Research Article

A Retrospective Assessment of Proton Pump Inhibitors Use in A Tertiary Care Hospital, Chennai, India

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ABSTRACT

Background: Proton Pump Inhibitors (PPIs) are the most widely utilized medications worldwide, both in the ambulatory and inpatient clinical setting. PPI is a class of medication that significantly reduces stomach acid output. PPIs became a class of drugs with a high prevalence of being prescribed for unsubstantiated and poorly defined reasons or for conditions where they are not beneficial., The significant misuse of PPIs was increased recently. There is growing concern regarding the utilization of PPIs.

Aim and Objectives: To assess and evaluate the utilization of Proton pump inhibitors at a tertiary care hospital and to determine the most frequently prescribed Proton pump inhibitor, to assess the frequency of usage of PPIs along with their dosage and to evaluate the Drug-Drug interaction of Proton pump inhibitors with co-prescribed drugs.

Methodology: A retrospective observational study was conducted in a multispeciality tertiary care hospital during the period of March to August 2022. Data were collected using a pre-structured patient data collection form and analyzed using Microsoft Excel datasheet.

Descriptive statistics including frequencies and percentages were used to summarize the data.

Result and Discussion: A total of 220 study participants were included in the study. Pantoprazole (73%) was the most frequently prescribed PPI followed by Rabeprazole and Esomeprazole. Among the study participants, approximately 88% of the PPI prescription were prescribed according to the NICE guidelines. High-dose therapy was prescribed in 53% of the patients. Majority of the patients (74%) were prescribed with PPI for NSAIDs/Aspirin-induced ulcer prophylaxis.

Conclusion: In our study, PPIs were most frequently used as a gastroprotective agent along with NSAID's and Pantoprazole was the most commonly prescribed PPI. As per NICE guidelines, out of 220 patients, appropriateness of indication for PPI use was seen in 88% of the prescriptions, whereas inappropriateness of dose (80mg/day) of PPI was seen in 49% (108 patients) of the patients. Drug interactions were also seen in 13% of the prescriptions and pantoprazole has the greatest number of interactions with other co-prescribed drugs. Unnecessary use of proton pump inhibitors should be minimized and awareness about PPI indications, drug interactions and economic burden should be created so that appropriate prescription will improve the patient care at low cost.

Keywords: Proton pump inhibitor, guidelines, drug interactions, gastroprotective agent.

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INTRODUCTION

Proton Pump Inhibitors (PPIs), which were first made available in 1989, are most frequently prescribed both in ambulatory and inpatient therapeutic settings. A class of drugs known as proton-pump inhibitors (PPI) greatly lowers the production of stomach acid.

The H+/K+ATPase pump in the parietal cell is where it binds irreversibly to do its work. The prevalence of acid peptic disorders (APDs) is increasing globally as a result of evolving dietary and lifestyle trends. Peptic ulcer disease (PUD), non-ulcer dyspepsia, and GERD are all highly prevalent in India [1].

Proton pump inhibitors (PPIs), a class of potent medications that control acid production, have revolutionized the treatment of disorders connected to acid production and reduced the need for surgery.

The main and generally accepted indications for their use include the management of gastroesophageal reflux disease, the elimination of Helicobacter pylori infection in conjunction with antibiotics, the treatment of H. pylori-negative peptic ulcers, the healing and prophylaxis of gastric ulcers brought on by non-steroidal anti-inflammatory drugs, and the management of a number of acids hypersecretory conditions[2].

Six different PPIs have been licensed by the US Food and Drug Administration (USFDA).

They are **Omeprazole, Esomeprazole, Pantoprazole, Rabeprazole, Lansoprazole, Dexlansoprazole.**

These PPIs share a similar pharmacological mechanism of action, but they act for varying lengths of time. Nowadays, PPIs are being overutilized because of their easy availability, high efficacy, and expanded indications[3].

All of the PPIs that are currently on the market are benzimidazole derivatives, which are heterocyclic organic compounds that connect the pyridine and benzimidazole moiety through a methyl sulfinyl group.

Omeprazole was the first clinically effective PPI and serves as the model for this structure. Lansoprazole, pantoprazole, rabeprazole, as well as the stereo-isomeric medicines esomeprazole and dexlansoprazole, were later released as medications. Despite having various mutations on their pyridine and/or benzimidazole rings, each of these medications' pharmacological characteristics is very comparable in the overall sense[4].

Increasing prices and an increased risk of adverse outcomes, the expanding use of PPI has caused a significant issue for several regulatory bodies.

PPIs on a long-term basis for gastroesophageal reflux disease and other common, chronic conditions, the long-term potential adverse effects are receiving more attention.

