College of Health Sciences

School of Pharmacy

Department of Pharmacology and Clinical Pharmacy

Evaluation of stress ulcer prophylaxis use and associated factors at adult medical ward and intensive care unit of Tikur Anbessa Specialized Hospital; A Cross-sectional Study

By: Samiya Yassin (BPharm)

A Thesis Submitted to the Department of Pharmacology and Clinical Pharmacy, School of Pharmacy, College of Health Sciences, Addis Ababa University in Partial Fulfillment for the Requirements of Master of Science Degree in Pharmacy Practice.

July, 2021

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July, 2021

Addis Ababa, Ethiopia

Addis Ababa University

School of Graduate Studies

This is to certify that the thesis prepared by Samiya Yassin, entitled with: Evaluation of stress ulcer prophylaxis use and associated factors at adult medical ward and intensive care unit of Tikur Anbessa Specialized Hospital; A Cross-sectional Study. Submitted in partial fulfillment of the requirements for the degree of Master of Science in Pharmacy Practice complies with the regulations of the University and meets the accepted standards with respect to originality and quality.

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Addis Ababa, Ethiopia

July, 2021

Abstract

Stress ulcer is an inflammatory condition involving the gastric mucosa that may appear at some point of physiological stress such as serious illness. Prophylaxis against stress ulcers using Acid-suppressive therapy (AST), such as proton pump inhibitors (PPIs) and histamine-2 receptor antagonists (H_2RAs), often is used to prevent gastric complications, in patients with serious illnesses as they have a high risk of developing gastric ulceration and bleeding. Currently there is a growing concern about improper use of stress ulcer prophylaxis (SUP) in hospitalized patients. Hence, this study was aimed to determine appropriateness and associated factors for the use of SUP among patients treated at adult medical ward and intensive care unit of TASH. An institutional based Cross-Sectional study was conducted from August 9th, 2019 to December 9th, 2019. Data was collected prospectively from 368 patient medical records. The data were entered into Epi-info version 7 and then exported to and analyzed using Statistical Package for Social Sciences, version 25. Descriptive statistics were used to summarize the data while multivariable binary logistic regression analysis was used to determine factors associated with appropriateness of SUP use. *P*-value <0.05 was considered as statistically significant. The median age of the study participants was 32 years. Of the included study participants, 144 (39.13%) were on SUP; among patients on SUP more than one-third of them (39.13%) received SUP without an appropriate indicationand140 (62.50 %) patients had indications but did not receive SUP. In multivariable logistic regression, patients who were on NG tube feeding, patients with coagulopathy and history of UGIB, PUD and gastritis showed statically significant association with inappropriateness of SUP use. Inappropriate SUP use was observed in significant number of study participants. Greater proportion of this inappropriateness was attributed to the underutilization of SUP for high-risk patients. Hence, it is necessary to implement and comply to standardized SUP guidelines for ICU and medical ward patients in our hospital setting.

Key words: Tikur Anbessa Specialized Hospital, Stress Ulcer Prophylaxis, Acid Suppressive Therapy, Hospitalized Patients

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Alhamdulillah, first and foremost I thank Allah, the almighty, who gave me courage and helped me complete this thesis work. I would like to express my deep gratitude to my advisors Tefera Abula (Professor, PhD), and Oumer Sada (Assistant Professor) for their full support and guidance throughout the study. I'm also thankful to all data collectors and supporting staff who are working in medical ward and ICU of TASH for their cooperation in the data collection process. My special thanks are addressed to Addis Ababa University, College of Health Sciences and School of Pharmacy for giving me this educational opportunity. Deepest appreciation to my cheerful group of friends, without their assistance and guidance this thesis could not have been a success. Finally, I would like to thank my family and friends for their valuable advice, patience and support.

Contents

Abbreviation and acronyms

ASHP	American Society of Health-System Pharmacists
AST	Acid suppressive therapy
Alb	Albumin
CI	Confidence interval
CrCl	Creatinine clearance
GI	Gastrointestinal
GIB	Gastrointestinal bleeding
H_2RAs	Histamine 2 receptor antagonists
ICU	Intensive care unit
NSAIDs	Non-steroidal anti-inflammatory drugs
PI	Principal investigator
PPIs	Proton pump inhibitors
PUD	Peptic ulcer disease
SCr	Serum creatinine
SUP	Stress ulcer prophylaxis
TASH	Tikur Anbessa Specialized hospital
UGIB	Upper Gastrointestinal bleeding

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1. Introduction

1.1. Background

Stress ulcer is an inflammatory condition involving the gastric mucosa that may appear at some point of physiological stress such as serious illness. It is the main concern in hospitalized, particularly in critically ill patients and that may lead to gastric ulceration and significant life-threatening bleeding if it is left untreated. The possible risk factors related with stress ulcer may also be seen in patients who suffers from serious injuries after trauma or surgical treatment(Armstrong *et al.*, 1999; Anderson, 2013;Malhis *et al.*, 2019). This is the cause behind the majority of stress ulceration cases in intensive care unit (ICU)in contrast to general medical patients who are considered at low chance of developing stress ulceration (Anderson, 2013).Majority of ICU patients are subjected to acquire stress related mucosal damage after their admission (Malhis *et al.*, 2019).

Based on some SUP guidelines and from studies by previous authors, certain risk factors for stress related mucosal damage have been categorized. Individuals most at risk include, critically ill patients on mechanical ventilation (>48 hours) without enteral nutrition, and patients with a coagulopathy, hypoperfusion (shock, or organ dysfunction), requirement high-dose corticosteroids (>250 mg/day hydrocortisone or equivalent) and significant burn injury (total body surface area 20%)(Armstrong *et al.*, 1999; Parsons,Chung-Esaki and Berte, 2015; Smith, Cheathamand Smith, 2017). Other recognized risk factors include spinal cord injury, former history of GI hemorrhage, organ failure, sepsis, use of non-steroidal anti-inflammatory drugs (NASIDs) and antiplatelet agents, and increased ICU length of stay(Heidelbaugh and Inadomi, 2006; Horsa, Ayele and Ayalew, 2019).

Numerous features can influence the pathophysiology of stress ulcer, including gastric acid secretion, mucosal ischemia as a result of splanchnic hypoperfusion, and reflux of upper intestinal contents into the stomach(Abdi *et al.*, 2017). Critical illness is frequently related alongside hypotension and catecholamine-induced vasoconstriction, which can result in splanchnic hypoperfusion and mucosal ischemia (Stollman and Metz, 2005). These factors can unite to impair the integrity of the mucosal lining winding up with mucosal damage. The ischemia is further more

responsible for a reduced ability to remove hydrogen ions from diffusing into the lumen, which can be a reason to cell death and ulceration(Cook and Guyatt, 2018).

