Project

Survey on Beyond the Prescription: Unraveling the Irrational Dependency on PPI Medications

Submitted To

The Department of Pharmacy,

Faculty of Health & Life Sciences,

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In the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy

Submitted By

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APPROVAL

This project Survey on Beyond the Prescription: Unraveling the Irrational Dependency on PPI Medications, submitted to the Department of Pharmacy, Faculty of Health & Life Sciences, Daffodil International University, has been accepted as satisfactory for the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy and approved as to its style and contents.

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DECLARATION

Firstly, I'd like to express my heartfelt gratitude to Allah, the All-Powerful, for providing me with the ability to complete my project work and the opportunity to focus on this topic, Alhamdulillah. I'm also grateful to my honorable project advisor, **Ms. Sultana Juhara Mannan**, Assistant Professor, Faculty of Health & Life Sciences, Daffodil International University, for his brilliant guidance and steady supervision, as well as for providing critical information about the challenge and his assistance in completing it. I would like to express my humble regards to **Dr. Muniruddin Ahmed**, Professor and Head, Department of Pharmacy, Daffodil International University. I wish to offer my respect to all of the teachers of Pharmacy Department, Daffodil International University and thankful to other members for their excellent cooperation, support and motivation in helping me to complete this project.

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ABSTRACT

Proton pump inhibitors (PPIs) are widely prescribed for acid-related disorders like gastroesophageal reflux disease (GERD) and peptic ulcers due to their effectiveness in reducing gastric acid secretion. However, their overuse has become a significant concern in clinical practice. Several factors contribute to the irrational use of PPIs, including inappropriate prescribing, over-the-counter availability, and increased patient demand for quick symptom relief. Physicians often prescribe PPIs without clear diagnostic indications or fail to discontinue therapy when it's no longer necessary, leading to prolonged and unnecessary use. Over-the-counter availability exacerbates this issue, allowing patients to self-medicate without proper medical guidance, unaware of the risks associated with long-term use, such as nutrient malabsorption, increased infection risk, and kidney complications. Patient demand also plays a role, as many individuals expect rapid relief from gastrointestinal symptoms, pressuring healthcare providers to continue or initiate PPI therapy unnecessarily. The consequences of this overuse are far-reaching, including adverse health outcomes and increased healthcare costs due to unnecessary prescriptions and the management of related complications. Addressing this issue requires a multi-pronged approach, emphasizing evidence-based prescribing practices, patient education about the risks of long-term PPI use, and regulatory interventions to limit over-the-counter availability or ensure proper usage. By promoting the judicious use of PPIs and encouraging regular reassessment of therapy, healthcare systems can reduce the risks associated with prolonged use, minimize unnecessary costs, and optimize patient outcomes while maintaining the therapeutic benefits of PPIs for those who genuinely need them.

Keywords: Proton Pump Inhibitors (PPIs), Irrational Use, Over the Counter, Adverse Effects, Patient Education, Judicious Use.

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Introduction

1.1. PPI (Proton Pump Inhibitors)

Proton-pump inhibitors (PPIs) are a group of medications that induce a substantial and enduring reduction in the production of acid by the stomach. This is secretion that are presently available. Proton-pump inhibitors have substantially supplanted antacids and medications classified as H2-receptor antagonists. These medications are administered in a manner that is distinct from that of proton-pump inhibitors despite their effects being comparable. PPIs are consistently regarded as one of the most frequently purchased pharmaceuticals globally. The World Health Organisation (WHO) has compiled the List of Essential Medicines, which includes pharmaceuticals that inhibit proton pumps [1].

