



# Patients, Prescribers, and Institutional Factors Associated with Inappropriate Use of Acid Suppressive Therapy in Medical Wards: An Experience of a Single-Center in Saudi Arabia

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**Purpose:** To identify factors associated with inappropriate acid-suppressive therapy (AST) use in hospitalized medical ward patients.

**Patients and Methods:** This was a combined retrospective cohort study reviewing the electronic medical records of medical ward in a secondary university hospital between January 2018 and July 2019, in addition to prescriber surveys about AST knowledge. We included adult patients ( $\geq 18$  years old) admitted to the medical ward who received at least one dose of AST during their hospitalization. Statistical analyses included descriptive statistics and logistic regression.

**Results:** A total of 335 patients were included. Most of the patients were female (66.6%), with a mean age of  $42.37 \pm 17.72$  years; 76% ( $n=256$ ) of the study subjects were prescribed AST for an inappropriate indication. Patients who were not receiving any home medications associated with high bleeding risk had higher odds of being prescribed AST inappropriately (OR, 4.06; 95% CI, 1.09–13.8). A total of 27 physicians completed the prescriber survey, and the average prescriber's knowledge score was  $46.8 \pm 15.6\%$ . This score did not differ by the prescriber's position.

**Conclusion:** This study demonstrated the overuse of AST in the medical ward. Therefore, improving providers' awareness about AST and implementing an AST stewardship program in institutions is necessary to limit this long-lasting issue.

**Keywords:** acid suppressive therapy, overuse, hospital practice, medical ward

## Introduction

The use of acid-suppressive therapy (AST), including proton pump inhibitors (PPIs) and histamine H<sub>2</sub>-receptor antagonists (H<sub>2</sub>RAs), for presumed stress ulcer prophylaxis (SUP), has been well established in hospitalized patients admitted to the intensive care unit (ICU).<sup>1</sup> Even though the guidelines support the use of AST for SUP in ICU patients,<sup>1</sup> the practice of using AST has been extended to non-ICU hospitalized patients without supporting evidence and has been associated with serious adverse effects.<sup>2</sup> Previous reports have shown that between 40% and 76% of AST in the non-ICU wards of hospitals are prescribed inappropriately.<sup>3–6</sup> In Saudi Arabia, the reported incidences of inappropriate AST use in medical wards was even higher, ranging from 59.5% to 71.1%, while PPIs were the first choice among prescribers.<sup>7,8</sup>

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Even though there are no non-ICU specific guidelines for SUP for hospitalized patients, many prescribers follow the general guidelines that can be used whether patients are hospitalized or not. These guidelines include recommendations from the American College of Cardiology (ACC/AHA) for all patients using two or more antithrombotic agents<sup>1,9,10</sup> and the American College of Gastroenterology (ACG) for the prevention of nonsteroidal anti-inflammatory drug (NSAID)-related ulcer complications.<sup>11</sup>

AST may be prescribed inappropriately for many reasons related to the patient's health status, age, and medications.<sup>12,13</sup> Previous studies have shown that sicker, older patients receiving multiple medications were associated with higher odds of being prescribed PPIs inappropriately.<sup>3,12,14</sup> Other factors may be related to the prescriber's perception since many practitioners in the medical ward perceive AST as harmless.<sup>15,16</sup> The inappropriate use of PPIs and H2RAs in hospitalized patients can incur significant health care expenditure as a result of serious adverse effects.<sup>2,17,18</sup> The overuse of AST in medical wards remains a common problem worldwide.<sup>3–8,19</sup> However, most previous studies have focused on assessing the incidences of inappropriate indications or routes of AST and the consequences of AST overuse in non-ICU wards. In contrast, few studies have investigated the factors associated with inappropriate AST use beyond patient factors, such as institutional or prescriber factors. Thus, this study aims to identify the patient-, institution-, and prescriber-related factors associated with the inappropriate use of AST in hospitalized medical ward patients.

## Methods

The study design was divided into two phases. The first phase was a retrospective cohort study reviewing the electronic medical records of patients admitted to the medical wards at King Abdullah bin Abdulaziz University Hospital (KAAUH) in Riyadh, Saudi Arabia, between January 2018 and July 2019. The second phase was a cross-sectional survey distributed to medical ward prescribers at KAAUH via an email questionnaire submission. KAAUH is a 300-bed secondary teaching hospital that encompasses two medical wards, each with 28 beds. The study was reviewed and approved by the Princess Nourah bint Abdulrahman University (PNU) institution review board (IRB) for patient data collection and prescribers survey (IRB Log Number: 20–0218), and conducted in accordance with the Declaration of Helsinki. The Ethics

Committee at PNU did not require informed consent from patients, since there was no direct contact with patients, and all patients' data were de-identified.