Moreover, normal defensive mechanisms including epithelial turnover in the gastric mucosa, secretions of mucus and bicarbonate production are compromised throughout stressful conditions(Stein*et al*., 1991; Stollman and Metz, 2005). These events, along with the release of various inflammatory mediators such as arachidonic acid metabolites, cytokines, and oxygen free radicals can directly injure the gastric mucosa(Armstrong *et al.*, 1999).

Prophylaxis against stress ulcers using Acid Suppressive Therapy (AST), such as proton pump inhibitors (PPIs) and histamine-2 receptor antagonists (H2RAs), often is used to prevent gastric complications, in patients with serious illnesses as they have ahigh possibility of attaining gastric ulceration and hemorrhage(Abdi *et al.*, 2017). Some consensus guidelines for stress ulcer prophylaxis (SUP) have been published(Smith, Cheathamand Smith, 2017;Parsons,Chung-Esaki and Berte, 2015; Tryba and cook, 1997).These published guidelines allow evidence based suggestions for SUP use in critically ill ICU and non-critically ill medical and surgical patients, as well as pediatric populations(Armstrong *et al.*, 1999; Malhis *et al.*, 2019).

On the other hand, there are also literatures indicating that, SUP does not associate with mortality benefit in patients with GI bleeding(Jain, Jabeen and Vallurupalli, 2013; Agee, Coulter and Hudson, 2015; Buendgens, Koch and Tacke, 2016). Currently, there is a growing concern about improper use of SUP in non-critically patients(Horsa, Ayele and Ayalew, 2019). This study is important because a significant number of patients may benefit from use of prophylactic acid suppressive agents where they are indicated and discontinuation when unnecessary.

Hence, assessing SUP use, determining the inappropriateness, assessing if the practice is in-line with the guidelines and identifying contributing factors for inappropriate use of AST at Tikur Anbessa Specialized Hospital (TASH) through a continued research can assist in planning interventions, and improve patient treatment outcome. This study attempted to show the prevalence of SUP use among patients treated at medical ward and ICU of TASH.

1.2. Statement of the problem

Significant number of evidences are stated regarding overutilization of SUP in both critically and non-critically ill patients(Heidelbaugh and Inadomi, 2006; Buckley *et al.*, 2015; Buendgens, Koch and Tacke, 2016). Over prescription without proper indication in non-ICU settings has been reported, despite the low incidence of GI bleeding(Cook and Guyatt, 2018).Several studies showed occurrences of inappropriate SUP use close to70% in medical and ICU patients(Buckley *et al.*, 2015; Parsons, Chung-Esaki and Berte, 2015).In addition, a significant proportion of ICU patients are inappropriately continued on prophylactic AST upon transfer to the medical-surgical wards and discharge (Jain, Jabeen and Vallurupalli, 2013; Buckley *et al.*, 2015).

Furthermore, the frequency of inappropriate continuation of acid suppression therapy upon hospital discharge is estimated as high as 73-90%(Jain, Jabeen and Vallurupalli, 2013). This has major economic and patient safety implications. The economic burden is significant when considering both inpatient and outpatient use (Jain, Jabeen and Vallurupalli, 2013; Buckley *et al.*, 2015).

Improper use of AST poses significant health risks and increases healthcare costs(Agee, Coulter andHudson, 2015). Overutilization and inappropriate prescription of SUP in particular Proton pump inhibitors (PPIs) may contribute to risks and long-term sequels, involving pneumonia, Clostridium difficile associated diarrhea, malabsorption, osteoporosis, and bone fracture(Jain, Jabeen and Vallurupalli, 2013).PPIs may also be responsible to increase the risk for hospitalization and added health care costs due to adverse drug interactions (Heidelbaugh, Goldberg and Inadomi, 2009; Wang *et al.*, 2009). Other potential complications of PPIs therapy are an increased risk of acute interstitial nephritis, gallbladder dyskinesia, vitamin and mineral deficiency as well as gastrointestinal-related cancers(Abraham, 2012).In addition, PPI-induced hypomagnesaemia may result cardiac disturbances involving prolongation of the QT interval(Chen *et al.*, 2012; Vaezi, Yang and Howden, 2017).Moreover, parenteral PPIs are relatively expensive, and inappropriate use can increase the treatment cost significantly for patients, especially in developing countries(Churi and Jogani, 2014).In general, the overuse of SUP has been associated with unwanted side effects as well as added economic costs(Agee, Coulter and Hudson, 2015).

On the other hand, it is claimed that a considerable number of patients required SUP but still not get an appropriate prophylaxis while hospitalization. Even though overutilization was highly reported, there were also patients who did not get prescription for SUP while there were clear risk factors for SRMD. Because of low percentage of underutilized patients, reasons for underutilization is not widely stated in previous studies (Issa *et al*., 2012; Farsaei, Ghorbani and Adibi, 2017; Horsa, Ayele and Ayalew, 2019; Mahmoudi, Mohammadi and Niknam, 2019). Although SUP use is controversial, evidence-based guidelines for SUP recommend prophylactic AST for high-risk patients (Armstrong *et al.*, 1999). Without SUP, approximately 6% of critically ill patients experience clinically significant bleeding (Agee, Coulter and Hudson, 2015).

1.3. Significance of the study

Around the world, clinicians order SUP for 80%–90% of critically ill and injured patients(Stein *et al.*, 1991; Buendgens, Koch and Tacke, 2016).Acid suppressant prescriptions are also prevalent in less critically ill patients. Consequently, inappropriate SUP utilization has grew concerns and is related with rise in adverse drug events and added health care costs (Heidelbaugh, Goldberg and Inadomi, 2009; Cook and Guyatt, 2018).

As the prevalence of inappropriate SUP use in other countries appeared higher, there is a need to examine the current practice of SUP among patients in our local setting. So far, there is no study that evaluated the use of SUP in TASH. This study made an effort to evaluate the magnitude and appropriateness of SUP use at medical ward and ICU of TASH. The result of this study will promote rational drug use, developing institutional based guidelines, create awareness about appropriate use of SUP, improving quality of life, and clinical outcomes of the patient, cutback duration of hospitalizations and reducing healthcare associated costs.

2. Literature review

2.1. Background

Stress ulcer can cause a broad range of clinical manifestations from superficial mucosal erosions or mild-severe ulceration to life threatening bleeding. It is the main concern in hospitalized critically and non-critically ill patients(Armstrong *et al.*, 1999; Anderson, 2013; Malhis *et al.*, 2019).

A prospective observational study conducted in Saudi, in2017,revealed that more than 75 in every 100 intensive care unit (ICU) patients develops stress-related ulcers within the first 3 days of admission(Malhis *et al.*, 2019). Estimates of the incidence of GI bleeding range from 0.1% to 31%, but most studies conclude that less than 6% of critically ill patients will develop GI bleeding during their hospitalization(Hammond *et al.*, 2017). The incidence of GI bleeding in hospitalized non–critically ill patients is approximately 0.2% to 0.4%(Qadeer, Richter and Brotman, 2006).