The long-term effect of chronic acid suppression on vitamin and nutrient absorption is an understudied area that is receiving a lot of attention. This also increased focus on the reported potential adverse effect of chronic PPI treatment on the occurrence of bone fractures[5]. PPIs have been linked to a higher risk of a variety of adverse effects, including dementia, kidney disease, Clostridium difficile infection, community-acquired pneumonia, vitamin B12 deficiency, and fractures due to osteoporosis[6].

The main causes of this overuse of PPIs are the overtreatment of functional dyspepsia, the overtreatment of gastro-duodenal ulcer prevention in low-risk patients, the stress ulcer prophylaxis in non-intensive care units, steroid therapy alone, anticoagulant treatment without risk factors for gastro-duodenal injury [2].

Indication:

PPI is the first-line agent among gastroenterologists for the following:

1. Gastroesophageal reflux disease (GERD)
   - ✓ Erosive Esophagitis,
   - ✓ Non-Erosive Reflux Disease (NERD)
   - ✓ Barrett's esophagus (BE)
2. Peptic ulcer disease
3. Prevention of Nonsteroidal anti-inflammatory drug-induced ulcers
4. Prevention of Steroid-induced ulcers
5. Zollinger-Ellison syndrome
6. Helicobacter pylori infections [7].

Drug Interactions

1. Clopidogrel + Esomeprazole/ omeprazole/ rabeprazole – Major interaction- Concurrent use of Clopidogrel and Esomeprazole or Omeprazole may result in reduced plasma concentrations of clopidogrel active metabolite and reduced antiplatelet activity.

Solution: Switch to pantoprazole, lansoprazole, dexlansoprazole which have less effect on the antiplatelet activity of clopidogrel. Consider using alternative antiplatelet therapy in patients requiring esomeprazole. The platelet aggregation of clopidogrel was not significantly altered by the coadministration of ranitidine, a histamine-2 receptor antagonist.

2. Levothyroxine + All PPIs – Moderate interaction - Concomitant use of levothyroxine and a proton pump inhibitor may cause clinically significant increases in TSH levels. Proton pump inhibitors may cause low stomach acid, decrease levothyroxine absorption, and affect intragastric pH.

Solution: Administer levothyroxine 4 hours before or after drugs that are known to decrease absorption and monitor patients appropriately.

3.Iron + All PPIs – Moderate interaction -Concurrent use of Iron and proton pump inhibitors may result in reduced iron bioavailability.

Solution: Monitor the patient for iron efficacy if rabeprazole is being used concurrently.

4. Warfarin + All PPIs – Moderate interaction - Concurrent use of Pantoprazole and Warfarin may result in increased International Normalized Ratio (INR) and prothrombin time.

Solution: Monitor prothrombin time or INR (International Normalized Ratio) when omeprazole is added to, changed during, or discontinued from concomitant treatment with warfarin. Adjust the warfarin dose as necessary in order to maintain the desired level of anticoagulation.

5. Digoxin +Omeprazole/ Esomeprazole/ Lansoprazole - Moderate interaction - Concurrent use of Digoxin and omeprazole or lansoprazole may result in an increased risk of digoxin toxicity (nausea, vomiting, arrhythmias).

Solution: Monitor digoxin levels and for signs and symptoms of digoxin toxicity in patients requiring concomitant digoxin and omeprazole therapy, particularly when initiating or discontinuing omeprazole therapy. Switch to pantoprazole

6. Ampicillin + Pantoprazole/ rabeprazole/ Lansoprazole/ Deslansoprazole – Moderate interaction - Concurrent use of Ampicillin and Pantoprazole/ Rabeprazole/ Lansoprazole/ Dexlansoprazole may result in loss of ampicillin efficacy.

Solution: monitoring the patient for antimicrobial efficacy if dexlansoprazole is being used concurrently with ampicillin[8].

Guidelines: National Institute for Clinical Excellence (NICE)[9].

Aim of the Study

- ✓ To assess and evaluate the utilisation of Proton pump inhibitors at a tertiary care hospital
- ✓ To determine the most frequently prescribed Proton pump inhibitor.
- ✓ To assess the frequency of usage of PPIs along with their dosage.
- ✓ To evaluate the Drug – Drug interaction of Proton pump inhibitors with co-prescribed drugs.

MATERIALS AND METHODS

A retrospective observational study was conducted in a multispeciality tertiary care hospital during the period of March to August 2022. Study population included the Patients admitted and prescribed with at least one proton pump inhibitors at different departments of the tertiary care hospital.