To investigate the prescriber-related factors and institution-related factors, we developed an English language survey including factors identified in previous studies and published questionnaires to construct the survey questions.<sup>18,20–22</sup> Initially, the questionnaire was piloted on five prescribers for phase and content validity. The data from the pilot were not included in the analysis. Prescribers' inclusion criteria were physicians who covered the medical floor with prescribing privileges between January 2018 and July 2019. Prescribers participated voluntarily in filling out the self-administered questionnaire, knowing that their information would be de-identified.

The survey was distributed to prescribers in non-ICU wards containing three main sections. The first section included demographic information, and the second section had 13 multiple-choice knowledge questions. These questions were developed to assess the knowledge about AST indication, dose, duration, side effects, and interactions based on national practice guidelines, including ACC and ACG recommendations.<sup>9,10</sup> The knowledge score was calculated as one point for each question answered appropriately. For the side effects and interaction questions, the mean grade of the selected choices among all correct options was used. The total knowledge score was out of 13 and then converted to a percentage. The detailed survey is available in the supplementary material ([Additional file 2](#)). The last section of the survey was about the prescribers' perceptions of barriers affecting AST prescribing in the medical ward, including institutional factors, such as the ordering system and the absence of hospital protocols or clinical pharmacists.<sup>18</sup>

## Study Participants

We included patients who were adults (age  $\geq 18$  years) admitted to the medical ward (non-ICU) who were prescribed and received at least one dose of either a PPI (omeprazole 20 mg tablet and 40 mg IV, or esomeprazole 20–40 mg tablet and 40 mg IV) or H2RA (ranitidine 150 mg tablet and 50 mg IV) alone or in combination during their hospitalization. Each patient record was followed for one year after the initiation of AST. Patients who were on a PPI or H2RA as an outpatient prior to admission, prescribed AST for a treatment indication, or in the ICU ward were excluded from the study. Patients were enrolled using consecutive sampling, including all patients

who met the inclusion criteria within the study window, even if the predefined sample size was achieved. Patients were categorized as having an “appropriate AST indication” if they met any of the criteria. Patients who did not meet any of the appropriate criteria were considered to be using AST for an “inappropriate indication.” Detailed definitions about AST indication are available in [Supplementary Table S1](#).

## Data Collection

A patient master list was obtained from the institution, including adults who were admitted to medical wards using any AST agent. Patients were included in the analysis after assuring that AST was not used before admission nor used for treatment. Patient data, including demographics, past medical history, admission information (including pre-admission and during hospitalization), high GI risk bleeding medications, and AST prescribing order, were collected to identify factors related to patients.

## Study Outcomes

The primary outcome was the number of patients prescribed AST for inappropriate indication in the medical ward. “Appropriate use” was defined as using PPIs and H2RAs with the proper indication, dosage, and route as specified in the clinical practice guidelines (ACC or ACG).<sup>9–11</sup>

The secondary outcomes were factors associated with inappropriate indications for AST, including institutional factors, prescriber factors, and patient factors. Detailed definitions about appropriate AST dose, route, and duration are available in [Supplementary Table S1](#).

