

# Appropriateness of Proton Pump Inhibitor Use in Hospitalized Patients: A Cross Sectional Study in a Tertiary Care Hospital in North India

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## Abstract

**Background:** Proton Pump Inhibitors (PPIs) are often prescribed inappropriately among hospitalized patients and same is often continued even after their discharge from the hospital. The inappropriate use of PPIs leads to an increased risk of adverse effects, drug interaction, and unnecessary hospital expenditure for such patients. Aim of this study was to determine the appropriateness of PPIs use among hospitalized patients.

**Methods:** A cross sectional observational study was conducted on hospitalized patients in a tertiary care hospital in Northern India. The clinical records of adult patients hospitalized during April- May 2022 were assessed for the prescribing pattern and appropriateness of PPI use as per the National Institute of Health and Care Excellence (NICE) guidelines.

**Results:** A total of 192 patient's records were included in this study with the mean age 57 years and 61% of the study participants were males. Overall, 72% (138) of the study participants were prescribed PPIs by intravenous route and only in 28% (54) cases an oral route was preferred. Pantoprazole was the most commonly prescribed PPI in 112 (58%) patients and it was administered by intravenous route among 87 patients (78%) and by oral route in 25 (22%) patients. PPI use was appropriate in 54% of the cases and they were most commonly prescribed for ulcer prophylaxis. This study identified higher use of PPIs was seen in low risk patients for longer duration than indicated.

**Conclusion:** PPIs are being prescribed inappropriately among hospitalized patient unrelated to their widely accepted clinical indications and are often continued unnecessarily once patient is discharged. These results suggest the need of regular audits on use of PPIs clubbed with educational initiatives to promote rational use of PPIs among hospitalized patients.

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**Keywords:** Proton Pump Inhibitors; Prescribing; Rational Use; Drug Safety

## Introduction

Proton Pump Inhibitors (PPIs) are one of the most commonly prescribed classes of medications among hospitalized patients (1). PPIs have revolutionized the treatment of peptic ulcer disease and gastroesophageal reflux disease (GERD) due to their superior gastric acid suppression providing better control of intra-gastric pH as compared to histamine type-2 receptor antagonists (H2RA) (2). Also, PPIs have been used for other indications like treatment of *Helicobacter pylori* (H. pylori) infection, Zollinger- Ellison syndrome, treatment

or prophylaxis of Non-steroidal anti-inflammatory drugs (NSAIDs) induced peptic ulcer, etc.(2,3).

However, over recent years, the use of PPIs has increased dramatically in hospitals and ambulatory care settings. The overutilization of PPIs is attributed to their low costs, high efficacy, good safety profile, and competitive marketing (4,5). The widely accepted clinical indications for intravenous PPI therapy is limited and it is indicated in exceptional circumstance like in patients with gastric hypersecretion associated with neoplastic conditions like Zollinger-Ellison syndrome; inability to take oral medications; severe non-variceal upper gastrointestinal

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bleeding; and in the prevention of stress-related mucosal disease bleeding (stress ulcer prophylaxis) in high-risk Intensive Care Unit (ICU) patients without enteral feeding access or “nothing by mouth” status (1). The data from the previous studies, suggests that up to 75% of the hospitalized patients are prescribed PPIs intravenously without any proper justification, indicating their inappropriate use (6).

Also, the widespread inappropriate use of PPIs which could potentially lead to serious and adverse health outcomes has been reported in previous studies (5). The inappropriate use of PPIs is not only increases healthcare cost but also has potential risk of iatrogenic harm by causing gastric polyposis, vitamin B12 and magnesium deficiency, acute interstitial nephritis, Clostridium difficile infection, or bacterial overgrowth in cirrhotic patients with an increased risk of spontaneous bacterial peritonitis, etc. have been documented previously (7). PPI are often over used in hospitalized patients which not only increases health care cost but also increases the risk of drug interactions. The aim of the present study was to observe the prescribing pattern and the appropriateness of PPI use among adult patients admitted in our hospital. The PPI overuse has been commonly reported in various healthcare setting across the world and prescription audit based feedback is important method to promote appropriate usage of these acid suppressive medications in medical inpatients (8).

**Methods**

This was a register based cross-sectional study carried out on hospitalized patients in a tertiary care hospital over a period of two months from 1st April 2022 to 31st May 2022. The study was a part of regular medication audits being carried out in the hospital and aimed at characterizing the PPI prescription for hospitalized patients. The data regarding patient demographics name, dosage indication and duration of PPI used at the time of hospital admission and after discharge was collected using a semi-structured proforma.

