only two drugs used for SIUP. Factors associated with inappropriate use of SIUP was being female (AOR=3.80, 95% CI: 1.65-8.74, P value: 0.002) and patients taking cimetidine (AOR=2.83, 95% CI: 1.54-5.21, P-value: 0.001).

**Conclusion:** The overall adherence level was found to be half and major criteria's were used for majority of patient which received SIUP. Strengthening of clinical pharmacist involvement in drug utilization process and adhering to the standard guidelines will reduce the burden of inappropriate SIUP use.

**Keywords:** Prescription pattern, Stress induce ulcer prophylaxis

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## Introduction

Stress-Related Mucosal Damage' (SRMD) is the broad term used to describe the spectrum of pathology attributed to the acute, erosive, inflammatory insult to the upper gastrointestinal tract associated with critical illness [1,2]. Putative mechanisms underlying SRMD include reduced gastric blood flow, mucosal ischemia and reperfusion injury, all of which occur frequently in the critically ill patients with severe physiological stress [3], and ranges from numerous diffuse superficial erosive mucosal lesions to major deep ulceration [4].

An estimated 4.4 million patients are admitted to intensive care units (ICUs) each year. Of these, about 12%, or 500,000 patients, die in the ICU [5]. The frequency of mucosal injury (*via* endoscopic studies) in critically ill patients ranges from 75% to 100% with occult bleeding occurring in roughly 5-25% [6]. However, the prevalence of Clinically Important Bleeding (CIB) due to stress ulceration in a study published in 2015 reported the frequency of CIB as 2.6% [2].

Critically ill patients are at risk as CIB develops due to stress ulceration because of physiologic stress leading to impaired

mucosal defense mechanisms and mucosal ischemia. Studies showed respiratory failure, coagulopathy, greater than or equal to three coexisting diseases, liver disease, use of renal replacement, and higher organ failure as independent risk factors for CIB [7,8].

In addition to the above risk factors the following has also been documented: spinal cord injury, traumatic brain injury (Glasgow Coma Score,  $\leq 10$ ), thermal injury (body surface area,  $>35\%$ ), sepsis, partial hepatectomy, hepatic or renal transplantation, major trauma (Injury Severity Score,  $\geq 16$ ), alcohol abuse, *Helicobacter pylori* colonization, ICU length of stay more than 1 week, occult or overt bleeding for more than or equal to 6 days, and high-dose corticosteroids [9-12].

Recently the utilization of proton pump inhibitors for Stress Induce Ulcer Prophylaxis (SIUP) has become prominent across the globe [13-15]. This may be due to the superiority of proton pump inhibitors for achieving and maintaining a gastric pH of greater than 4, which is a historical target for SIUP due to minimization of gastric acid mediated fibrinolysis [16-18]. This trend may complement with evidences suggesting lower CIB rates with proton pump inhibitors compared with histamine-2 receptor antagonists [19].

Non-adherence to guidelines for prescription of SIUP may stretch to 96.4% [20]. Inappropriate uses of SIUP may result in economic burden to the patient and Concerns have been raised about the association between non-judicious acid suppression and increased risk of bacterial infections, namely *Clostridium Difficile* Infection (CDI) and pneumonia [21,22]. In Ethiopia, no previous studies were attempted to assess practice of stress induce ulcer prophylaxis in hospitals. Therefore, the aim of the study was to assess prescription pattern and appropriateness of stress induce ulcer prophylaxis in Dessie Referral Hospital, northeast Ethiopia. We present the following article in accordance with the Strengthening the Reporting of Observational studies in Epidemiology reporting checklist.

## Methods

**Study area and period:** The study was conducted in four unit of Dessie Referral Hospital (internal medicine, surgical unit, and emergency unit), from May 1-June 22, 2018. Dessie is a town in Amhara National Regional State; North East Ethiopia located 401 km from Addis Ababa. The hospital is being serving to the populations of Dessie town and the surrounding population.