## Statistical Analysis

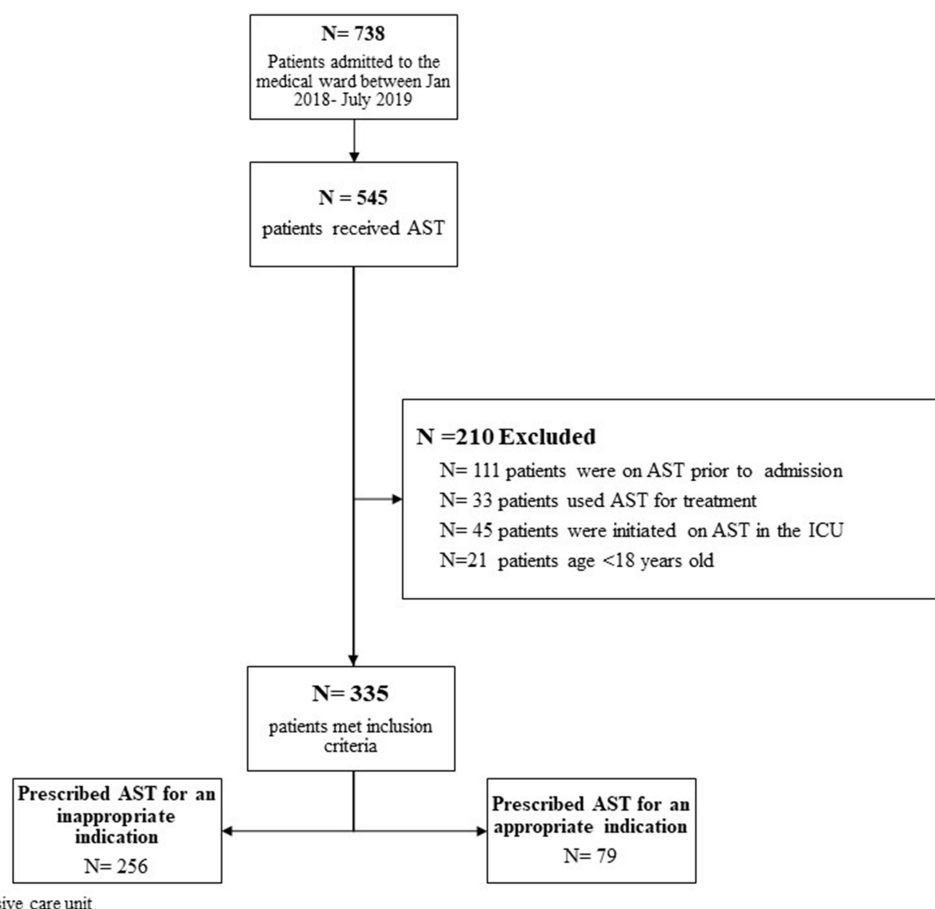
Data were collected from the electronic medical records of patients using Research Electronic Data Capture (REDCap<sup>®</sup>) 7.3.6 software. To identify the proportion of inappropriate indications compared to those reported in previous studies, a sample size of approximately 200 participants was required to achieve a power of 80%. Chi-square and Fisher exact tests were used to determine the percentages and frequencies for categorical variables comparing the two groups (inappropriate and appropriate). Means and standard deviations (SD) were calculated using the *t*-test for continuous variables. Univariable and multivariable logistic regression models were used to measure the association between clinical characteristics and

the outcomes of inappropriate indications. We conducted the statistical analysis using “R” version 4.1.0.

## Results

A total of 545 patients were admitted to the medical ward and received AST during the study window. However, only 335 patients met the inclusion criteria; the remaining were excluded, as presented in the patients’ flow chart in [Figure 1](#). Most of the included patients were females ( $n = 233$ , 66.6%). The mean age of all patients was  $42.37 \pm 17.72$  years. Patients were grouped into two groups based on the appropriateness of the indication for AST. Among the included patients, 76.4% ( $n = 256$ ) were prescribed AST for an inappropriate indication. Most of the patients received PPIs, while only 13% of the patients received H2RAs. Most of the baseline characteristics among the appropriate and inappropriate groups were balanced, as shown in [Table 1](#). Variables deemed significantly different at the baseline between the groups were those included in the regression model to identify associated factors. Overall, 100% of the study subjects received AST for either an inappropriate indication, dosage, route, or duration. However, there was no significant difference in prescribing inappropriate dosage, route, or duration between the inappropriate and appropriate AST indication groups. Even though 23.5% of the patients were prescribed AST for an appropriate indication, only 12.7% of the patients received an appropriate dose of AST, and only 29% of the patients received AST through an appropriate route. Almost all of the study subjects (98.5%) in the two groups received an inappropriate duration of AST, with 61% of patients continuing AST after discharge ([Table 2](#)).

A total of 27 prescribers (out of 35) completed the survey. The response rate was 77% for physicians covering the internal medicine service. The majority of the physicians who completed the questionnaire were residents (37%), followed by consultants (33.3%) and associate consultants (29.6%). About two-thirds of the prescribers had more than five years of working experience. [Table 3](#) presents prescriber information categorized by position and their responses to the knowledge and perception questions. The average prescriber’s knowledge score was  $46.8 \pm 15.6\%$ . This score did not differ by education level, years of experience, or specialties. The questions about AST indication and duration were mainly answered correctly, whereas all prescribers missed sucralfate as one of the agents used for AST. The most commonly reported barrier to appropriately prescribe AST was



**Figure 1** Patient flowchart.

the absence of a hospital protocol. In contrast, in another question, when prescribers were asked about the presence of an institutional protocol, nine prescribers (33%) reported an existing one while in fact, there is no protocol in the institution.

## Secondary Outcomes

### Patient Factors

In the Univariable logistic regression analysis, the number of comorbidities, preadmission NSAIDs and antiplatelet use, age and gender were significantly associated with lower odds of lower odds of prescribing AST for inappropriate indication. In contrast, the absence of preadmission medications was significantly associated with higher odds of AST inappropriate prescription, as shown in Table 4. In the multivariable regression analysis, being admitted for rheumatological reasons was associated with significantly lower odds of inappropriate AST prescription (Odds Ratio (OR) 0.07; 95% confidence interval [CI]

0.01–0.30). In contrast, patients who were not receiving any home medications associated with high bleeding risk had higher odds of being prescribed AST inappropriately (OR 4.06; 95% CI 1.09–13.8), as presented in Table 4.