The risk factors associated with stress ulcer might be found in patients with serious injuries after trauma or surgery (Armstrong *et al.*, 1999). It is stated in different literatures that mechanical ventilation and coagulopathy are the major risk factors for developing stress related ulcer(Issa *et al.*, 2012; Cohen *et al.*, 2017; Hammond *et al.*, 2017; Sridharan, Sivaramakrishnan and Gnanaraj, 2017). A retrospective cross-sectional study done in Gondar, in 2017, states the most widely recognized acute risk factors to stress ulcer are coagulopathy (18.4%), followed by hypoperfusion (9.8%). The concomitant NSAID use (16.7%), mild-to-moderate brain or spinal cord injury (11.1%), and concomitant or recent corticosteroid use (9.4%) were the most frequent potential risk factors that required administration of prophylaxis for patients who were on nothing by mouth (NPO)(Horsa, Ayele and Ayalew, 2019).

During stressful events normal protective mechanisms are altered, including epithelial turnover in the gastric mucosa and secretions of mucus and bicarbonate(Stein*et al.*, 1991). Cellular defense is primarily mediated by gastric prostaglandins, which prevent ulcer formation and accelerate the healing process. This seems to occur partly because prostaglandins reduce acid secretion. More importantly, they have been shown to exert a direct cytoprotective effect against agents that kill mucosal cells on contact (Stollman and Metz, 2005).When homeostasis of the gastric mucosa is disrupted, combined with the release of various inflammatory mediators such as arachidonic acid

metabolites, cytokines, and oxygen free radicals can directly damage the gastric mucosa(Armstrong *et al.*, 1999).Thus, prevention of stress ulceration can be achieved using acid suppressing agents or therapies that enhance the protective mechanisms.

Proton pump inhibitors were the most frequently used acid suppressing agents followed by H_2blockers(Sheikh-taha *et al.*, 2012; Farsaei, Ghorbani and Adibi, 2017; Horsa, Ayele and Ayalew, 2019; Mahmoudi, Mohammadi and Niknam, 2019). Because of the efficacy of PPIs, they have become clinicians' first choice for SUP use(Alshamsi*et al.*, 2016).Significant GI bleeding is seen in critically ill patients and rarely in non-critically ill patients. Despite the fact that, consequence of GI bleeding is relatively low in non-critically ill patients (0.41%), but they also could benefit from SUP (Agee, Coulter and Hudson, 2015; Farsaei, Ghorbani and Adibi, 2017).

2.2. Prevalence of SUP use

Regardless of an often weak rationale, administration of SUP for hospitalized patients is common, with previous studies stating that up to 60% of patients receive SUP(Khalili *et al.*, 2010; Jain, Jabeen and Vallurupalli, 2013; Abdi *et al.*, 2017; Hammond *et al.*, 2017; Cook and Guyatt, 2018; Mahmoudi, Mohammadi and Niknam, 2019). An observational prospective study done in Northern Cyprus showed, 60.86% of patients received AST for prophylaxis (Abdi *et al.*, 2017). Also, in a pre- and post-interventional study, SUP was prescribed to 74.1% of all patients during their hospital stay(Jain, Jabeen and Vallurupalli, 2013). This is also similar with a study done in Iran 2019, which reported (81.2%) patients received prophylactic AST(Mahmoudi, Mohammadi and Niknam, 2019).Prevalent use of SUP by clinicians were also reported in another exploratory, prospective pre- and post-intervention study, stating that the prevalent use of SUP may be attributed to the misconception that the side effects of PPIs and H_2RAs are occasional, and their relatively low cost of these agents(Khalili *et al.*, 2010). Other possible reason for prevalent use of SUP stated by Hammond *et al*, was the unfamiliarity of physicians with the tones of SUP guidelines and new literatures drawing indications and choice of prophylactic agents(Hammond *et al.*, 2017). Similarly, it is stated in previous studies that initiation of prophylactic ASTs that were not based on the available SUP guidelines attributed to the higher number of SUP use(Jain, Jabeen and Vallurupalli, 2013; Mahmoudi, Mohammadi and Niknam, 2019).

2.3. Appropriateness of SUP use

Currently, there is a growing concern in overutilization of SUP. Overutilization of stress ulcer prophylaxis (SUP) in both critically and non-critically ill patients poses significant health risks and increases healthcare costs(Agee, Coulter and Hudson, 2015). Events of improper utilization of SUP have been expressed both in retrospective and prospective studies. A cross-sectional prospective study done in Iran, revealed that among 195 patients both over and under inappropriate use of SUP upon admission, during hospital stay and at discharge were 61%, 80% and 77.4%, respectively. Among included patients, 155 received SUP upon hospital ward admission, 109 (70.33%) patients did not fulfill the criteria to receive SUP. In addition, 10 out of 40 (25%) patients did not receive SUP properly upon admission while they had clear or valid indication (Farsaei, Ghorbani and Adibi, 2017).

Similarly, an exploratory, prospective pre- and post-intervention study done in 2010, showed of the 262 patients in the pre-intervention period, 80.9% (n = 212) received AST compared with 113 of 240 patients (47.1%) in the post-intervention period. Of the 23 patients in the pre-intervention period with an indication for SUP according to the internal ASHP-based guideline, 78.3% (n = 18) received AST versus 85.7% (n = 12 of 14) in the post intervention period. Of the 239 patients without an indication for SUP, 194 (81.2%) received AST in the pre-intervention period versus 101 of 226 (44.7%) in the post-intervention period. Of the 212 patients who received AST in the pre intervention period, 194 (91.5%) did not have an indication for SUP versus 101 of 113 (89.4%) in the post-intervention period (Khalili *et al.*, 2010).

A retrospective cohort study done in University of Texas Medical School at Houston, United States of America (USA), reviewed 774 patients, in 2011. From those 545 patients were included in the study. Patients were more likely to receive SUP if they had more risk factors for stress ulcer bleeding. Nevertheless, 37.7% of the patients with no risk factors were given SUP, representing 10.6% of the entire group of non-critically ill patients. Overall, 54.9% (299 of 545) of patients received SUP. Of these 299 patients, at least 58.5% did not warrant SUP, depending on the criteria used. Of the entire cohort of 545 non-critically ill patients, 32.1% to 54.9% received unjustified SUP, depending on the criteria applied(Hwang *et al.*, 2007).Similarly, other studies also identified that SUP is frequently prescribed to hospitalized patients lacking risk factors for stress ulcer(Qaisar, 2013; Mohamad, Shamsuddin and Tan, 2015; Malhis *et al.*, 2019).