- ✓ **Inclusion Criteria** - Inpatients of General Medicine and Multi-speciality ward who were prescribed with PPIs (oral/IV), Both gender, Patient over 18 years old.
- ✓ **Exclusion Criteria** - Out Patients, Patients not prescribed with PPIs (oral/IV), Paediatric, OBG and Emergency departments.
- ✓ **Data Collection**-Data were collected using a pre-structured patient data collection form.

Statistical Analysis-analyzed using Microsoft Excel datasheet. Descriptive statistics including frequencies and percentages were used to summarize the data.

RESULTS

A total of 220 study participants were include in the study conducted at a Tertiary care hospital during the study period.

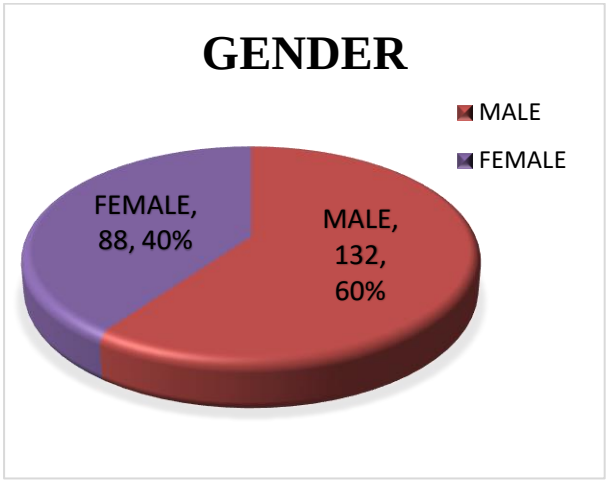


Figure 1: Percentage distribution of gender

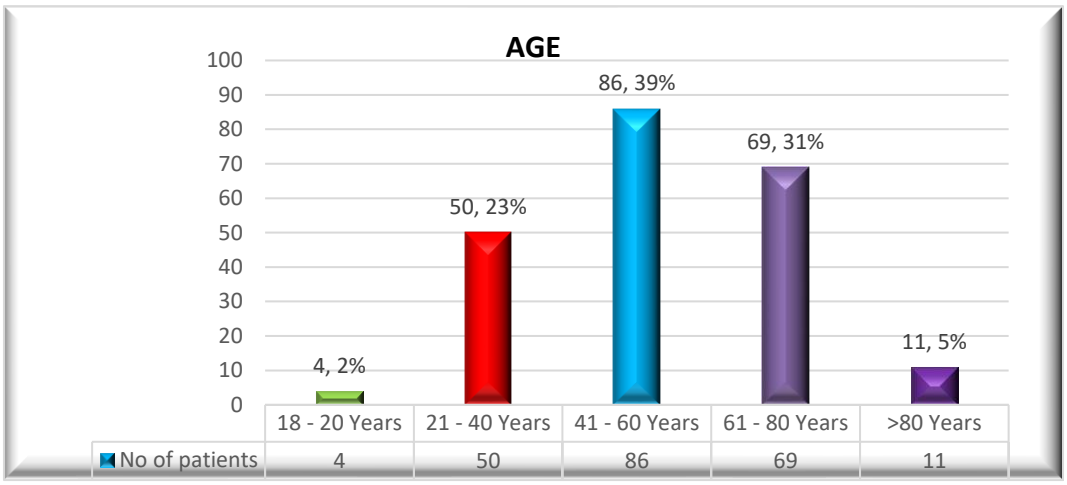


Figure 2: Percentage distribution of age group

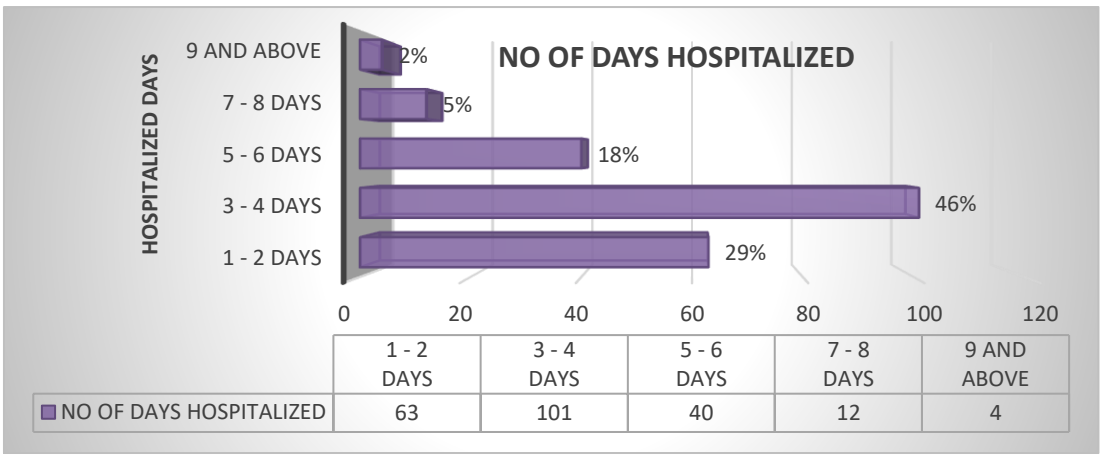


Figure 3: Percentage distribution of hospital stay

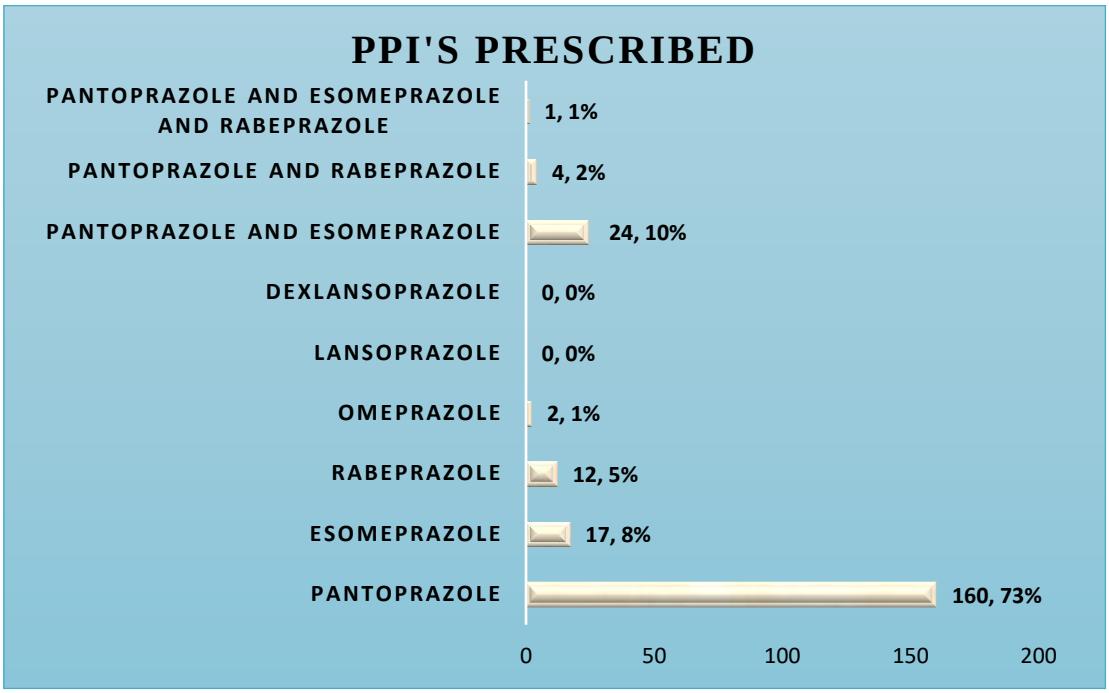


Figure 4: Percentage Distribution of PPI prescribed

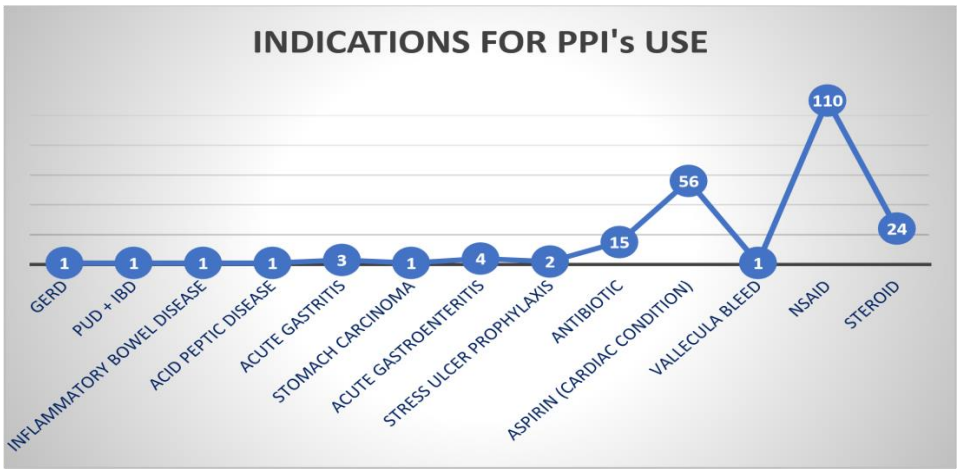
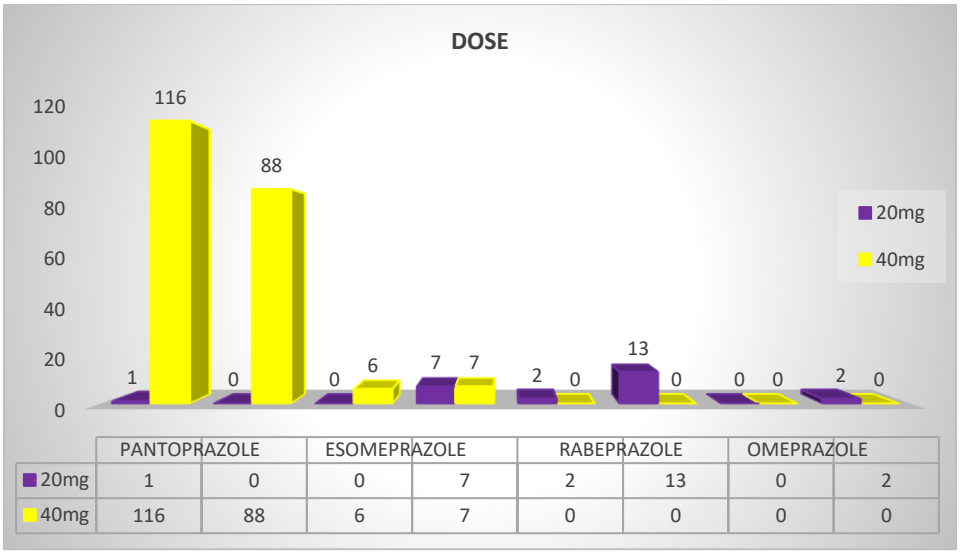