### Prescriber Factors

Overall, prescribers' mean  $\pm$  SD grade (percentage) of the knowledge questions was low ( $46.8 \pm 15.6\%$ ). Even though assistant consultants scored the highest ( $59.08 \pm 19.15\%$ ) among the provider groups, the grade did not significantly vary between consultants and residents. More than half of the prescribers correctly answered questions related to the proper duration of AST (59%). Still, only 41% correctly responded to questions about the indications in the medical ward. In contrast, the mean grade for selecting the correct PPI side effects was  $3.04 \pm 1.58$  out of 6, and for H2RA side effects, it was  $3 \pm 4.1$  out of 5. The most commonly reported barrier for appropriately prescribing AST included the

**Table 1** Baseline Characteristics Comparison of Patients Prescribed AST for an Appropriate Indication and for an Inappropriate Indication in the Medical Ward

Patient's Characteristics	Total N=335	Patients Prescribed AST for an Inappropriate Indication (n =256)	Patients Prescribed AST for an Appropriate Indication (n=79)	P value
Male, n (%)	112 (33.4)	76(29.7)	36 (45.6)	0.013
Age in years, mean (SD)	42.37 (17.72)	38.52 (15.6)	54.85 (18.5)	<0.001
BMI, mean (SD)	31.03 (8.83)	30.89 (9.22)	31.47 (7.48)	0.616
The presence of significant past medical history, n (%)	148 (44.2)	90 (35.2)	58 (73.4)	<0.001
Cardiovascular disease*, n (%)	30 (9)	5 (2)	25 (31.6)	<0.001
Hypertension, n (%)	99 (29.6)	52 (20.3)	47 (59.9)	<0.001
Chronic kidney disease, n (%)	7 (2.1)	4 (1.6)	3 (3.8)	0.445
Diabetes mellitus, n (%)	101 (30.1)	61 (23.8)	40 (50.6)	<0.001
Dyslipidemia, n (%)	61 (18.2)	31 (12.1)	30 (38)	<0.001
Gastrointestinal (GI) disease, n (%)	28 (8.4)	23 (9)	5 (6.3)	0.608
Number of comorbidities, n (%)				
No comorbidities	173 (51.6)	153 (59.8)	20 (25.3)	<0.001
1 comorbidity	69 (20.6)	56 (21.9)	13 (16.5)	
2 comorbidities	36 (10.7)	21 (8.2)	15 (19)	
≥ 3 comorbidities	57 (17)	26 (10)	31 (39.2)	
Reason of Hospital admission, n (%)				
GI	104 (31)	96 (37.5)	8 (10.1)	<0.001
Neurological disease	20 (6)	13 (5.1)	7 (8.9)	0.333
Orthopedic disease	1 (0.3)	0 (0)	1 (1.3)	0.533
Pulmonology disease	90 (26.9)	74 (28.9)	16 (20.3)	0.17
Endocrinology disorder	17 (5.1)	14 (5.5)	3 (3.8)	0.765
Hematology disorder	17 (5.1)	11 (4.3)	6 (7.6)	0.382
Metabolic disorder	3 (0.9)	1 (0.4)	2 (2.5)	0.279
Infectious disorder	91 (27.2)	79 (30.9)	12 (15.2)	0.01
Psychiatry disorder	1 (0.3)	1 (0.4)	0 (0)	1
Renal disorder	6 (1.8)	5 (2.0)	1 (1.3)	1
Rheumatology disorder	9 (2.7)	3 (1.2)	6 (7.6)	0.007
Urology disorder	12 (3.6)	9 (3.5)	3 (3.8)	1
Other disorders	26 (7.8)	18 (7)	8 (10.1)	0.51
Pre-admission GI bleeding risk medications, n (%)				
None	280 (83.6)	238 (93)	42 (53.2)	<0.001
NSAID	12 (3.6)	5 (2)	7 (8.9)	0.011
Antiplatelets	35 (10.4)	7 (2.7)	28 (35.4)	<0.001
Anticoagulation	5 (1.5)	2 (0.8)	3 (3.8)	0.161
Corticosteroids	6 (1.8)	4 (1.6)	2 (2.5)	0.934

**Notes:** \*Cardiovascular disease included coronary heart disease, cerebrovascular disease, peripheral arterial disease, rheumatic heart disease, congenital heart disease, venous thromboembolism.