An observational prospective study done in Northern Cyprus showed, 60.86% received AST therapy for SUP (stress ulcer prophylaxis). Out of 42 rationally managed patients 13 (18.84%) patients had an absolute indication for SUP, 29 (42.02%) patients had 2 or more relative indications for SUP. 18 (26.08%) patients received AST without any appropriate indication (Abdi *et al.*, 2017).In addition according to a hospital based retrospective study, of 153 admitted patients, 130 (85%) were started on AST, out of which 11 (8.5%) were non-SUP indications and had a diagnosis that supports the use of this therapy (GI bleed, gastritis, esophagitis and GERD),16 (12.3%) had an absolute indication for SUP, 59 (45.4%) had 2 or more relative indications for SUP and 44 (33.8%)received AST without an appropriate indication. In addition, one patient with an absolute indication for SUP and four with two or more relative indications did not receive AST(Sheikh-taha *et al.*, 2012).

2.4. Predictive factors for inappropriate SUP use

To improve this improper utilization of SUP, pharmacists could play an important role in reducing inappropriate prescribing of SUP. Few studies showed reduction of the duration of inappropriate stress ulcer prophylaxis during hospitalization and continuation upon hospital discharge after clinical pharmacists' interventions (Khalili *et al.*, 2010; Buckley *et al.*, 2015; Agee, Coulter and Hudson, 2015; Belfield *et al.*, 2017). Pharmacist led educational sessions improved appropriateness of SUP by decreasing inappropriate SUP prescribing from 55.5% to 30.5%(Agee, Coulter and Hudson, 2015).

A retrospective interventional study that consisted of formulation of a guideline, education to the hospitalist service, and intervention by clinical pharmacists was done in Hackensack University Medical Center, at Hackensack, USA. They enrolled 61 patients in the historical group and 81 patients in the interventional group. Their intervention resulted in a 31% absolute reduction of inappropriate use of AST between the historical and interventional samples, representing a relative reduction of 48%. In addition, there was 24% absolute reduction of patients discharged on inappropriate AST, representing a 75% relative reduction. And there were 23 successful interventions(Belfield *et al.*, 2017).

In another interventional study, of the 262 patients in the pre-intervention period, AST use declined from 80.9% (n = 212) to 47.1% (113 of 240) patients in the post-intervention period. Of the 23

patients in the pre-intervention period with an indication for SUP according to the internal ASHP-based guideline, 78.3% (n = 18) received AST versus 85.7% (n = 12 of 14) in the post intervention period. Of the 239 patients without an indication for SUP, 194 (81.2%) received AST in the pre-intervention period versus 101 of 226 (44.7%) in the post-intervention period. Of the 212 patients who received AST in the pre intervention period, 194 (91.5%) did not have an indication for SUP versus 101 of 113 (89.4%) in the post-intervention period. The introduction of a treatment guideline for SUP by pharmacists was associated with reduction in use of AST overall and in patients without an absolute indication for SUP (Khalili *et al.*, 2010).

Previous studies stated that advanced age, male gender, prolonged hospitalization, type of ward, types of comorbidities, reason for admission (CNS disorder), and having more than 2 minor risk factors for stress ulcer had an association with the outcome variable (Issa et al., 2012; Farsaei, Ghorbani and Adibi, 2017; Malhis *et al*., 2019; Horsa, Ayele and Ayalew, 2019). The possible justification for significant association between inappropriate SUP use and longer hospital stay may be because patients with longer stay had more chances of unnecessary SUP prescription as a result of a greater number of physicians' visits over the longer periods of stay (Horsa, Ayele and Ayalew, 2019). Increased age was stated as major predictor variables in previous studies, the fact that medical diseases do increase with age therefore be the rationale behind frequent SUP prescription (Issa et al., 2012; Farsaei, Ghorbani and Adibi, 2017).

3. Objective

3.1. General objectives

- ✓ To determine the appropriateness and associated factors for the use of SUP among patients treated at medical ward and ICU of TASH, Addis Ababa, Ethiopia.

3.2. Specific objectives

- ✓ To determine the prevalence of SUP use among patients treated at medical ward and ICU of TASH
- ✓ To determine the appropriateness of SUP among patients treated at medical ward and ICU of TASH
- ✓ To identify predictive factors associated with inappropriate use of SUP among patients treated at medical ward and ICU of TASH

4. Methods

4.1. Study Setting

The study was conducted at adult medical wards and ICU of TASH, which is the tertiary specialized hospital in Ethiopia that gives service for the community The hospital found in Lideta Sub-City, Addis Ababa, Ethiopia and built up in 1972(Niguse, Engidawork and Amogne, 2016).It is the biggest teaching hospital affiliated with Addis Ababa University, College of health Sciences(Worku*et al.*, 2017).

The hospital has around 465 physicians, 76 pharmacists, 992 nurses and 115 other health care experts committed to giving wellbeing care administrations. It moreover has 950 administrative and support staff (College of health sciences human resource management, 2018). It serves approximately 250,000 patients per year in its outpatient division and approximately 24,000 within the inpatient and same number within the emergency divisions(Sisay*et al.*, 2018). The major services provided by the hospital includes: internal medicine, emergency, surgery, gynecology and obstetrics, pediatrics, oncology/chemo-radiology, radiology, psychiatry and dermatology(Niguse, Engidawork and Amogne, 2016)

4.2. Study design and period

This is an institutional based Cross-Sectional study, which was conducted from August 9th to December 9th2019. Data was collected prospectively from medical records of patients and communicated with respective physicians in order to confirm the indication of AST. And intervention was made about the use of SUP.

4.3. Source and study population

4.3.1. Source population

All patients who were admitted at medical ward and ICU for any type diagnosis at TASH were considered as source population.

4.3.2. Study population

All patients who were admitted at medical ward and ICU at TASH for any type diagnosis from August 9th 2019 to December 9th 2019 constituted the study population and those patients who fulfilled the inclusion criteria were the sample population.

4.4. Sampling and sample size determination

All patients who fulfill the eligibility criteria and those admitted at medical and ICU wards of TASH at the time of data collection period were included in the present study. Three hundred ninety-one patients were included. Among them, 23 patients were excluded due to exclusion criteria. Finally, data of 368 patients was considered for the final analysis.