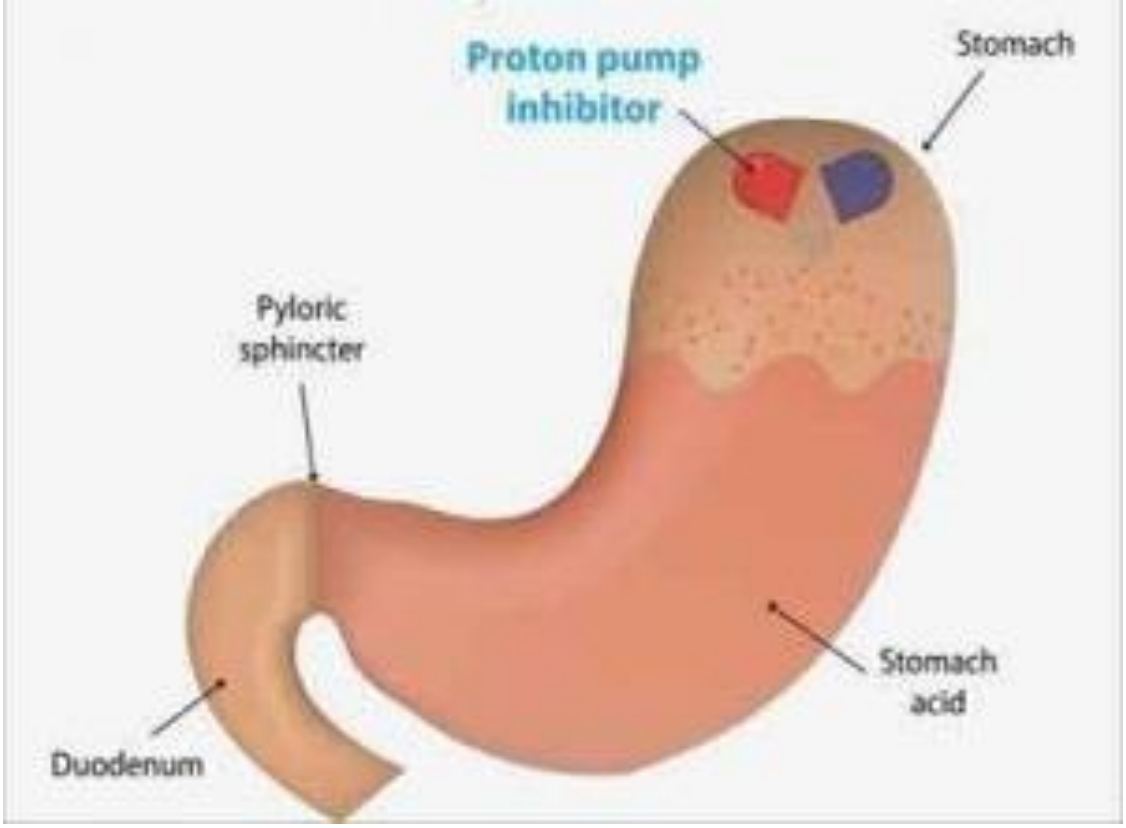

Fig 01: PPI

1.2. Medical uses

1.2.1. Dyspepsia

Indigestion is a condition that is defined by an insufficient metabolism. It is also known as dyspepsia and an unsettled stomach. The symptoms may include dyspepsia, discomfort, regurgitation, vertigo, or upper abdominal congestion. Belching may be one of the supplementary symptoms. Specific individuals experience a sensation of fulfillment earlier than anticipated when they consume sustenance. Indigestion is a condition that impacts approximately one in five individuals at some point in their lives. Indigestion is most frequently caused by gastritis and gastro-oesophageal reflux disease (GERD). Determining the type of dyspepsia a patient has can be challenging for clinicians, as it can be classified as "functional" or "organic." Organic dyspepsia is the term used to describe indigestion resulting from condition, such as gastritis, peptic ulcer disease (an ulcer that may develop in either the stomach or the duodenum), or malignancy. Functional indigestion, previously known as nonnuclear dyspepsia, is a term used to describe indigestion that does not exhibit symptoms of an underlying illness.

Fig 02: Dyspepsia

Functional gastritis is the most common cause of dyspepsia, which approximately 15% of the general population in Western countries. An endoscopy is a procedure that involves the

implantation of a flexible tube containing a camera into the stomach and down the esophagus. Patients who are either older (60 years of age or older) or who exhibit concerning symptoms, such as weight loss, blood loss, or difficulty consuming, are advised to undergo this procedure. This procedure aims to conduct a more thorough evaluation and identify a potential cause. It is recommended that patients under the age of 60 undergo testing for the bacterium H. pylori. If the test results are affirmative, the condition should be addressed. Additional information regarding dyspepsia's diagnosis and treatment can be located further down this page [2].

1.2.2. Peptic ulcer disease

A peptic ulcer, also called peptic ulcer disease (PUD), is a rupture in the interior membrane of the stomach, the first section of the small intestine, or the lower esophagus in specific instances. A gastric ulcer is an ulcer localized in the stomach, while a duodenal ulcer is an ulcer located in the duodenum. The two symptoms that are most indicative of a duodenal ulcer are the presence of pain in the upper abdomen and the presence of distress in the upper abdomen that is alleviated by ingesting, which is present upon awakening in the morning. If you consume it while experiencing a gastrointestinal ulcer, the discomfort may become more severe. Individuals frequently use "burning" or "dull ache" to characterize the anguish. The additional symptoms are belching, vomiting, weight loss, and a loss of appetite. Symptoms are not present in approximately one-third of elderly individuals. Potential complications include obstruction of the intestines, perforation, and bleeding. Bleeding is observed in up to 15% of the cases [3].

Fig 03: Peptic ulcer disease

Helicobacter pylori and non-steroidal anti-inflammatory medications (NSAIDs) are two of the most prevalent causes of peptic ulcer disease. Among the less common causes of cirrhosis are Behcet's illness, Zollinger–Ellison syndrome, Crohn's disease, liver cirrhosis, and tension caused by other significant health disorders. Furthermore, tobacco consumption is a contributing factor. The ulcer-causing effects of NSAIDs are more prevalent in senior individuals than in their younger counterparts. In general, a diagnosis is only hypothesized based on the present symptoms and is validated through either endoscopy or a barium swallow. Potential diagnostic methods for H. pylori include the investigation of the defecation for evidence of the bacterium, utilizing a stomach biopsy, testing the breath for urea, and screening the blood for antibodies. Additional conditions that may induce symptoms comparable to those of GERD include coronary heart disease, inflammation of the stomach membrane, gastric malignancy, and biliary inflammation [4].