**Abbreviations:** AST, acid-suppressive therapy; BMI, body mass index; GI, gastrointestinal; NSAID, non-steroidal anti-inflammatory drug.

prescriber's workload (33%) and patients' polypharmacy (22%). Looking at the AST orders from the profiles of patients in both groups of the study (appropriate vs inappropriate indication), most of the

prescribers who used AST for an inappropriate indication were residents (n = 302), followed by assistant consultants and then associate consultants, as shown in Table 2.

**Table 2** Acid Suppressive Therapy (AST) Order Information Among Patients Who Were Prescribed AST in the Medical Ward for Appropriate and Inappropriate Indication

AST Order Information	Total N=335	Patients Prescribed AST for an Inappropriate Indication (n =256)	Patients Prescribed AST for an Appropriate Indication (n=79)	P value
Dose, n (%)				0.644
Omeprazole 20 mg daily	17 (5.1)	14 (5.5)	3 (3.8)	
Omeprazole 40 mg daily	18 (5.4)	15 (5.9)	3 (3.8)	
Omeprazole 20 mg bid	2 (0.6)	1 (0.4)	1 (1.3)	
Esomeprazole 20 mg daily	55 (16.4)	42 (16.4)	13 (16.5)	
Esomeprazole 40 mg daily	176 (52.5)	128 (50.0)	48 (60.8)	
Esomeprazole 20 mg bid	6 (1.8)	6 (2.3)	0 (0.0)	
Esomeprazole 40 mg bid	14 (4.2)	12 (4.7)	2 (2.5)	
Ranitidine 150 mg daily	3 (0.9)	2 (0.8)	1 (1.3)	
Ranitidine 150 mg bid	19 (5.7)	15 (5.9)	4 (5.1)	
Ranitidine 50 mg daily	7 (2.1)	7 (2.7)	0 (0)	
Inappropriate dose, n (%)	58 (17.3)	208 (81.2)	69 (87.3)	0.28
AST route, n (%)				0.69
Oral	188 (56.1)	141 (55.1)	47 (59.5)	
Intravenous	146 (43.6)	114 (44.5)	32 (40.5)	
Nasogastric	1 (0.3)	1 (0.4)	0 (0.)	
Inappropriate Route, n (%)	76 (22.7)	203 (79.3)	56 (70.9)	0.16
AST Duration, n (%)				0.883
Until the resolution of GI risk factors	2 (0.6)	2 (0.8)	0 (0)	
NSAID induced ulcer for 6 months	1 (0.3)	1 (0.4)	0 (0)	
Extended beyond the presence of the indication	102 (30.4)	77 (30.1)	25 (31.6)	
Shorter than indicated	26 (7.8)	19 (7.4)	7 (8.9)	
Continued upon discharge	204 (60.9)	157 (61.3)	47 (59.5)	
Inappropriate Duration, n (%)	329 (98.2)	5 (2.0)	1 (1.3)	0.99
Prescribers position, n (%)				0.308
Associate consultant	6 (1.8)	3 (1.2)	3 (3.8)	
Assistant consultant	23 (6.9)	18 (7.0)	5 (6.3)	
Residents	302 (90.1)	231 (90.2)	71 (89.9)	
Interns	4 (1.2)	4 (1.6)	0 (0.0)	
Concomitant Medications with GI bleeding risk, n (%)				
NSAID	42 (12.5)	11 (4.3)	31 (39.2)	<0.001
Antiplatelets	57 (17.0)	8 (3.1)	49 (62.0)	<0.001
Anticoagulation	186 (55.5)	117 (45.7)	69 (87.3)	<0.001
Systemic corticosteroids	62 (18.5)	50 (19.5)	12 (15.2)	0.482
Length of hospital stay in days, mean ± SD	4.24 (4.51)	3.98 (3.84)	5.10 (6.15)	0.052

**Abbreviations:** AST, acid-suppressive therapy; GI, gastrointestinal; NSAID, non-steroidal anti-inflammatory drug.

## Institutional Factors

There were no implemented clinical guidelines or institutional protocols at the study site to help identify eligible

patients needing AST for SUP in the medical wards. Even though the ordering system requires entering an indication for the use of any medication, the prevention of GI