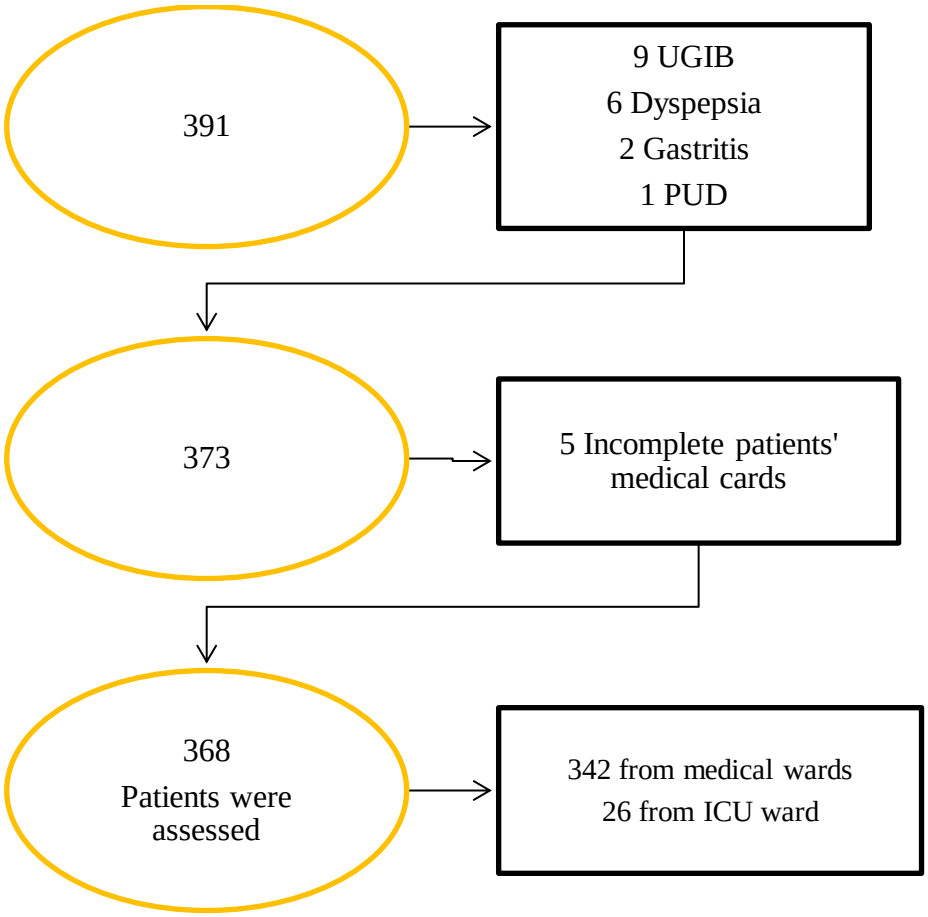

Figure1.Diagrammatic scheme of study participant recruitment process of patients attending in adult medical and ICU wards of TASH, n=368.

4.5. Inclusion and exclusion criteria

4.5.1. Inclusion criteria

- ✓ Patients admitted for any type of diagnosis at adult medical ward and ICU of TASH.

4.5.2. Exclusion criteria

- ✓ Patients with incomplete medical records
- ✓ Patients with acid suppressive therapy for indication of GI disease

4.6. Study variables

4.6.1. Dependent variables

- ✓ Appropriateness of stress ulcer prophylaxis (SUP) use

4.6.2. Independent variables

Socio-demographic variables

- ✓ Age
- ✓ Sex

Clinical/ medication related variables

- ✓ Duration of hospitalization
- ✓ Reason for admission
- ✓ Coagulopathy
- ✓ Hypoperfusion (shock, or organ dysfunction)
- ✓ High-dose corticosteroids (>250 mg/day hydrocortisone or equivalent)
- ✓ Concomitant use of a non-steroidal anti-inflammatory drugs (NSAIDs)
- ✓ Concomitant or recent corticosteroid use
- ✓ History of upper GI hemorrhage, peptic ulcer disease, or gastritis
- ✓ Feeding status

4.7. Data collection instruments and techniques

The data collection tool was adopted from evidence-based medicine Guidelines for stress ulcer prophylaxis after reviewing similar articles. Specifically, the Orlando Regional Medical Center (ORMC) SUP guideline was used to collect all necessary information like socio demographic and risk factors for developing a stress-related ulcer, drugs prescribed for prevention of stress ulcer, and the rationality of SUP (Smith, Cheathamand Smith, 2017).). For comprehensive information, medication history of patients was assessed for any acid suppressive therapy and past GI diseases.

According to the guideline, stress ulcer prophylaxis is indicated in patients with acute risk factors or in patients that are nothing by mouth (NPO) and have at least two potential risk factors for stress ulceration. The five absolute indications include, mechanical ventilation (>48h) without enteral nutrition, coagulopathy, hypoperfusion (shock, or organ dysfunction), high-dose corticosteroids (>250mg/day hydrocortisone or equivalent), and significant burn injury (total body surface area 20%). The potential risk factors for stress ulcer are concomitant use of a non-steroidal anti-inflammatory drug (NSAID), concomitant or recent corticosteroid use, history of upper GI hemorrhage, peptic ulcer disease, or gastritis(Smith, Cheatham and Smith, 2017).

4.7.1. Data collector recruitment and training

One clinical pharmacist and one BSc nurse from ICU were enlisted as data collectors. The data collectors were trained on the use of data collection tool, sampling techniques, how to collect the necessary data from patient's chart, and the ethical principles of confidentiality and data management prior to their involvement with data collection.

4.7.2. Data quality control

The data collection instruments were reviewed by senior experts of the area for clarity and comprehensiveness of its contents. Following that pre-testing of both data collection tools were done in ten selected hospitalized patients who had been admitted at internal medicine and ICU wards of TASH. Accordingly, all the necessary modifications and adjustments were done before implementing the main study. Throughout the data collection process close supervision was made by the principal investigator. The collected data were checked for completeness and accuracy.

After data entry, data cleaning was performed and maximum effort was also done at the analysis and interpretation.

4.7.3. Data analysis and interpretation

The data was checked for completeness and consistency. At that point, information was traded to statistical package for social science (SPSS) window adaptation 25 for investigation. Categorical variables were presented in numbers and percentages. Continuous variables are presented as mean ± standard deviation. Upon univariable regression a p-value ≤0.2 were taken into multivariable logistic regression to determine the presence of significant association between the appropriateness of SUP and independent variables. Statistical significance was declared at p-value less than 0.05.

4.8. Ethical considerations

Before starting of the study, ethical clearance was obtained from Addis Ababa University, School of Pharmacy ethical review committee as well as permission also taken from the ICU and internal medicine ward. Confidentiality and anonymity of subject was maintained by not recording identifying details, such as name or any other personal identifiers. Only numerical identifications used as a reference. Informed consent was obtained from patients and patients' attendants. No disclosure of any name of the patients, the healthcare provider or drug product will make in relation to the findings.

4.9. Operational definition

- Organ dysfunction= Renal insufficiency (CrCl<40mL/min or Scr>2.8mg/dL), Hepatic impairment (bilirubin >8.8mg/dL, serum AST >500 U/L, Alb<4g/L).
- SUP was viewed as appropriate in every one of those patients who had an absolute risk or 2 or more potential risk factors.
- Inappropriate SUP use was defined as per Orlando medical center SUP guideline, that is in those patients who had risk factors for SRMD but who did not receive SUP or those who were on SUP but who were not candidates for prophylaxis.

5. Results

5.1. Sociodemographic and clinical characteristics

Three hundred sixty-eight patients were included in this study. Among the study participants there was a predominance of male study participants 208 (56.5%). The median age of the study participants was 32 years (range: 13–83 years), and the mean ± SD 35.88 ± 16.15.