Barrett's esophagus

A metaplastic (anomalous) alteration in the mucosal cells that line the lower portion of the esophagus is the defining characteristic of Barrett's esophagus. The cells transition from stratified

squamous epithelium to simple columnar epithelium with interspersed goblet cells. This cell type is typically found exclusively in the small and large intestines. The development of malignancy may result from this condition. This modification is classified as a premalignant condition due to its increased risk of developing esophageal adenocarcinoma, a cancer that is frequently fatal. It is widely accepted that Barrett's esophagus is predominantly the result of an adaptation to persistent acid exposure, which is most likely the result of reflux oesophagitis. Barrett's esophagus is diagnosed through endoscopy. The initial stage of the procedure involves conducting a direct examination of the lower esophagus to identify the indicative symptoms of the condition. This is followed by a microscopic examination of tissue obtained from the affected location through a biopsy. Barrett's esophagus cells may be nondysplastic, exhibit low-grade dysplasia, high-grade dysplasia, or be a frank malignancy. Barrett's esophagus cells are classified into four subtypes based on the severity of dysplasia. Endoscopic excision or radiofrequency ablation may be implemented to manage the initial phases of adenocarcinoma and high-grade dysplasia. Surgical resection or palliative care may be considered as a treatment option in the advanced stages of adenocarcinoma. Individuals with nondysplastic or low-grade dysplasia undergo annual surveillance with endoscopy, while those with dysplasia undergo radiofrequency ablation. The probability of a patient developing cancer is approximately 10% per patient-year in cases of high-grade dysplasia [5].

Eosinophilic esophagitis

Eosinophilic esophagitis, or EoE, is an allergic inflammatory disorder that impacts the esophagus. Eosinophils are a type of white blood cell implicated in the condition's development. Eosinophils are uncommonly detected in the esophagus of individuals otherwise in excellent health. A substantial number of eosinophils migrate to the esophagus in patients with EoE. Eosinophils are responsible for tissue injury and inflammation, which are induced by the consumption of a trigger meal. Some of the symptoms include dyspepsia, difficulty imbibing, food impaction, and vomiting. Although eosinophilic esophagitis was initially identified in neonates, it may also be present in adults. The precise cause of the condition is not well understood; however, an allergy to specific

substances may be a significant factor. The therapy will likely involve the ingestion of medication to reduce the immunological response, in addition to the elimination of any known or potential triggers. In severe cases, an endoscopic operation may be necessary to expand the esophagus to accommodate additional food. Despite the rapid advancement of our comprehension of EoE, the diagnosis may be challenging because neither the symptoms nor the histopathologic findings are particularly distinctive [6].

Specialized professional organizations advise their members to prescribe the lowest effective dosage of PPI to their patients to achieve the desired therapeutic outcome when used to treat gastro-esophageal reflux disease on a long-term basis. According to the Food and Drug Administration (FDA) in the United States, it is not recommended to administer over-the-counter proton pump inhibitors (PPIs) such as Prilosec OTC for more than three treatment sessions of 14 days each within a single calendar year. Despite their widespread use, the quality of the data supporting their use in treating specific disorders is inconsistent. There is insufficient evidence to demonstrate that PPIs are effective in all situations. For example, they do not seem to affect the length of the esophagus, even though they decrease the risk of esophageal cancer in patients with Barrett's esophagus. Moreover, research conducted in the United Kingdom has demonstrated that PPIs are not an effective treatment for symptoms that persist in the esophagus over time.

1.3. Indications for stopping PPIs

PPIs are frequently implemented for an extended period before they are necessary. In approximately 50% of patients hospitalized or treated in primary care clinics, there is no medically substantiated justification for the long-term use of PPIs. Some experts recommend that clinicians discontinue the use of proton pump inhibitors (PPIs) in a significant number of patients due to the high cost, the potential for injury, and the absence of evidence regarding their long-term efficacy. Patients may be able to discontinue the use of PPIs for gastritis, gastro-oesophageal reflux disease (GERD), or modest esophageal inflammation after four weeks if their symptoms have improved and their condition no longer necessitates treatment. It is not recommended that smokers who have Barrett's esophagus or an ulcer that is bleeding into their stomachs cease smoking. By initially

decreasing the dosage or directing the individual to consume the medication exclusively when symptoms are present, it is feasible to discontinue medication intake.

1.4. Adverse effects

Proton pump inhibitors are generally well-tolerated, and the incidence of short-term adverse effects is typically low. This is because proton pump inhibitors prevent the production of hydrogen ions. Although omeprazole has been documented more frequently, the frequency and extent of potential adverse effects are comparable for all PPIs. This may be due to its extended existence, which has resulted in a higher level of clinical expertise [7].

Exhaustion, disorientation, diarrhea, vertigo, migraines, and gastrointestinal distress are among the most frequently observed adverse effects. Rash, irritation, constipation, anxiety, melancholy, and flatulence are among the few adverse consequences that may occur. The development of myopathies, including the potentially fatal response known as rhabdomyolysis, has been associated with the use of PPIs in exceedingly uncommon instances.

It is imperative to assess the treatment's relative risks and benefits when using PPIs for an extended period. Although numerous primary reports have established a correlation between long-term PPI use and various adverse consequences as of March 2017, assessments have classified the quality of the evidence in these studies as "low" or "very low." They clarify that there is insufficient evidence to establish causal relationships between PPI treatment and many of the reported correlations resulting from the studies' design and the modest estimations of the impact size. The hazards of PPIs were outweighed by their benefits when they were implemented effectively in March 2017. Nevertheless, the relatively insignificant concerns became substantial when they were implemented insufficiently. They favor using PPIs in patients with a confirmed indication at the lowest effective dosage. However, they are opposed to the escalation of dosages and the continuance of chronic medication in those who are not responsive to the initial empiric therapy [8].