Patients over 18 years old and hospitalized in either ICUs (Medical & Surgical) or wards during study duration were included in the study.

The primary outcome was the appropriateness of PPI use among hospitalized patients in terms of their indication and dosage prescribed, based on the National Institute of Health and Care Excellence (NICE) guidelines “Gastro-oesophageal reflux disease and dyspepsia in adults: investigation and management” and criteria used by Lenoir et al., (2019) (8).

**Statistical analysis**

The data was collected anonymously and included patient demographics and PPI usage at the time of hospital admission and after discharge. The data analysis was performed using descriptive statistics. The continuous variables were expressed as mean ± standard deviation and categorical variables were expressed as percentages.

**Results**

A total of 192 hospitalized patients were prescribed PPIs during the study period, 114 patients (59%) were from ICU (Medical ICU & Surgical ICU) and 78 (41%) from wards. The average age of patients was 60.6 ±17.49 of which 118 (61%) were male and 74 (39%) were female participants (Table 1). NSAIDs were found to be the highest concomitantly prescribed medication among such patients accounting for 48% cases followed by anti-coagulants (24%), anti-platelets (16%), and corticosteroids (12%).

**Table 1. Demographic details of the study participants.**

Variable	N (%)
Age (years)	60.6 ±17.49
Gender	Female: 74 (39%) Male: 118 (61%)
Admission site	ICU: 114 (59%) Wards: 78 (41%)
Diagnosis	Gastrointestinal disease: 18 Other diseases: 174
Concomitant medications	NSAID: 111 (48%) Anti-platelet: 38 (16%) Anti-coagulants: 56(24%) Corticosteroids: 27(12%)

The intravenous PPIs were administered in 138 patients (72%) and remaining 54 (28%) patient received PPIs by oral route. Majority of the patients in both ICUs and wards were prescribed Pantoprazole, followed by other PPIs and combination with prokinetic agents (Table 2). Out of the 138 patients who were initially prescribed intravenous PPIs, 68 were switched to oral route while remaining 70 patients were continued on intravenous route. Among 54 patients who were initially prescribed oral PPIs, about four patients were switched to intravenous route while remaining 50 continued on oral therapy. The average duration of PPIs therapy during the hospital stay was found to be 4±3 days.

**Table 2. The choice of PPI for initial management in hospitalized patients.**

PPIs	IV route	PO route	TOTAL (n=192)
Esomeprazole	51	7	58 (30%)
Pantoprazole	87	25	112 (58%)
Rabeprazole	0	3	3 (2%)
Pantoprazole + Domperidone	0	17	17 (9%)
Rabeprazole + Domperidone	0	2	2 (1%)
Total	138	54	192

The clinical indications for prescribing PPIs were mentioned in very few clinical records of patients and were given for appropriate indications in only half of the cases (N=105; 54.68%) cases. Also PPIs were predominantly

(N=153; 85.5%) used for ulcer prophylaxis in patients receiving NSAIDs, anti-platelets or anti-coagulants (Table 3). Most patients (N=179; 93%) also received PPI as their discharge medication. Among them, Pantoprazole was found to be the highest prescribed medication (n=

80, 45%) followed by Pantoprazole + Domperidone combination and Esomeprazole respectively. The duration of PPI prescribed was not specified in discharged notes in 64% cases while it was up to 1 week in 18% cases and up to 1 month in 17% cases (Table 4).

**Table 3. Indication for prescribing PPI in study participants.**

PPI indication	N (%)
<b>Appropriate PPI indication</b>	<b>105 (54%)</b>
Ulcer prophylaxis in high-risk patients on NSAIDs	51
Ulcer prophylaxis in high-risk patients on anti-platelets or anti-coagulants	33
Dyspepsia	5
Peptic ulcer and H-pylori	1
Upper gastrointestinal bleeding	5
Stress ulcer prophylaxis in high risk patients	10
<b>Inappropriate PPI indication</b>	<b>87 (45%)</b>
Gastroenteritis	2
Ulcer prophylaxis in low risk patients on NSAIDs	59
Ulcer prophylaxis in low risk patients on anti-platelets or anti-coagulants	10
Ulcer prophylaxis in low risk patients on corticosteroids	8
Stress ulcer prophylaxis in low risk patients	8

**Table 4. Duration of PPIs used among the patients at the time of discharge.**

Duration of PPI use (n=179)	N (%)
3-7 days	33(18)
Up to 1 month	31(17)
>1 month	1(1)
Not mentioned	114(64)

## Discussion

PPIs were inappropriately used only in 54% of the cases and were most commonly (85.5%) used for peptic ulcer prophylaxis. The present study was done to evaluate the prescribing pattern of PPIs in 192 patients admitted in a tertiary care hospital. The average age of patient who were prescribed PPI was 60.6 years and 60% of them were males. The data from previous studies also indicate that PPIs prescription increases significantly with age and a similar study by Lenoir et al., (2019) (8) evaluating PPI usage in hospitalized patient found average age of patients prescribed PPI as 64.4 years and about 48% of these were males.