Around half of the study participants stayed in the hospital for less than ten days (46.2%). The mean ± SD duration of hospital stay was 11.39 ± 6.52 days. Infectious disease, cardiovascular diseases and oncologic diseases were among the commonest reasons for hospitalization recorded in the 37.5%, 24.5% and 22.8% of study participants, respectively. Most majority of the study participants 317 (86.1%) were on enteral feeding. Among 368 study participants 26 (6.8%) were admitted to the ICU ward of TASH and from ICU admitted patients majority of them were 24 (96%) on mechanical ventilation for >48hours. However, the rest of the study participants 342 (92.93%) which were from medical ward were not on mechanical ventilation during their hospital stay (table1).

Table 1: Socio-demographic and clinical characteristics of patients attending in adult medical ward ICU unit of TASH, Addis Ababa, Ethiopia, from August 2019- December 2019, (N=368)

Characteristics	Category	Appropriate vs inappropriate SUP		Number of patients (%)
Age	< 25years	60 (16.3)	61 (16.6)	121 (32.8)
	26-45 years	74 (21.1)	88 (23.9)	162 (44.0)
	>46 years	44 (11.9)	41 (11.1)	85 (23.1)
Sex	Male	99 (26.9)	110 (29.9)	209 (56.8)
	Female	77 (20.9)	82 (22.3)	159 (43.3)
Length of hospital stay	≤10 days	130 (35.3)	120 (32.6)	250 (67.9)
	>10 days	47 (12.8)	71 (19.3)	118 (32.1)
Feeding status	Enteral	149 (40.5)	168 (45.7)	317 (86.1)
	NG tube	28 (7.6)	23 (6.3)	51 (13.9)

Reasons for admission	Cardiovascular diseases	55 (14.9)	36 (9.8)	91 (24.7)
	Infectious diseases	61 (16.6)	77 (20.9)	138 (37.5)
	Oncologic diseases	40 (10.9)	43 (11.7)	83 (22.5)
	CNS diseases	8 (2.2)	11 (3.0)	19 (5.2)
	GI diseases	1 (0.3)	3 (0.8)	4 (1.1)
	Respiratory diseases	2 (0.5)	7 (1.9)	9 (2.4)
	Renal diseases	2 (0.5)	7 (1.9)	9(2.4)
	Others**	7 (1.9)	8 (2.2)	15(4.1)

**Central Nerves System, GI; Gastrointestinal*

***Others; Endocrine diseases, metabolic complications, immunological diseases*

5.2. Indication for stress ulcer prophylaxis

According to the Orlando Regional Medical Center (ORMC) stress ulcer prophylaxis guideline, the most common acute risk factors for use of to stress ulcer prophylaxis in this study were coagulopathy 134 (36.4%), followed by organ dysfunction and hypoperfusion 115 (31.3%). Concomitant or recent corticosteroid uses were reported around one-fifth of the study participants (20.7%) and history of UGIB, PUD or gastritis 66 (17.9%) were the most frequent potential risk factors (table2).

***Table 2*: Indications of Stress ulcer prophylaxis of patients attending in adult medical ward ICU unit of TASH, Addis Ababa, Ethiopia, from August 2019- November 2019, (N=368)**

Category	Indications for stress ulcer prophylaxis	Number of patients (%)	
		Yes	No
Acute risk factors	Mechanical ventilation (>48 hours)	24 (6.5)	344 (93.5)
	Coagulopathy	134 (36.4)	234 (63.3)
	Organ dysfunction and hypoperfusion	115 (31.2)	253 (68.8)
	High-dose corticosteroids (>250 mg/day hydrocortisone or equivalent)	48 (13)	320 (87)
Potential risk factors	Concomitant or recent corticosteroid use	75 (20.4)	293 (79.6)

History of UGIB, PUD or gastritis	66 (17.9)	302 (82)
Concomitant use of a NSAID	43 (11.7)	325 (88.3)

5.3. Prevalence and Appropriateness of SUP use among patients treated at medical and ICU wards of TASH

Among 342 patients admitted at adult medical wards, which were included in our study 118 one-third (34.5%) were on SUP. On the other hand, all patients from ICU ward received SUP. Of all the included patients, almost 40% of the study participants were on SUP, from these around two-third of them (64.58%) had an indication for SUP, and the rest one-third (35.41%) received SUP without an appropriate indication. Besides this, there are a huge number of patients that had an indication for SUP but did not receive SUP 140 (62.5%).

Among the study participants, 177 (48.1%) patients were appropriately managed regarding their SUP use according to the Orlando medical center SUP guideline. However, 191 (51.9%) patients SUP use was inappropriate. 51(26.7%) had no clear indication for SUP but received prophylaxis. In addition, 140 (73.3 %) patients with indications did not receive SUP (table 3). Intervention was made for the inappropriately managed patients, among them 79 (41.4%) were accepted, 48 (25.1%) partially accepted and the rest 64 (33.5%) were rejected.

Table 3: **Number of patients with appropriate SUP use, overuse, and underuse among patients attending in adult medical ward ICU unit of TASH, Addis Ababa, Ethiopia, from August 2019- November 2019, (N=368)**

Assessment of rationality	**Number of patients**	**(%)**
Appropriate (n=177)		
No indications for SUP and no SUP	84	47.7
Indication and SUP were given	93	52.5
Inappropriate (n=191)		

	No indications for SUP but SUP was given (Overutilization)	51	26.7
	There is indication but no SUP was given (Underutilization)	140	73.3

5.4. Pharmacologic agent used for SUP

Of patients who received SUP, majority of them (90.3%) received PPIs of which, exclusively omeprazole, and the rest of the study participants 14 (9.7%) received H2-RAs of which cimetidene was the most commonly prescribed. Almost half of the participants (48.6%) received AST by the oral route, while 74 patients (51.9 %) received it intravenously.

Table 4: **Drugs used for stress ulcer prophylaxis among patients attending in adult medical ward ICU unit of TASH, Addis Ababa, Ethiopia, from August 2019- November 2019, (N=368)**

Drugs used for SUP	Dosage form		Frequency of use	Percent (%)
	IV	PO		
Proton pump inhibitor (PPIs)	60	70	130	90.3
Histamine 2 receptor antagonist (H_2RA)	14	0	14	9.7

5.5. Predictive factors associated with inappropriateness of SUP

All variables with a p-value of ≤0.2 were included in multivariable logistic regression for final analysis. Patients who were on NG tube feeding, patients with coagulopathy and history of UGIB, PUD or gastritis had showed a significant association with inappropriate use of SUP. The odds of inappropriate use of SUP in patients with NG tube feeding are 2.92 times, compared to those who were on enteral feeding in their hospital stay (AOR=2.92, 95% CI: 1.165-7.321, P=0.022).