**Study design:** Institution-based cross sectional study design was used. Chart review was executed on patient admissions to collect demographics data and clinical variables (indication for stress ulcer prophylaxis and type of drug used).

**Study population:** All Patients who were in the three department of Dessie Referral Hospital (medicine, emergency and surgery) and took SIUP or have risk factors for stress ulcer during the study period.

**Inclusion and exclusion criteria:** patients above 18 years old, who had risk factor for stress induce ulcer according to American Society of Health-System Pharmacists (ASHP), and who were taking SIUP were included. Patients who were less than 18 years old, patients with incomplete medical information and patients

who received Acid Suppressive Therapy (AST) for treatment purposes such as gastro intestinal bleeding, gastro esophageal reflux disease, peptic ulcer disease and dyspepsia.

## Variables

**Dependent variable:** The dependent variable was appropriateness of stress induce ulcer prophylaxis.

**Independent variables:** The independent variables were socio-demographic characteristics and clinical variables.

**Sample size determination and sampling procedure:** Single population proportion formula (50% prevalence, 95% confidence level, and 5% tolerable sampling error) was used to estimate the sample. Since the source population was less than 10,000 (149 chronic cases), the sample size was an adjustment with a total of 107 participants. A total of 107 patients who satisfies the inclusion criteria in study period were included in study. Simple random sampling technique was used to select the study participants.

**Data collection and quality assurance:** Structured data extraction format was used and the appropriateness of SIUP use was evaluated against the modified ASHP guideline. To be a candidate for SIUP, a patient must have one major risk factor or two and above minor risk factor [11].

The data was collected by one nurse who had no working relation to the hospital with the supervision of the principal investigators. Pretested was done in five percent of the sample size in Dessie health center. During and after data collection, data were checked for completeness, accuracy, and consistency, and confidentiality was maintained. To reduce bias, the validated method was used. Study participants were also selected using rigorous criteria to avoid confounding.

**Data analysis:** Statistical Package for Social Sciences version 20 was used for data entry and analysis. Initially, binary logistic regression was run and variables with a p-value of less than 0.25 were transferred to multivariate logistic regression. In the logistic regression analyses, variables with a p-value of less than

0.05 with 95% confidence intervals were taken as statistically significant. This study did not examine subgroups and interactions. In this study, there was no missing data and sensitivity analysis was not done.

**Major risk factor:** Head injury with Glasgow Coma Score of  $\leq 10$  or inability to obey simple commands, thermal injury involving  $>35\%$  of body surface area, respiratory failure patients requiring mechanical ventilation for more than 48 hours, coagulopathies a platelet count of  $<50,000 \text{ mm}^3$ , an International Normalized Ratio of 1.5, or a partial thromboplastin time of  $>2$  times the control value, partial hepatectomy, hepatic or renal transplantation, multiple trauma with Injury Severity Score of  $\geq 16$ , spinal cord injury, hepatic failure, and history of gastric ulceration or bleeding during year before admission [9].

**Minor risk factor:** Sepsis, ICU stay of  $>1$  week, occult or overt bleeding for  $\geq 6$  days, and corticosteroid therapy ( $>250 \text{ mg}$  of hydrocortisone or equivalent daily) [9].

**Appropriate use:** A patient is a candidate for SIUP, if he/she has one major risk factor or has two or more minor risk factors [9].

## Results

Socio-demographic and clinical data: The response rate of the study was 93.15% due to refusal to participate in the study. A total of 100 patient's medical profiles were reviewed during the study period. Of 100 patients, 54 (58.7%) were female and the age range of study subjects ranges from 19-81 with mean  $46.53 \pm 1.67$ . From all study participants, 82 had been received SIUP. One-third (33%) of participants had more than three morbidities. The number of morbidities ranged from 1-5 with a mean  $2.11 \pm 0.99$ . On average,  $4.56 \pm 1.54$  (1 to 9) number of drugs per patient was prescribed (**Table 1**).