Figure 5: Distribution of indication of PPI use



	PANTOPRAZOLE		ESOMEPRAZOLE		RABEPRAZOLE		OMEPRAZOLE	
20mg	1	0	0	7	2	13	0	2
40mg	116	88	6	7	0	0	0	0

Figure 6: Distribution of dosing of proton pump inhibitors.

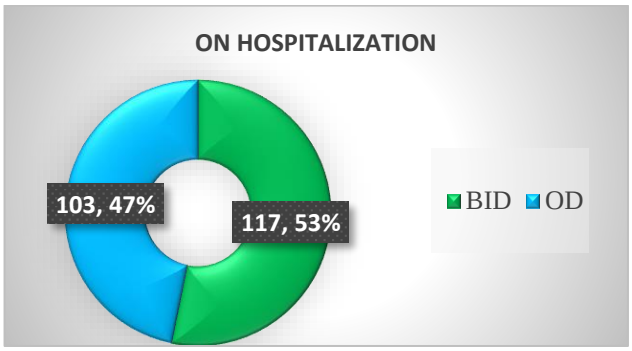


Figure 7: Percentage distribution of PPI prescribed during hospitalization

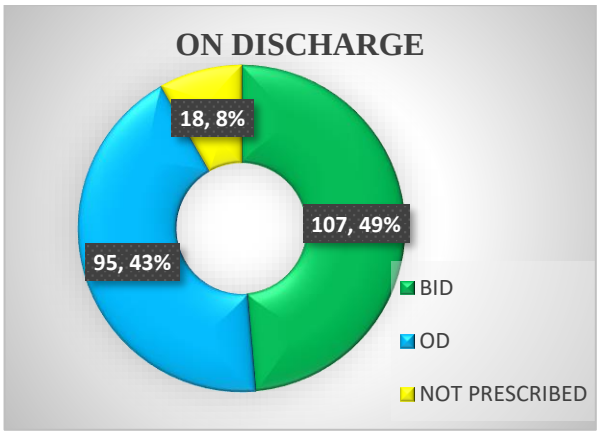


Figure 8: Percentage distribution of PPI prescribed during discharge

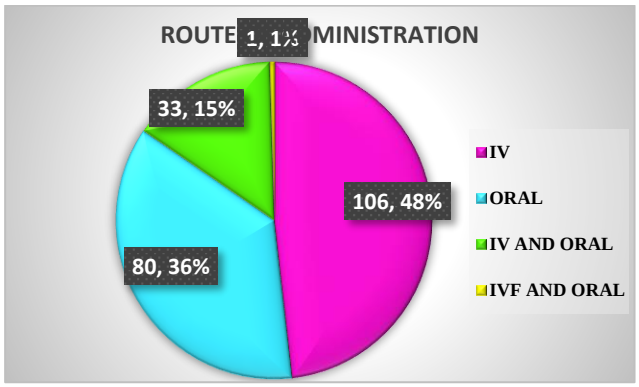


Figure 9: Percentage Distribution of Route of administration

DISCUSSION

Proton pump inhibitors (PPIs), a class of potent medications that control the production of acid, have revolutionized the treatment of disorders connected to the production of acid and reduced the need for surgery. The main and generally accepted indications for their use include the management of gastroesophageal reflux disease, the elimination of Helicobacter pylori infection in conjunction with antibiotics, the treatment of H. pylori-negative peptic ulcers, the healing and prophylaxis of gastric ulcers brought on by non-steroidal anti-inflammatory drugs, and the management of a number of acids hypersecretory conditions.