In addition, patients without coagulopathy had showed a 51.2% reduction towards the occurrences of inappropriate uses of SUP compared to patients with coagulopathy (AOR=0.488, 95% CI: 1.200-3.308, P=0.008). Similarly, patients without any history of UGIB or PUD or gastritis had

50.6% lower risk than patients with any of the above indications towards inappropriate SUP use (AOR=0.494, 95% CI: 1.024-3.705, P=0.042).

***Table 3*: Predictive factors associated with appropriateness of SUP use of study participants attending in adult medical ward and ICU unit of TASH, Addis Ababa, Ethiopia, from August 2019-November 2019, (N=368)**

Variables	Appropriate vs inappropriate SUP use		COR (95% CI)	AOR (95% CI)	P-Value
Age					
≤25 years	60 (16.3)	61 (16.6)	1.00		
26-45	74 (21.1)	88 (23.9)	2.384 (0.551-4.948)	1.952 (0.992-3.841)	0.053
≥45	44 (11.9)	41 (11.1)	0.872 (0.411-6.187)	1.774 (0.558-7.367)	0.211
Gender					
Male	99 (26.9)	110 (29.9)	1.00		
Female	77 (20.9)	82 (22.3)	1.002 (0.384-6.271)	1.002 (0.613-1.637)	0.995
Hospital stay					
≤10 days	130 (35.5)	120 (32.6)	1.00		
≥10 days	47 (12.8)	71 (19.3)	0.059 (0.799-0.845)	0.599 (0.354-1.014)	0.058
Feeding status					
Enteral feeding	207 (56.3)	110 (29.9)	1.00		
NG tube feeding	13 (3.5)	38 (10.3)	9.107 (1.144-3.726)	2.920 (1.165-7.321)	**0.022***
Coagulopathy					
Yes	56 (15.2)	78 (21.2)	1.00		
No	171 (46.5)	63 (17.1)	2.442 (0.982-14.66)	0.488 (1.2-3.308)	**0.008***
High dose steroid use					
Yes	24 (6.5)	24 (6.5)	1.00		

No	153 (41.6)	167 (45.4)	0.125 (0.816-12.88)	0.612	(0.296-1.263)	0.184
Organ dysfunction						
Yes	56 (15.2)	59 (16.0)	1.00			
No	121 (32.9)	132 (35.9)	1.356 (0.665-9.485)	1.356	(0.779-2.360)	0.281
Concomitant NSAIDs use						
Yes	29 (7.9)	14 (3.8)	1.00			
No	149 (40.5)	177 (48.1)	0.472 (0.603-4.804)	0.472	(0.197-1.128)	0.091
History of UGIB, PUD or gastritis						
Yes	23 (6.3)	43 (11.7)	1.00			
No	175 (47.6)	128 (34.8)	1.948	0.494	(1.024-3.705)	**0.042***

**Variables that showed a significant association with the outcome variable*

6. Discussion

This study is the first study in TASH aimed to determine the prevalence and appropriateness of SUP use among patients admitted at medical and ICU wards. The Orlando Regional Medical Center derived guideline was used to evaluate appropriateness of SRMD prophylaxis practice. The rationality why this guideline was selected to evaluate appropriates of SUP use was due to its simplicity to practice in clinical terms and easy to evaluate the practice of SUP use among hospitalized patients.

This study had found that 144 (39.13%) patients were on SUP in their hospital stay which was comparable to a study done in Gondar (35%) Boressa et al(Horsa, Ayele and Ayalew, 2019).However, previous studies reported greater number of patients were receiving SUPs than the current study (Khalili *et al.*, 2010; Nasser, Nassif and Dimassi, 2010; Jain, Jabeen and Vallurupalli, 2013; Abdi *et al.*, 2017; Hammond *et al.*, 2017; Luo *et al.*, 2017; Mahmoudi, Mohammadi and Niknam, 2019).The higher SUP use in the above studies could be due to prescribing SUP routinely at admission and lack of guidance from senior physicians afterwards contributes to the widespread use of SUP(Jain, Jabeen and Vallurupalli, 2013; Luo *et al.*, 2017). Lack of consistency in practice of prescribing SUP among physicians with the real practice and prescription of these SUP medications were not based on the available guidelines (Jain, Jabeen and Vallurupalli, 2013; Hammond *et al.*, 2017; Mahmoudi, Mohammadi and Niknam, 2019).The higher prevalent use of SUP by prescribers in other centers compare to this study might also be attributed to the wrong perception that the adverse effects of PPIs and H2RAs are occasional when used for short period(Khalili *et al.*, 2010).

According to the Orlando regional medical center derived guideline, in the present study inappropriateness of SUP use was encountered among 51.9% of patients. Among them around three-fourth (73.3%) of medical and ICU patients were not prescribed prophylaxis while there were clear indications (underutilization). Discrepancy between current practice in the hospital and available guidelines could be related to underutilization of SUP in this setting. In addition, the absence of regular clinical pharmacy service in the hospital might be another reason for underutilization of SUP. The rest one-fourth (26.7%) of the patients were inappropriately prescribed SUP in the absence of clear indication. Whereas almost half 48.1% of the patients were

appropriately managed regarding their SUP use on the basis of the Orlando Regional Medical Center SUP guidelines.

The high prevalence of inappropriateness in this study was attributed to the underutilization of SUP. It was seen in 73.3% of patients, which was higher than most studies. Mahmoudi *et al*, Shadi Farsaei, and boressa *et al* reported a 4.5%, 9.8%, and 18.4% of patients did not receive prophylaxis for SRMD while they had risk factors(Farsaei, Ghorbani and Adibi, 2017; Horsa, Ayele and Ayalew, 2019; Mahmoudi, Mohammadi and Niknam, 2019). However, issa*etal,*2012 reported 33% of patients were candidates for SUP but did not receive AST(Issa *et al.*, 2012). The reason for varied results could be their study designs, settings and period, as well as in the current study, the number of days of hospitalization of study participants was lower when compared to some other studies(Issa *et al.*, 2012; Farsaei, Ghorbani and Adibi, 2017).

In this study, overutilization is seen in 26.7% of patients, which is consistent with Mahmoudi *et al*, Abdikarim *et al*, and Boresa *et al* who reported inappropriate SUP use among 28.3%, 26.08% and 22.2% respectively of study subjects who lack risk factors for stress ulcer(Abdi *et al.*, 2017; Horsa, Ayele and Ayalew, 2019; Mahmoudi, Mohammadi and Niknam, 2019). However, this figure is a lesser compared to other studies, which reported >65% of inappropriate SUP use(Khalili *et al.*, 2010; Zeitoun, Zeineddine and Dimassi, 2011; Rph *et al.*, 2012; Jain, Jabeen and Vallurupalli, 2013; Qaisar, 2013; Mohamad, Shamsuddin and Tan, 2015; Farsaei, Ghorbani and Adibi, 2017). According to a prospective observational study conducted in 2015 M.S Mohammed *et al*, 96.4% of the patients had inappropriate prescriptions for SUP(Mohamad, Shamsuddin and Tan, 2015). Perception of need for prophylaxis in patients with different clinical circumstances, increased age of study participants and different hospital protocols could be the reasons of the higher inappropriate SUP use in the above studies compared with our study. The absence of standard guidelines in the institutions, and no regular review for the necessity of SUP once initiated were the possible justification for overutilization in other studies(Khalili *et al.*, 2010; Rph *et al.*, 2012).