Nutritional

Despite its critical function in digesting food and releasing micronutrients, gastric acid may impede the absorption of iron, calcium, magnesium, and vitamin B12. Specific studies have demonstrated this. The data regarding iron and vitamin B12 needs to be improved, and several variables that may need to be more accurate with the results have been identified.

Patients who have been prescribed proton pump inhibitors (PPIs) are at an increased risk of experiencing decreased magnesium levels; however, this adverse effect may be mitigated by transitioning to medications that inhibit H2 receptors [9].

Bone fractures

In 2010, the FDA included a warning on the labels of PPI medicines to inform consumers of the increased risk of bone fractures caused by their use. This risk was not observed when PPIs were used for a limited period at a low dosage. In neonates who are otherwise healthy and do not have gastro-oesophageal reflux disease, acid suppression is frequently used to treat symptomatic gastro-oesophageal reflux. This pertains to neonates not yet diagnosed with gastro-oesophageal reflux disease. An elevated risk of bone fracture was associated with the use of proton pump inhibitors (PPIs) alone or in combination with histamine H2-receptor antagonists, according to a 2019 study. The risk was multiplied by the number of days of usage and the earlier the medication was initiated. One hypothesis is that osteoclast activity has increased even though the precise cause of this phenomenon is unknown [10].

Gastrointestinal

In specific studies, the use of proton pump inhibitors (PPIs) has been associated with an elevated prevalence of Clostridioides difficile infection. The FDA was sufficiently concerned about the

potential for this adverse effect to mandate that a warning be included in the packaging of PPI medications. However, the evidence is inconsistent, and the theory is contested. Furthermore, there are concerns regarding spontaneous bacterial peritonitis (SBP) in senior individuals who are taking PPIs and in individuals with irritable bowel syndrome who are taking PPIs. Whether this is a class effect of PPIs is uncertain, as underlying conditions in these categories cause both infections. SBP is more probable in elderly individuals who are taking PPIs. Consuming probiotics may lead to an elevated risk of developing bacterial or fungal proliferation in the small intestine. A substantial quantity of ascites and impaired esophageal motility due to varices may precipitate GERD in cirrhotic individuals. Varices may rupture due to irritation from a corrosive source [11]. Proton pump inhibitors are frequently and consistently administered to cirrhotic patients to treat GERD and prevent variceal bleeding.

Conversely, it was recently discovered that the l infections associated with PPIs [12]. These infections may contain Helicobacter pylori, which can increase the risk of gastric cancer and ulceration in individuals who are genetically predisposed to these conditions. This species is not attracted to an acidic environment. Proton pump inhibitors (PPIs) may also be linked to an increased risk of gastric cancer in patients who have undergone treatment to eradicate H. pylori [13]. The validity and robustness of this correlation and the lack of a distinct causal relationship between the two variables have been evaluated. It is recommended that individuals with a history of H. pylori infection, in particular, exercise caution when using long-term proton pump inhibitors (PPIs), as determined by an evaluation of their risk-benefit scenario.

Additionally, it is recommended that additional prospective studies be conducted with suitable construction. The formation of benign polyps from fundic glands is linked to the prolonged use of proton pump inhibitors (PPIs), which should not be confounded with fundic gland polyposis. Upon discontinuing the use of PPIs, these lesions do not develop into malignancy and cease to exist. An increasing body of research has demonstrated that the use of proton pump inhibitors (PPIs) may obscure gastric malignancies and other severe gastrointestinal conditions. The development of microscopic colitis in specific patients has also been associated with the use of PPIs [14].

1.5. Mechanism of action

The of the stomach's parietal cells is inhibited by proton pump inhibitors. This enzyme system is also referred to as the H+/K+ ATPase or, more commonly, the gastric proton pump. Proton pump inhibitors can exert their effects by inhibiting this enzyme system. This process is irreversible. The proton pump is an exceptional candidate for restricting acid production in the stomach, as it is the final stage in the production of gastric acid and is directly responsible for the discharge of H+ ions into the gastric lumen. An inhibitor of the H, K-ATPase enzyme is more efficacious than receptor antagonists in reducing gastric acid production [15]. This is knstage in the acid secretion process. This is the case as a result of the antecedent clause. Given the concentrations of these medications in the circulation, the duration of their effects is significantly prolonged than one would expect. This results from the H, K-ATPase enzyme located in the stomach, forming covalent connections with each of these medications. The development of a new class of pharmaceuticals has resulted from the irreversible nature of the inhibition and the targeting of the terminal stage of acid production [16]. These treatments can decrease the amount of acid produced by the stomach by up to 99%. It is feasible to expedite the healing process of duodenal ulcers and mitigate the distress associated with dyspepsia and reflux by decreasing the amount of acid the stomach generates.

Nevertheless, gastric acids are essential for assimilating diverse substances, such as calcium, vitamin B12, and proteins. Hypochlorhydria is a condition that may arise when the stomach is unable to produce an adequate amount of acid. The patient is administered a PPI medication devoid of its active constituent [17].