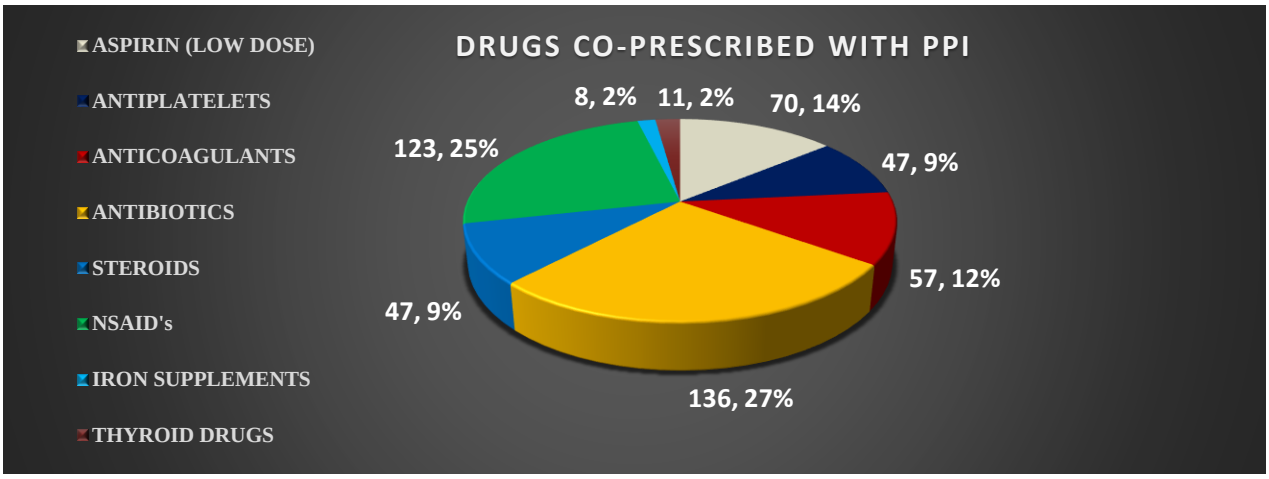


Figure 10: Percentage distribution of co-prescribed medications with PPI's

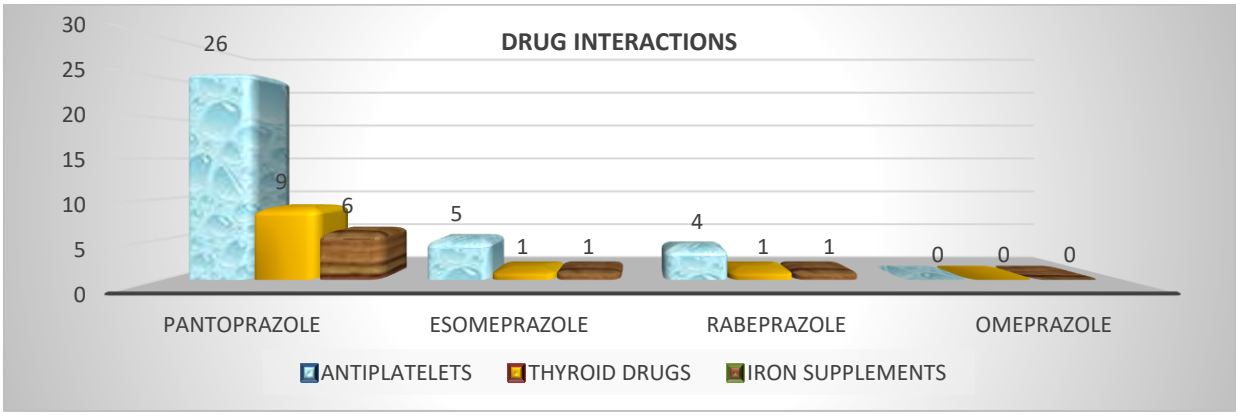


Figure 11: Distribution of drug interaction of proton pump inhibitors with Co-prescribed drugs