The most commonly used PPI at our hospital was Pantoprazole which was prescribed in 58% (n= 112) cases, followed by Esomeprazole (30%) and other PPIs. A similar study by Verma et al., (2019) (9) in a tertiary care hospital in North India also identified pantoprazole as the most commonly prescribed PPI. In most cases pantoprazole was prescribed as standard dose of 40 mg once daily but in 33% (n=37) cases it was given as 40 mg twice daily, which is not a recommended dose and has no rational basis. The inappropriate dosage of PPIs have also been reported in many previous studies across various countries (8,10-11). Also, none of the patients was prescribed omeprazole, a PPI which is listed in the National List of Essential Medicines of India and cheapest PPI available in Indian markets (12).

In 72% (n=138) of participants PPI was administered by intravenous route and in about half of them were later switched to oral route. In remaining 28% cases (n=54) patients PPIs were administered by oral route and only four patients needed escalation to intravenous route. Verma et al., (2019) (9) also report that 79% of hospitalized patients in a tertiary care hospital in north India were given PPI by intravenous route. Similar studies conducted by Ahad et al (2021) (13), Luo et al., (2018) (14) and Kadam et al., (2022) (15) also found that PPIs were predominantly used by parenteral route among hospitalized patients. However, evidence suggest that PPIs given by oral route have similar efficacy as injectable formulations at equivalent doses and are less costly, while intravenous PPIs are need only limited patients like those with upper gastrointestinal bleed (15,16).

In most patients PPIs were prescribed on the first day of hospitalization but clinical indication for the same were rarely documented in the medical records. In addition, we observed that many patients received PPIs for indications other than widely accepted clinical recommendations. PPI were prescribed for recommended indications in 53% (n=102) of cases while in 47% (n=90) cases they were used inappropriately. We found that ulcer prophylaxis in low risk patients on NSAIDs, anti-platelet drugs, corticosteroid or an anti-coagulant was the most common off label use of PPI. Thus, the most common irrational use of PPI was for prophylaxis of stress ulcers among low risk individuals. A study by Bez et al., (2013) (17) found that PPI prophylaxis was given in 79% patients who did not have any risk factor for stress ulcer. A similar study by Shabazi Khamas et al., (2022) (18) found inappropriate use of PPI for stress ulcer prophylaxis in 63.5 per 100 patient days.

Despite not having a rational basis of using PPIs the same was not reassessed at the time of discharge from hospital and PPI therapy were continued in 93% of cases after discharge for variable duration from 1 week to 1 month. This finding is consistent with the study by Biswas et al., (2017) (19) in which 87.17% of the patient received PPIs as their discharge medication. Al- Dosari et al., (2021) (5) identified 92% of the patients received PPIs for 1 to 3 months as a take-home medication after hospital discharge. This may further lead to long term inappropriate use of PPIs in community and also adds to the overall health care cost. It is known that overuse of PPIs can lead to rebound acid hypersecretion (RAHS) due to which discontinuation of PPIs may be challenging in such patients receiving inappropriate and duration of PPI therapy (8).

Limitations of the study are firstly, the data was collected from patient's medical records which were limited by the quality of documentation in our hospital. Secondly, in most medical records the indication for using PPI was not clearly documented and had to be assumed based on the patient history, examination findings or concomitant medications. Finally, we did not follow up with patients once they were discharged for any adverse effect or problems related to use of PPIs.

The inappropriate use of PPIs is a multifactorial problem with its roots in the presumption that their short term use is generally well tolerated and lack of awareness among prescribers about the adverse effects of long term PPI therapy. The over use of PPIs in hospitalized patients can lead to drug interactions and promote their use in community when such patients leading to additional expenditure. Proper documentation is imperative for rationalizing the use of PPI therapy and the reasons for using a PPI should be clearly documented in medical records. The re-evaluation of the adequacy of PPI therapy should be done in hospitalized patients and their usefulness should be reconsidered for patient's benefit by reducing health cost and possible adverse effects. Interventions such as educational programs, institution-specific prescribing guidelines and PPI stewardship program may be developed and implemented for more appropriate use of this therapeutic class.

### Conflict of interest

The authors declare no conflict of interest, financial or otherwise.

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