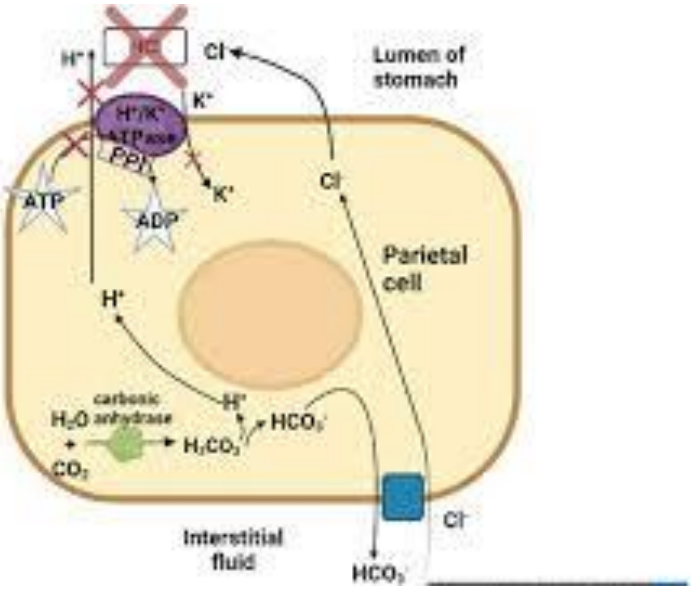

Fig 04: PPI Mechanism of Action

This form is lipophilic, which implies that it is uncharged. Subsequently, it can effortlessly cross cell membranes to access acidic intracellular compartments, including the parietal cell canaliculus. Protonation and structural transformation are the processes by which the substance transforms from an inactive to an active state when subjected to an acidic environment. I have previously stated that the active form will establish a covalent and irreversible bond with the gastric proton pump. Consequently, the pump will be unable to function conventionally [18]. Because of their ability to elevate the pH of the stomach, proton pump inhibitors (PPIs) are an effective treatment for eradicating H. pylori. Consequently, the bacteria are compelled to transition from their coccoid form, which is impervious to both acids and antibiotics. Although they are of diminished significance, PPIs have been demonstrated to have a few additional effects during the elimination process [19].

1.6. Cellular Mechanism of Proton Pump Inhibitors in the Stomach

The stomach is the only human body region with a pH level below 4. The concentration of these proton pump inhibitors (PPIs) in the acidic area of the secretory canaliculus of the activated parietal

cell was immediately apparent upon their identification as weak bases with a pKa ranging from 4.0 (omeprazole, lansoprazole, and pantoprazole) to 5.0 (rabeprazole). The acid space-dependent concentration of the PPIs initially determines the therapeutic index of these medications. The concentration of these medications at the luminal surface of the pump is approximately one thousand times greater than that of the blood as a result [20]. The second critical phase is distinguished by the low pH-dependent transformation of the accumulating prodrug into the activated species, a highly reactive cationic thiophilic reagent. The pH value is a determining factor in this transformation. This suggests that the protonation of these compounds is crucial for their activation, which is necessary to produce disulfides with the cysteines included in the H+, K+-ATPase. The order of acid stability is as follows: pantoprazole > omeprazole > lansoprazole > rabeprazole. The pH dependency of activation was found to mirror the protonation of the benzimidazole moiety when the rate of conversion of various compounds was assessed as a function of pH [21]. This was discovered while investigating the conversion rate of a diverse array of compounds with pH. This elucidated the diverse activation rates that the PPIs observed. Protonation is essential for the efficacy of PPIs, which is why they are classified as prodrugs. The protonation process is initiated to produce the thiophilic drug, which subsequently interacts with luminally accessible cysteines on the acid pump enzyme. This occurs after the substance is bonded to the gastric H+, K+-ATPase, accumulating in the parietal cell's activated secretory canaliculus. Consequently, the efficacy of these agents is contingent upon the presence of acid secretion [22]. It is recommended that the pumps be administered approximately thirty minutes before a meal to ensure that they are operational during the peak concentrations of PPIs in the circulatory system. Furthermore, it is imperative to protect them from the acid produced by the stomach before their absorption. The steady state of acid secretion is obtained after approximately three days when a balance is achieved between the covalent inhibition of the active pump, the subsequent stimulation of inactive pumps after the drug has been eliminated from the circulation, and the de novo synthesis of new pumps. This is due to the fact that PPIs have a comparatively brief half-life, and not all pumps are activated. The rat pump protein has a half-life of approximately 54 hours, which may be comparable to that of humans. Consequently, approximately 20% of new turbines are produced every 24 hours. Furthermore, the quantity of pump synthesis is higher at night than during the day. The medication will not provide any additional benefits if administered before bed, as it will no longer be present in the body when night-time acid production is evident. This is due to the

inhibitory effect on nocturnal acid breakthrough. The steady-state inhibition of a once-daily dose is approximately 66% of the maximal acid production if it is presumed that approximately 70% of pumps are engaged by breakfast and that the PPI is administered between 30 and 60 minutes prior. Once the optimal dosage has been determined, there is minimal impact when the dosage is increased. However, the delayed release formulation of dexlansoprazole demonstrates that the frequency of administration has an effect [23].

The linear relationship between the covalent binding of proton pump inhibitors and the inhibition of gastric acid secretion has been established. The amount of omeprazole bound in vivo was compared to the quantity of acid secretion inhibited (Shin, unpublished data). The quantity of PPIs bound to the pump enzyme was linearly proportional to the inhibitory activity of PPIs. To complete inhibition, radioactive omeprazole was administered orally at a 10 mg/kg dose in this experiment. Throughout the investigation, the drug concentration in the plasma and the inhibition of acid secretion were monitored at predetermined intervals. The pump enzyme was extracted from each stomach at a predetermined time during the animal's stomach removal. The quantity of radioactive omeprazole affixed to the enzyme was quantified, and the enzyme's amount was determined. The maximal amount of acid pumping that could be inhibited by the binding of omeprazole to the pump enzyme was determined to be 2.5 nmol/mg of the enzyme, which follows the published data. The suppression of acid secretion was less effective when the receptors were bound to reduced concentrations of omeprazole. The inhibition or binding quantities and the plasma level of the medication did not exhibit any correlation except at the initial administration time, where the relationship was a straight line. The drug concentration in the blood was rapidly eliminated in rodents, with an elimination half-life of approximately 7–10 minutes. Conversely, the inhibition was sustained for an extended period due to the covalent binding of activated omeprazole. This is a distinct indication that the efficacy of the medication cannot be determined by assessing its concentration in plasma [24].