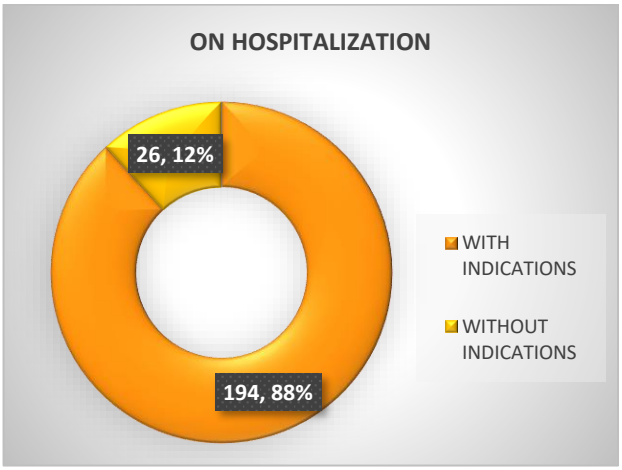


Figure 12: Percentage distribution of PPI utilization on hospitalization

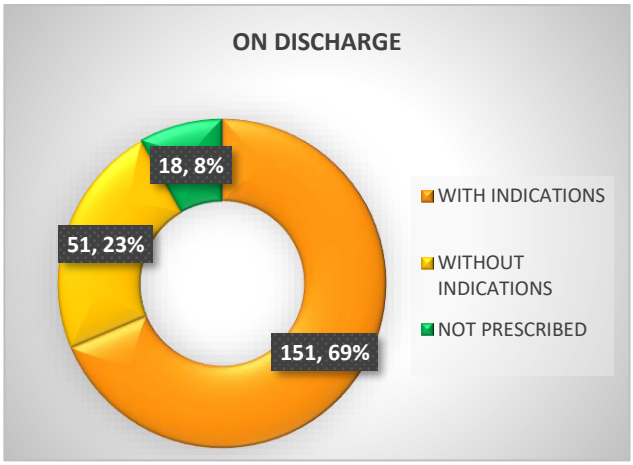


Figure 13: Percentage distribution of PPI prescribed during discharge

PPIs became a class of drugs with a high prevalence of being prescribed for unsubstantiated and poorly defined reasons or for conditions where they are not beneficial., The significant misuse of PPIs was increased recently. There is growing concern regarding the utilization of PPIs. They are available for over-the-counter purchase resulting in increased public access. The aim of our study is to evaluate the pattern of proton pump inhibitors use in a tertiary care hospital.

In the study conducted, we found that PPIs were prescribed to approximately 90% of the patients who were admitted to the hospital and most of the patients who were prescribed with PPIs were males (60%), which is similar to the study conducted by Mathew et al., where it was reported that males (55%) were more than females (44%).

In our results, patients prescribed with PPIs were more in the age group of 40-59 years. The probable reason for the increase in PPI prescription in males may be due to social habits, stress and irregular meal eating habits hence commonly male population are more prone to conditions, for which Acid Suppressant Drugs are prescribed. Patients above age 50 years are more prone to co-morbid conditions because of their decreased physiology, immune system, and altered pharmacokinetic and pharmacodynamics properties, which may be the reason behind more hospital admissions which leads to increased PPI prescriptions in these age groups. This result is similar to the study conducted by Lama Madi et al., 2019 [3]. Another study conducted by Bodoor S AL-Dosari et al., 2021[9] reported that PPIs were prescribed almost equally in terms of frequency for both male and female patients, most of whom were aged 60 years.

Our study shows that Pantoprazole is utilized with higher prescription frequency than other PPIs as prophylaxis for NSAID-induced ulcers. This indicates that PPIs are preferred and prescribed as gastroprotective agents along with NSAIDs. Thus, they will reduce the gastrointestinal adverse effects of NSAIDs. The results of our study were found to be comparable with some of the studies like Lama Madi et al., 2019 [3] and Shabbir Rafik Pendhari et al.[11] In our study, we found that about 10% of the patients were prescribed with pantoprazole (IV) and esomeprazole (Oral). Switching from Pantoprazole (intravenous route) to Esomeprazole (oral route) shows that esomeprazole more effectively suppresses intragastric acid compared with switching from Pantoprazole IV to oral pantoprazole. This result is confirmed in the study done by Philip B Miner Jr et al., [12] in which the Complete data collection for 286 patients was used to assess intravenous (IV) PPI utilization.

We found that in our study Patients who were initiated on PPIs via the IV route were about 63%, of which one-fourth of the candidates were switched from IV to the oral form (15%) during their hospitalization. Most patients received a 40 mg IV dose twice daily for a period during hospitalization. The high prescribing pattern (40mg twice daily dose) of IV PPIs is similarly found in the study done by Soumana C Nasser et al., (2010). [10] The majority of the patients were prescribed intravenous PPIs. The main reason behind this was the patient's physical condition, inability to swallow the drug, use of corticosteroids and NSAIDs

According to the NICE guidelines, in our study, we found that high-dose therapy (40mg twice daily dose) was most frequently prescribed in 53% of the patients. Patients with severe or complicated reflux disease were required higher than standard doses of a Proton pump inhibitor for sufficient acid suppression. This result was similar to the findings of the result conducted by Yujuan Liu et al., (2020).[11]

PPI was prescribed both for primary and secondary prophylaxis against NSAIDs/aspirin-induced ulcers in 74% of patients.