Patients' with longer hospital stays tend to be sicker being on higher number of medication, thus prescribers may be urged to initiate unnecessary SUP to avoid further complications of GIB(Issa *et al.*, 2012; Horsa, Ayele and Ayalew, 2019). Moreover, recent studies stated that teaching or nonteaching study settings could have an effect on inappropriate SUP. Use of SUP is likely better

practiced in teaching hospitals where available standardized guidelines may be followed(Zeitoun, Zeineddine and Dimassi, 2011; Horsa, Ayele and Ayalew, 2019).

In the current study, patients who were on NG tube feeding, coagulopathy and patients with either history of UGIB or PUD or gastritis showed a statistically significant association with inappropriate use of SUP. On the other hand, previous studies stated that advanced age, male gender, prolonged hospitalization, type of ward, types of comorbidities, reason for admission (CNS disorder), and having more than 2 minor risk factors for stress ulcer had an association with inappropriateness of SUP use(Issa *et al*., 2012; Farsaei, Ghorbani and Adibi, 2017; Malhis *et al*., 2019; Horsa, Ayele and Ayalew, 2019).

During the time of data collection, the medical ward was under maintenance due to this significant number of study participants were from hematology side, and in those patients coagulopathy were common. These were the most commonly encountered acute risk factor in this study necessitating initiation of SUP, which contribute to the higher rate of underutilization in this study.

7. Limitations of the study

- ✓ There are no current established hospital guidelines in the study setting for the appropriate utilization of SUP to evaluate their practice.
- ✓ The study was performed at single teaching hospital which may be difficult to generalize to other hospital settings.
- ✓ Variation in prescribing behaviors may exist due to medical residents' rotation and this may affect the appropriateness of SUP prescribing as the skill of the residents may differ.
- ✓ Possible observational bias could limit the prevalence of inappropriately prescribed SUP.
- ✓ Appropriateness of SUP was evaluated based on the indications of patients even though appropriateness is inclusive of other parameters such as type of prophylactic agent used, the dose and duration of prophylaxis.
- ✓ There was poor record keeping system.

8. Conclusion

The result of the current study found that more than one-third (39.13%) of patients admitted at ICU and medical ward of TASH were prescribed SUP. Inappropriate SUP use was encountered in significant number of study participants. Almost 3/4th of inappropriateness was attributed to the underutilization of SUP. Study participants who were on NG tube feeding, coagulopathy and history of UGIB or PUD or gastritis showed a significant association with inappropriate use of SUP. Hence, it is necessary to develop and implement standardized SUP guidelines for ICU and medical ward patients in our hospital setting.

9. Recommendations

Based on the study findings, the following recommendations were made:

- ✓ Institutional based stress ulcer prophylaxis practice guidelines, for medical and ICU patients' needs to be developed and implemented within the institution (TASH) by the hospital's physicians and pharmacists to improve quality of SUP use.
- ✓ Frequent review of medications and reassessment for the need of SUP by the senior physicians and clinical pharmacists are essential to improve proper use of SUP.
- ✓ Future researches concerning SUP use should also be carried out in multi centers including surgery, and other hospital wards and need for intervention should be addressed. Furthermore, other possible factors contributing to inappropriate SUP use practice should be addressed.
- ✓ This study spots the need for interventional study and will help future researchers address impact and cost of inappropriate SUP use practice.

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11. Annex

11.1. Annex I: Data abstraction format

STUDY CHECKLIST

Sociodemographic data

1. Age
2. Sex: a) Male b) Female

Clinical characteristics

1. Reason for admission
2. Length of hospital stay in days
3. Feeding status of the patient
   a) NG tube feeding b) Enteral feeding c) NPO

Medication data

1. Is patient on stress ulcer prophylaxis (SUP)?
   a) Yes b) No
2. Which drug is used for SUP?
   a) Proton pump inhibitors: Omeprazole, Esomeprazole, Pantoprazole
   b) Histamine 2 receptor blockers: Cimetidine, Ranitidine
3. Duration of stress ulcer prophylaxis:

Acute risk factors

Risk factors			
Mechanical ventilation (>48 hours) without enteral nutrition	a) Yes	b) No	c) Unknown
Coagulopathy			

Platelet count <50,000mm^3 : INR>1.5: PTT 2x the baseline:	a) Yes a) Yes a) Yes	b) No b) No b) No	c) Unknown c) Unknown c) Unknown
Hypoperfusion (shock, or Organ dysfunction)	a) Yes	b) No	c) Unknown
Scr>2.8mg/dl: AST>500U/l: Albumin<4g/dl: Bilirubin Total> 8.8mg/dl:	a) Yes a) Yes a) Yes b) Yes	c) No b) No c) No b) No	d) Unknown c) Unknown d) Unknown e) Unknown
Significant burn injury (total body surface area 20%)	a) Yes	b) No	c) Unknown
High-dose corticosteroids (>250 mg/day hydrocortisone or 50 mg of methylprednisolone, 60 mg of prednisone, 10 mg of dexamethasone)	a) Yes	b) No	c) Unknown

Potential risk factors

Risk factors		
Concomitant use of a non-steroidal anti-inflammatory drugs (NSAIDs)	a) Yes	b) No
Concomitant or recent corticosteroid use	a) Yes	b) No
History of upper gastrointestinal (GI) hemorrhage, peptic ulcer disease, or gastritis	a) Yes	b) No

Appropriateness of SUP

Appropriateness of SUP	
Appropriate	
Inappropriate	
Intervention	
Yes (write Suggested intervention)	
No	
Interventions	
Accepted	
Partially accepted	
Rejected	

11.2. Annex II: Ethical clearance

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Addis Ababa University

School of Pharmacy
Ethical Review Board

ቀን Date: August 05, 2019

ቁጥር Ref. No.: ERB/SOP/119/08/2019

To: **Samiya Yassin**

School of Pharmacy

Re: **Ethical Clearance**

It is to be recalled that you submitted a study proposal entitled ***"Evaluation of stress ulcer prophylaxis use at adult medical ward and intensive care unit of Tikur Anbessa Specialized Hospital: A prospective study"*** for ethical approval by the School's Ethical Review Board (ERB). The Board thoroughly reviewed the proposal based on its operational guidelines and found it to fulfill all ethical requirements stipulated in the guidelines. This is, therefore, to inform you that the proposal is ethically approved for implementation.

With best regards,

Arebu Issa

Chairperson, ERB

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