Goal of my studies

Patients who take irrational PPIs for an extended period may develop an elevated risk of adverse effects, such as respiratory infections, infections caused by Clostridium difficile, bone fractures, vitamin B12 deficiency, and hypomagnesemia. Additionally, patients may develop hypomagnesemia.

I conducted this investigation to determine the most common form of PPI in Bangladesh.

- Determine the age group of individuals most likely to use PPI.
- Evaluate their level of familiarity with PPI.
- To provide a comprehensive examination of the irrational use of PPI pharmaceuticals.

Literature Review

2.1. Ali, O., Poole, R., Okon, M., Maunick, S., & Troy, E. (2019). Irrational use of proton pump inhibitors in general practice. Irish Journal of Medical Science (1971-), 188, 541-544.

Proton pump inhibitors (PPIs), which are frequently abbreviated as PPIs, are a trendy primary treatment option for a wide range of medically permissible maladies among both general practitioners (GPs) and hospital physicians. Nevertheless, proton pump inhibitors have a well-established side-effect profile that may be disregarded when their prescription is outside of the Food and Drug Administration (FDA)'s recommended indications. A total of one hundred seventy-four (n = 174) inpatient records were randomly examined during the investigation. Eighty-five percent of these individuals were consistently consuming PPIs. Despite the absence of a documented rationale, 54.7% of patients (n = 46) were administered PPIs. The average age of these patients, who accounted for 46.4% (n = 39), was over 75 years. Only 54.7% of the patients (n = 46) were advised to take esomeprazole. The primary justification for prescribing PPIs was to reduce the risk of gastric ulcers, which are associated with the use of NSAIDs. This was the case for 68.4% (n = 26) of the individuals prescribed a PPI per the recommendations.

2.2. Venkataraman, R., Rashid, M., & Shrestha, H. (2020). Inappropriate medication use and cost comparison analysis of proton pump inhibitors: evidence from an Indian tertiary care facility. Current Drug Safety, 15(2), 147-155.

Following the acquisition of ethical authorization, a prospective observational study was conducted for nine months, involving 253 inpatients. Participants in the trial were not subjected to discrimination based on gender or age, provided that they had received PPIs for any of the prospective reasons specified in the study. A cost comparison study of branded vs generic PPIs was also conducted, and the drug's appropriateness was assessed using criteria established by the US Food and Drug Administration (FDA). Most inpatients were male, comprising 62% of the total. Their average ages ranged from 46 to 19. The standard deviation was 1, and the average number of days spent in the hospital was 4.0. The standard deviation was 1.16, and the number of medications prescribed was 4.39. Pantoprazole was the PPI administered to the most patients

(76%) even though most patients were not within the FDA-approved indication. A drug interaction was documented in 14% of the population, and 9% of the population experienced an adverse drug reaction. The average cost of a hospital stay was determined to be 207.96 + 149.57 Taka. It was determined that generic substitution could save a total of 41582 Taka.

2.3. Bavishi, C., & Dupont, H. L. (2011). Systematic review: the use of proton pump inhibitors and increased susceptibility to enteric infection. Alimentary pharmacology & therapeutics, 34(11-12), 1269-1281.

The utilization of probiotics (PPIs) leads to an increase in the pH of the stomach, the promotion of the development of intestinal microflora, the increase in the translocation of bacteria, and the modulation of a variety of immunomodulatory and anti-inflammatory effects. The pH of gastric acid and acid tolerance levels have varying degrees of influence on the susceptibility of enteric infections. In a variety of distinct pathways, PPIs appear to increase the susceptibility to bacterial enteropathogens, including Salmonella, Campylobacter jejuni, invasive strains of Escherichia coli, vegetative cells of Clostridium difficile, Vibrio cholerae, and Listeria. We present the evidence that using PPIs increases the susceptibility to enteric infections caused by Salmonella, Campylobacter, and C. difficile. The adjusted relative risk ranges for these three organisms were 4.2–8.3 (two studies), 3.5–11.7 (four studies), and 1.2–5.0 (17 of 27 studies).

2.4. Hasan, M., Ferdous, J., & Islam, M. (2016). Flatulence awareness among the masses and its affinity with daily foods along with anti-ulcerant drugs in Bangladesh. Asian Pacific Journal of Tropical Disease, 6(5), 380-384.

It was a qualitative investigation that was founded on in-depth interviews. A series of questionnaires was distributed to three hundred individuals from one hundred and ten families. Each participant was interviewed regarding their dietary behaviors, comprehension of flatulence, potential causes, self-medication, and completion of their medical education. A main course that

included rice, fish, and vegetables was consumed by approximately 99.99% of the respondents. Furthermore, respondents self-medicated at a rate of 90%; however, only 2%–3% of respondents reported maintaining an appropriate quantity of medication. Proton pump inhibitors or other anti-ulcerate medications were administered to the remaining patients, while only about thirty percent utilized antacids.