In this study, some of the patients did not have high-risk factors (Age >65 years or concomitant use of corticosteroids, antiplatelet agents, or anticoagulants, or previous history of peptic ulcer disease) but were prescribed with PPI to prevent NSAID-related ulcers. However, it is not recommended to prescribe in gastroprotective strategies with PPIs in younger NSAID users (<65 years) and without other known risk factors, and

this is also one of the main causes of PPI misuse. Therefore, clinicians should be trained and guided on the exact indications of PPI to reduce unnecessary use of PPI and avoid serious adverse reactions. The majority of these prescriptions were for routine primary prophylaxis of NSAID/Aspirin-induced ulcers and is similar to the study done by Muhammad Haroon et al., (2013)[13].

Our findings showed that PPIs are frequently prescribed to most patients in the medical wards of tertiary care hospitals. In this, about 12% of the PPIs prescribed were indicated for complaints other than those approved by NICE guidelines used for this study. Such complaints included nausea and vomiting, epigastric pain, gastritis, irritable bowel syndrome, bleeding, oesophageal varices, stomach cancer, and antibiotic prescription. The inappropriate prescriptions suggest the need for prescribers to adhere to official monographs and guidelines to ensure rationale prescription and safe drug use. This is supported by the study done by Muhammad Haroon et al., (2013)[13].

In our study, out of 220 patients, 136 patients were prescribed proton pump inhibitors along with antibiotic prescriptions. In this, about 121 patients received antibiotics in combination with drugs like NSAIDs, corticosteroids, aspirin (low dose), and antiplatelet drugs. The remaining 15 patients received PPI only for antibiotic therapy (PPI for antibiotic therapy is not mentioned anywhere in the NICE guidelines). Some antibiotics like doxycycline, amoxicillin-clavulanic acid, etc., can cause esophageal ulcers. For which Antacids, histamine H2 receptor blockers, proton pump inhibitors, sucralfate, and even local anesthetic agents are often prescribed, but their value is unsubstantiated.

We also found that in our study, about 8% of the patients were not prescribed with PPI during discharge but they were prescribed with NSAIDs, corticosteroids, aspirin (low dose), and antiplatelet agents or anticoagulants. In this, some of the patients were found to be geriatric (> 60 years) and needed PPI therapy for the concomitant use of NSAIDs and corticosteroids.

All PPIs have different drug interaction, in which the same drug interact with different PPIs to various extents. Clopidogrel, Warfarin, Levothyroxine, digoxin, phenytoin, diazepam, citalopram, methotrexate, etc., these drugs interact with PPIs. In our study drugs like levothyroxine and iron supplements are concurrently prescribed along with PPIs, whereas drugs like warfarin, ampicillin, and digoxin were prescribed with PPIs but not concurrently used. Proton pump inhibitors may cause low stomach acid, decrease levothyroxine absorption, and affect intragastric pH and Concomitant use of levothyroxine and a proton pump inhibitor may cause clinically significant increase in TSH levels. Concurrent use of Iron with PPIs may result in reduced iron bioavailability.

Clopidogrel is the most commonly prescribed drug in cardiac conditions along with PPI. Our results also showed the predominance of pantoprazole being prescribed in patients receiving clopidogrel. This is assuring as clopidogrel prescribing information recommends avoiding concurrent use with omeprazole, rabeprazole, and esomeprazole due to the possibility that combined use may result in decreased clopidogrel effectiveness. This study is similar to the study conducted by Lama Madi et al., (2019) [3].

CONCLUSION

From the present study conducted, it can be concluded that, 90% of the patients were prescribed with Proton pump inhibitors for wide range of indications. In our study, PPIs were most frequently used as a gastroprotective agent along with NSAID's and Pantoprazole was the most commonly prescribed PPI.

As per NICE guidelines, out of 220 patients, appropriateness of indication for PPI use was seen in 88% of the prescriptions, whereas inappropriateness of dose of PPI was seen in 49% (108 patients) of the patients. Drug interactions were also seen in 13% of the prescriptions and pantoprazole has the greatest number of interactions with other co-prescribed drugs.

The unnecessary use of proton pump inhibitors should be minimized and awareness about PPI indications, drug interactions and economic burden should be created so that appropriate prescription will improve the patient care at low cost.

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