SIUP prescription pattern: From 82 participants who received SIUP, only 50 (50%) fulfilled the prescription criteria. From 50 patients who fulfill prescription criteria's, 36 (72%) were based on major and the remaining 14 (28%) were based on minor

criteria. Eighteen patients didn't receive SIUP while they fulfilled the criteria. From all patients which received SIUP, 55 (67.07%) were from medical ward (**Table 2**).

Patient conditions, types of SIUP agents used and their indication: Omeprazole and cimetidine were the only two drugs used for SIUP during the period. From 82 patients who received SIUP, only 50 had indications. Cimetidine was prescribed for 38 (76.0%) patients and intravenous route 45 (90.0%) was the most frequent rout of administration (**Table 3**).

Factors associated with inappropriate uses of SIUP: Bivariate analyses showed that being female and patients taking cimetidine were at higher risk of inappropriate use of SIUP adjusted odds ratio (AOR) (95% CI=3.80) 1.65-8.74 and 2.83 (1.54-5.21) and P=0.002 and 0.001 respectively, but other variables didn't show significant association with inappropriate use of SIUP (**Table 4**).

**Table 1:** Socio-demographic and clinical data of the study subjects (n=82).

Variable		Frequency	Percentage
Sex	Male	46	41.3
	Female	54	58.7
Age, years	less than 34	26	26
	35-45	30	30
	46-60	24	24
	greater than 60	20	20
Number of morbidities	One	32	32
	two	35	35
	>three	33	33
Number of drugs per patient	01-Mar	24	24
	4	30	30
	5	22	22
	>6	24	24
Types of ward	Medical	67	67
	ICU	16	16
	Surgical	17	17
Level of prescriber	General practitioners	29	29
	Intern	37	37
	Resident	16	16
	Senior	18	18

**Table 2:** Patient characteristic and prescription pattern for SIUP (n=82).

Variables		SIUP Number	Percentage
Sex	Female	39	47.56
	Male	43	52.44
Age	Less than 34	20	24.39
	35-45	23	28.05
	46-60	23	28.05
	Greater than 60	16	19.51
Presence of indication	Major criteria	36	72
	Minor criteria	14	28
Types of ward	Medical	55	67.07
	ICU	16	19.51
	Surgical	11	13.41
Number of morbidities	One	29	35.37
	Two	26	31.71
	>Three	27	32.93

**Table 3:** Patient conditions, types of SIUP agents used and their indication (n=50).

Variables		Indication for SIUP Number	Percentage
Types of SIUP agent	Cimetidine	38	76
	Omeprazole	12	24
Rout of administration	Intravenous	45	90
	Oral	5	10
Level of prescriber	General practitioners	18	36
	Interns	17	34
	Residents	15	30
Number of morbidities	One	23	33.8
	Two	25	36.8
	>three	20	29.4
Ward type	Medical	41	60.3
	ICU	15	22.1
	Surgical	12	17.6

**Table 4:** Factors associated with inappropriate use of SIUP.

Variable		Appropriateness of SIUP		P value	AOR (95% CI)
		Yes	No		
Sex	Male	31	15	0.002	3.80 (1.65 - 8.74)
	Female	19	35		
Age	Less than 34	12	14	0.433	0.65 (.22 - 1.88)
	35-45	17	13		
	46-60	14	10		
	Greater than 60	7	13		
Number of morbidity	One	20	12	0.089	2.11 (.89 - 4.99)
	> Two	30	38		
Types of ward	Medical	44	39	0.189	2.06 (.70 - 6.11)
	Others	6	11		
Level of prescriber	Intern	18	11	0.881	1.07 (.42 - 2.72)
	Physicians	32	21		
Types of prophylaxis	Cimetidine	38	28	0.001	2.83 (1.54 - 5.21)
	Omeprazole	12	4		