Methodology

3.1. Target Population:

The survey commences with 16 pertinent inquiries and an introduction. 145 individuals of varying ages are participating in it.

3.2. Research Design:

This survey's objective was to ascertain the public's perceptions of PPI pharmaceuticals and their utilization. The target population was invited to participate in field research, which required them to respond to each inquiry in person. It is an online survey.

3.3. Method of Data Analysis:

All data was analyzed for internal consistency and precision to eradicate any lacking or conflicting information. Any data that was deemed to be inaccurate was discarded. Microsoft's most frequently updated version was employed to conduct the information analysis.

3.4. Ethical Considerations:

The investigation members were granted verbal authorization before the commencement of the information collection. The respondents' anonymity was preserved, and the study subjects were advised that they were free to withdraw from the program at any time.

3.5. Survey Question:

1. Age range?

• 18-22

• 22-26

• 26-30.

• 30 Above

2. Gender?

• Male

• Female

3. Profession

• Job Holder

• Student

• House Holder

• Other:

4. Do you ever know about Gastric Medicine?

Yes

No

5. Why do you suppose to take Gastric medicine?

• Hyperacidity

• Gastroesophageal reflux disease

6. Most uses Antiulcer drug?

• Omeprazole

• Esomeprazole

• Lansoprazole.

• Rabeprazole

• Pantoprazole

• Other:

7. Do you use any alternative along with Gastric Medicine?

• Yes

• No

• Maybe

8. Do you face any adverse effect after taken Gastric drugs?

Nausea

Abdominal pain

Flatulence

Constipation

Diarrhea

9. Do you use Gastric medicine as a OTC (Over The Counter) drug?

• Yes

• No

10. Do you take any doctors instruction to take Gastric drugs?

• Yes

• No

11. Dose Gastric Medicine taken effect on health and life style?

• Yes

• No

12. Do you use Gastric medicine as a OTC (Over The Counter)drug?

• Yes

• No

13. Do you take any doctors instruction to take Gastric drugs?

• Yes

• No

14. Dose Gastric Medicine taken effect on health and life style?

• Yes

• No

Result & Discussion

4.1. Age

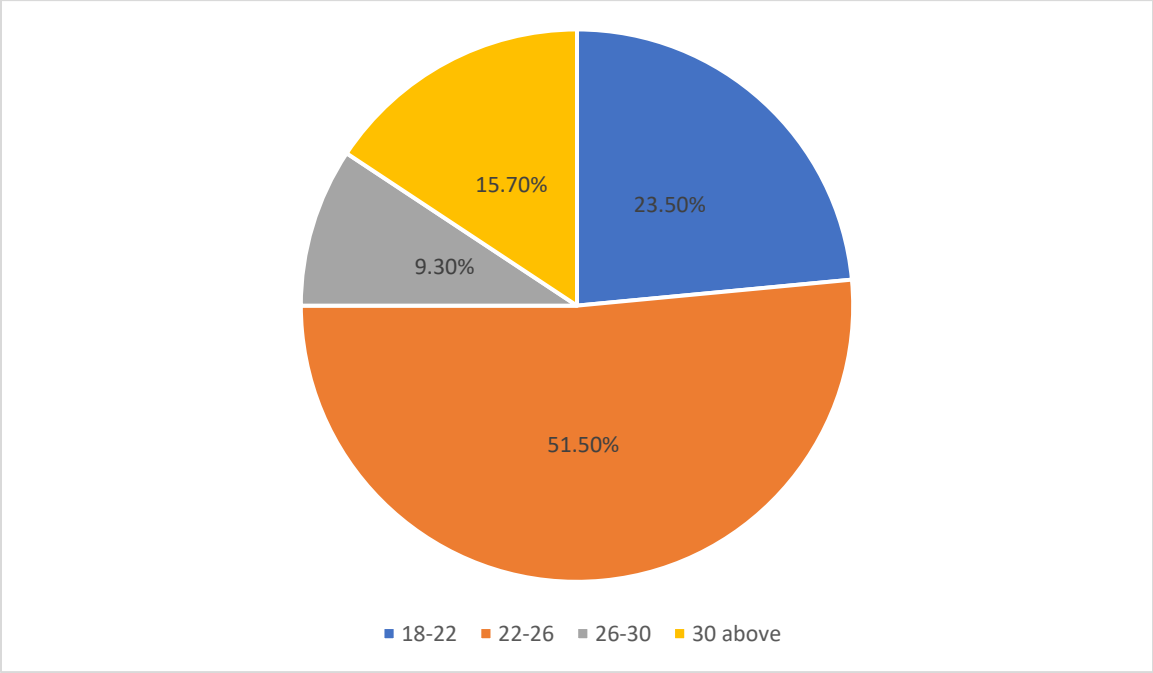

Fig 05: Age

The survey indicates that the youthful generation, aged 22-26, consumes 51.50% of the PPI. Of the total, 23.50% are between 18 and 22. 15.70% of the population is over the age of 30. 9.30% of the population is between the ages of 26 and 30. Therefore, it can be concluded that adolescents consume a greater quantity of PPI medications.