**Table 3** Prescribers' Demographics and Knowledge About AST

Prescribers by Position	Total (n=27)	Consultant (n =9)	Assistant Consultant (n=8)	Residents (n=10)	P value
Age in years, mean (SD)	39.33 (7.81)	45.33 (9.41)	39.5 (4.17)	33.80 (3.74)	0.002
Education, n (%)					
Bachelor	5 (18.5)	0 (0)	0 (0)	5 (50)	<0.001
Masters	9 (33)	0 (0)	6 (75)	3 (30)	
PhD	1 (3.7)	1 (11)	0 (0)	0 (0)	
Residency	2 (7.4)	0 (0)	0 (0)	2 (20)	
Fellowship	5 (18.5)	3 (33)	2 (25)	0 (0)	
Post doc	5 (18.5)	5 (55.6)	0 (0)	0 (0)	
Years of experience, n (%)					
1–5 years	3 (11)	0 (0)	3 (30)	0 (0)	0.015
6–10 years	10 (37)	3 (37.5)	5 (50)	2 (22)	
11–15 years	9 (33)	5 (62.5)	2 (20)	2 (22)	
16–20 years	1 (3.7)	0 (0)	0 (0)	1 (11)	
>20 years	4 (14.8)	0 (0)	0 (0)	4 (44)	
Specialty, n (%)					
Internal medicine	17 (63)	1 (11)	6 (75)	10 (100)	<0.001
Cardiology	3 (11)	1 (11)	2 (25)	0 (0)	0.245
Endocrinology	1 (3.7)	1 (11)	0 (0)	0 (0)	0.354
GI	1 (3.7)	1 (11)	0 (0)	0 (0)	0.354
Hematology	1 (3.7)	1 (11)	0 (0)	0 (0)	0.354
Infectious diseases	2 (7.4)	2 (22)	0 (0)	0 (0)	0.115
Nephrology	1 (3.7)	1 (11)	0 (0)	0 (0)	0.245
Rheumatology	1 (3.7)	1 (11)	0 (0)	0 (0)	0.354
Prescribers encountered patients who experienced AST side effects	4 (14.8)	3 (33)	1 (11)	0 (0)	0.128
Prescriber's knowledge					
Identified GI risk factors, n (%)	2 (92.6)	1 (11)	1 (12.5)	0 (0)	0.527
Identified AST indications f in the IM, n (%)	11 (40.7)	4 (44.4)	3 (37.5)	4(40)	0.957
Identified AST agents can be used, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	NA
Identified AST dose, n (%)	5 (18.5)	2 (22.2)	2 (25)	1 (10)	0.675
Identified AST duration, n (%)	16 (59.3)	5 (55.6)	4 (50)	7 (70)	0.666
Identified PPI common side effects out of 6, mean(SD)	3.04 (1.58)	3.33 (1.58)	1.88 (1.55)	3.70 (1.16)	0.034
Identified PPI common interactions out of 5, mean(SD)	2.93 (1.36)	2.67 (1.32)	2.38 (1.60)	3.60 (0.97)	0.126
Identified ranitidine common side effects out of 5, mean(SD)	3 (1.41)	2.78 (1.39)	2.38 (1.69)	3.70 (0.95)	0.118
Identified ranitidine common interactions out of 5, mean(SD)	3 (1.39)	2.33 (1.58)	2.88 (1.36)	3.70 (0.95)	0.092
Total score in knowledge questions out of 100%, mean (SD)	46.8 (15.6)	55.54 (13.31)	59.08 (13.31)	44 (11.69)	0.092
Factors Affecting Prescribing AST for SUP in the medical ward					
Prescriber's time, n (%)	3 (11)	0 (0)	3 (37.5)	0 (0)	0.018
Prescriber's workload, n (%)	9 (33)	2 (22)	4 (50)	3 (30)	0.461
Patient's preference, n (%)	5 (18.5)	1 (11)	1 (12.5)	3 (30)	0.498
Patient's polypharmacy, n (%)	6 (22)	2 (22)	1 (12.5)	3 (30)	0.675

(Continued)

**Table 3** (Continued).

Prescribers by Position	Total (n=27)	Consultant (n =9)	Assistant Consultant (n=8)	Residents (n=10)	P value
Absence of clinical pharmacist, n (%)	6 (22)	2 (22)	2 (25)	2 (20)	0.968
Absence of hospital protocol, n (%)	15 (55.6)	7 (77.8)	5 (55.6)	3 (33)	0.165
Institution ordering system, n (%)	1 (3.7)	0 (0)	1 (12.5)	0 (0)	0.291

**Abbreviations:** AST, acid-suppressive therapy; GI, gastrointestinal; IM, internal medicine; PPI, proton pump inhibitors; SD, standard deviation.