## Discussion

Although the indications of SUP in the ICU setting have been well defined in the medical literature, in recent years the practice of SUP has become increasingly common in general medical wards with little evidence to support this practice. The use of SIUP as an acid suppression therapy decreases mortality and morbidity rate in critically ill patients. But overuse of these medications has considerable cost burden on patients and healthcare systems that should be considered by healthcare providers [23,24]. This study was mainly aimed at assessing prescription pattern and appropriateness of stress induced ulcer prophylaxis in Desire referral hospital. In comparison with other studies, we assessed the appropriateness of SIUP based on an ASHP guideline that addresses SUP administration [8].

We found that there was a very high frequency of unnecessary use of acid-suppressive therapy in hospitalized patients. Overuse of both histamine-2 receptor antagonists (cimetidine) and proton pump inhibitors (omeprazole) was seen. In this study, from 100 study subjects, 82 received SIUP of which only 50 fulfilled the prescription criteria while 18 patients fulfill the criteria but

denied SIUP which resulted with 50% overall level of adherence to ASHP guideline. This might be attributed to poor diagnosis and prescribing practice.

Among 32 patients which received SIUP inappropriately, 28 patients were on cimetidine and 30 of them were on intravenous acid suppressant therapy. This might be justified by lower price and easily accessibility of cimetidine in the hospital. Medical intern students were responsible for prescription of 63% of inappropriate SIUP and 81% of these errors were committed in the medical ward. This might be partially explained the contribution of level of the prescriber for injudicious use of SIUP [25].

Our results agreed with previous reports on the overuse of SIUP in hospitalized patients [25-31]. Its lower when compared with a report in study conducted at medical wards of University of Gondar Hospital (63.4%) [32]. But, similar rate (50%) of guideline compliance in academic hospitalists was reported in an institutional based chart review study in USA [33].

Higher rate of inappropriate use of SIUP were reported in: a prospective observational study conducted in three general

medicine wards in University Malaya Medical Centre (96.4%) [20]; a hospital based prospective study in Lebanon (83%) [1]; prospective cross-section observational study conducted at a tertiary teaching hospital in Riyadh, Saudi Arabia (71%) [34]; in USA community hospital 68.5% of prescriptions were inappropriate. Most were for SIUP in low-risk patients [29]. Lower rate of inappropriateness was showed in studies conducted: in Lebanon, no critically.

ill patients in a teaching service hospital received SIUP, among those who received SIUP, one-third were inappropriate [31]; a one day-observational study, reviewing patients' medical records in Italy reported that 62.9% of patients received a PPI as a SIUP that only 29.1% of these were appropriate [35]. This difference might be due to study methods and settings where the studies conducted which can further depend on practicing academic level and the type of patient which can be served in these health settings.

In this study, being female and patients taking cimetidine are at higher risk of inappropriate use of SIUP (AOR=3.80 and 2.83) and P value=0.002 and 0.001 respectively. Being female in gender and putting patients on cimetidine acid suppressive therapy increased the risk of inappropriate SIUP use. Which correspond with findings elsewhere [25,36,37], but debated from other findings in USA and Lebanon [33,38]. Findings from studies showed significant reduction of inappropriate use of SIUP by encouraging involvement of clinical pharmacists during drug utilization process [39,40]. The limitations of the study should not be overlooked. This study was undertaken at a single teaching hospital so that the results could not be generalized to other centers. Besides, temporal relationship cannot be established. However, the present study was the representative of the whole of the population.

## Conclusion

The overall adherence level was found to be half and major criteria's were used for majority of patient which received SIUP. Statistically significant association was found between female gender and use of cimetidine and inappropriate SIUP use. Strengthening of clinical pharmacist involvement during drug utilization process and physicians should be encouraged to be adherent to the standard guidelines to reduce the burden of inappropriate SIUP use. We recommend future researchers to assess the cost and impact of inappropriate SIUP use.

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