**Table 4** The Association Between AST Inappropriate Indication and Patients' Characteristics Using Univariable and Multivariable Regression Analysis

	Univariable Regression Analysis			Multivariable Regression Analysis		
	Odds Ratio (OR)	95% Confidence Intervals (CI)	P value	Odds Ratio (OR)	95% Confidence Intervals (CI)	P value
Age	0.95	0.93, 0.96	<0.001	0.98	0.95, 1.00	0.025
Gender	0.50	0.30, 0.85	0.010	0.60	0.31, 1.16	0.124
Presence of past medical history	0.20	0.11, 0.34	<0.001	0.65	0.23, 1.89	0.416
Number of comorbidities	0.50	0.40, 0.61	<0.001	0.83	0.54, 1.26	0.371
Reason of admission; Rheumatology	0.14	0.03, 0.56	0.005	0.07	0.01, 0.30	<0.001
No medication use prior to admission	11.6	6.16, 22.8	<0.001	4.06	1.09, 13.8	0.027
Pre-admission NSAID	0.2	0.06, 0.66	0.009	0.41	0.07, 2.15	0.302
Pre-admission Antiplatelet	0.05	0.02, 0.12	<0.001	0.49	0.11, 2.10	0.341

bleeding represented only 19.4% of the indications for prescription of AST in the system. For AST ordering, the system is not preceded by a checklist, and the GI risk assessment score for further verification indicated the need to use AST for SUP. Prescribing AST was not restricted to a particular specialty in the hospital or restricted dosage forms. Starting in 2019, a clinical pharmacist started rounding with the medical team, reviewed the SUP eligibility of patients, and advised deprescribing if the patient had no appropriate indication for SUP. According to the prescribers, the most commonly reported barrier to prescribing an appropriate AST regimen in the medical wards was the absence of an institutional protocol (56%).

## Discussion

The overuse of AST in medical ward remains an issue that carries a risk to the health outcomes of patients. In this study, approximately 74% of patients admitted in medical wards received AST for inappropriate indications within the global rates reported in previous studies, between 22% and 79%.<sup>4,5,23</sup> Also, our rate is comparable to previously

reported numbers in Saudi Arabia.<sup>6,7</sup> A prospective study conducted in emergency and internal medicine departments in Saudi Arabia showed that 59.5% of patients received omeprazole using an inappropriate route and 1.4% of patients received an improper dose of omeprazole, while 42.9% of patients received an inappropriate frequency of ranitidine.<sup>6</sup> In contrast, we found that 17.3% of patients were prescribed an inappropriate dose of AST, and 23% of patients received AST using an inappropriate route.

Interestingly in this study, patients with no prior chronic medication use before their admission had a higher odds of being prescribed AST for an inappropriate indication. This may be related to practitioners commonly prescribing PPIs because they believe that AST-related side effects and complications are uncommon.<sup>15,16</sup> Thus, practitioners instead prescribe AST in the medical wards for most patients, rather than not prescribing it.<sup>3</sup> Our univariate analysis showed that increased age and the presence and increased number of comorbidities were associated with lower odds of prescribing inappropriate AST. Similarly, a retrospective study conducted in a tertiary hospital in the United States found that



age and number of comorbidities were associated with lower odds of inappropriate AST use (OR = 0.99; 95% CI 0.98–1.02 and OR = 0.97; 95% CI 0.88–1.08, respectively).<sup>13</sup>

Furthermore, a retrospective observational study using the claims from insurance companies of more than 1,000,000 patients reported that the female gender was associated with lower odds of inappropriate PPI prescribing.<sup>3</sup> Moreover, age, drugs with bleeding risk, and the number of chronic diseases were associated with higher odds of prescribing inappropriate PPI, however, this study also included outpatients.<sup>3</sup> Another prospective case-control study that included elderly patients admitted to the medical ward demonstrated that the use of blood thinner was an predictor of inappropriate PPI use.<sup>12</sup> In opposition to these findings, our study showed that gender, the presence of comorbidities, preadmission use of NSAIDs, and antiplatelets were associated with non-significantly lower odds of inappropriate AST prescribing. The variation in the identified factors for inappropriate AST prescribing may be attributed to the discrepancies between the “appropriateness” definitions between the studies and the included patient populations.<sup>3,12,13</sup>

One of the reasons behind the inappropriate use of AST suggested in this study is the knowledge of prescribers about the appropriate indications and complications of AST. Prescribers may perceive PPIs as safe drugs since they seldom reported (15%) witnessing AST-related side effects.<sup>3</sup> This was also apparent in the low knowledge scores on questions related to PPIs’ side effects and interactions. The prescriber knowledge scores were similar to a previous survey of 900 medical staff in China, where they reported a low score with regard to PPI-related awareness, scoring  $59.47 \pm 15.75$  out of 100.<sup>22</sup> Besides, a study that looked into all discharge patients over eight days reported that postgraduate year one (PGY-1) medical residents were more likely to prescribe AST inappropriately.<sup>23</sup> However, that study and ours were conducted in university teaching hospitals where most of the medication orders are entered by medical residents, as observed in this study with the AST order entry.

There is limited information available about the institutional factors in relation to inappropriate use of AST.<sup>18,20</sup> In our survey, we listed some of the factors identified in the literature, as well as the institutional factors that we thought to correlate with prescribing AST inappropriately.

The absence of institutional protocols regarding the use of AST in medical wards was the most common barrier

reported by prescribers. This issue is a consequence of the lack of solid evidence supporting the use of AST in non-ICU patients in relevance to their risk of GI bleeding. Relying on non-acutely ill patients, guidelines for hospitalized patients may be inadequate, as their recommendations may inflate the need to use AST in hospitalized patients.<sup>9–11</sup> This issue may be observed in hospitalized patients who are usually prescribed anticoagulation for the prevention of deep vein thrombosis. Meanwhile, the 2020 ACC guidelines include the use of two or more antithrombotic therapies as one of the criteria to determine the need for AST, but do not specify their indication (treatment or prevention) or the duration.<sup>9</sup>

Most of the available reports have identified factors related to the characteristics of patients associated with inappropriate prescription of PPIs.<sup>3,12,13</sup> However, years after these studies were published, the problem still exists. During AST prescription, the patient’s related factors identified in most previous reports were not modifiable at that time. However, prescribers need to be vigilant and review the eligibility of those patients against these identified factors. Looking deep into this global issue, the actual problem is more prescriber- and institution-related.

To our knowledge, this is one of the few studies that incorporate patients, prescribers, and institutional factors associated with the inappropriate prescription of AST in medical wards in one study. This provides a broader view of the defects in clinical practice that need to be addressed. Moreover, this study includes an updated definition of “appropriate indications” for AST use in patients using dual or more antithrombotic therapy following the recent 2020 ACC Expert Consensus Decision Pathway for Antithrombotics.<sup>9</sup> The sample size exceeded the number needed to meet power, thus increasing the validity of the results. However, this study remains to have several limitations. First, it is a single-center retrospective study that may limit both the patients’ retrieval of all needed data and the generalizability of the results. Second, we could not ensure that prescribers who answered the survey were the same ones prescribing AST in the medical wards. Third, the mismatch between the patients’ baseline characteristics may affect the results. However, these mismatched variables were considered in the regression models to identify patient factors.

This study highlights that the absence of non-ICU acutely ill-specific practice guidelines for AST limits the control of AST overuse in the medical ward. Therefore, this study calls for national and international

polymakers to develop practice guidelines or risk assessment models that can help determine GI bleeding risk in hospitalized patients to direct the appropriate use of AST for SUP in eligible patients. Additionally, medical institutions can implement AST stewardship programs to ensure the proper initiation and continuation of AST in patients admitted or discharged from hospitals. Pharmacists are medication experts and have demonstrated significantly higher knowledge related to PPI use.<sup>22</sup> The implementation of a pharmacist-led PPI stewardship program could help deprescribe inappropriate PPIs.<sup>20</sup> In addition, enhancing the prescriber's awareness about the appropriate use of AST and the detrimental consequences of improper use on the health outcomes of patients, as well as the therapy costs to institutions, by providing continuous education is also crucial.<sup>24</sup>

## Conclusion

AST is commonly overprescribed in the medical ward and for inappropriate indications, regardless of a patient's medication history. This issue may be attributed to the awareness of prescribers about the indications and adverse effects of AST. Thus, improving provider awareness about AST and implementing AST stewardship programs in institutions are necessary to limit this long-lasting issue. However, barriers to deprescribing will remain if no pre-defined criteria for AST prescribing are developed. A large prospective study to further investigate the factors and complications related to inappropriate AST use should be considered.

## Abbreviations

ACC, American College of Cardiology; AST, acid-suppressive therapy; SUP, stress ulcer prophylaxis; ICU, intensive care unit; NSAID, nonsteroidal anti-inflammatory drugs; H2RAs, histamine receptor antagonists; PPI, proton-pump inhibitors; NG, nasogastric; IV, intravenous; GI, gastrointestinal; AHA, American Heart Association; ACG, American College of Gastroenterology; KAAUH, King Abdullah bin Abdulaziz University Hospital; BMI, body mass index; OR, odds ratio; CI, confidence intervals; IM, internal medicine; SD, standard deviation.

## Disclaimer

The contents of this manuscript are solely the authors' views and may not be understood or quoted as being

made on behalf of or reflecting the position of the Saudi Food and Drug Authority.

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## Author Contributions

All authors contributed to data analysis, drafting or revising the article, gave final approval of the version to be published, agreed to the submitted journal, and agree to be accountable for all aspects of the work.

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