4.2. Gender

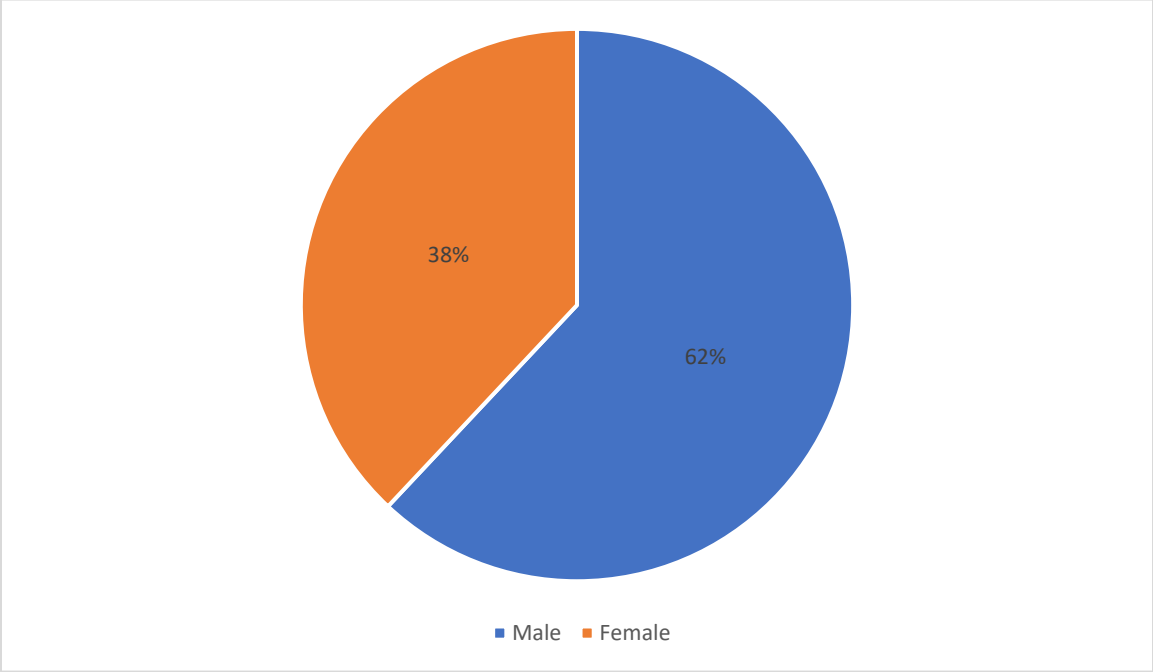

Fig 06: Gender

In this survey, 62% of males are taking PPI drugs more frequently. This is being consumed by 38% of women. Therefore, males are more susceptible to gastrointestinal issues.

4.3. Profession

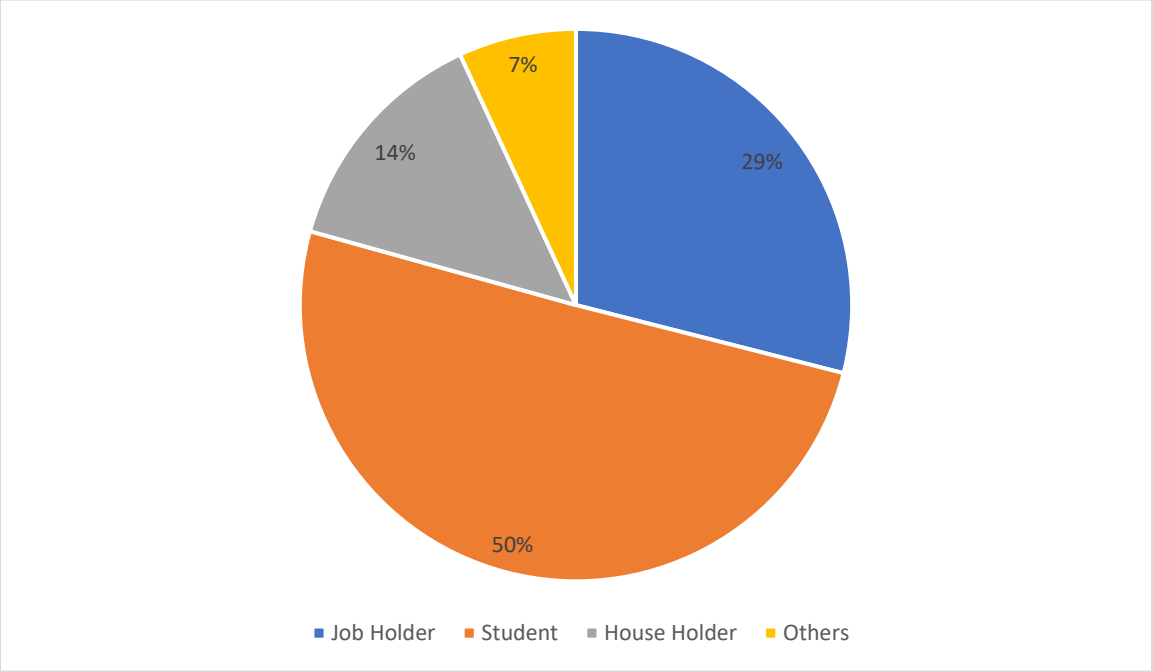

Fig 07: Profession

Gastric disease has affected 50% of students, according to this survey. Conversely, 29% of job holders and 14% of homeowners also experience gastric issues. Only 7% of individuals have others included in their list.

4.4. Knowledge about PPI

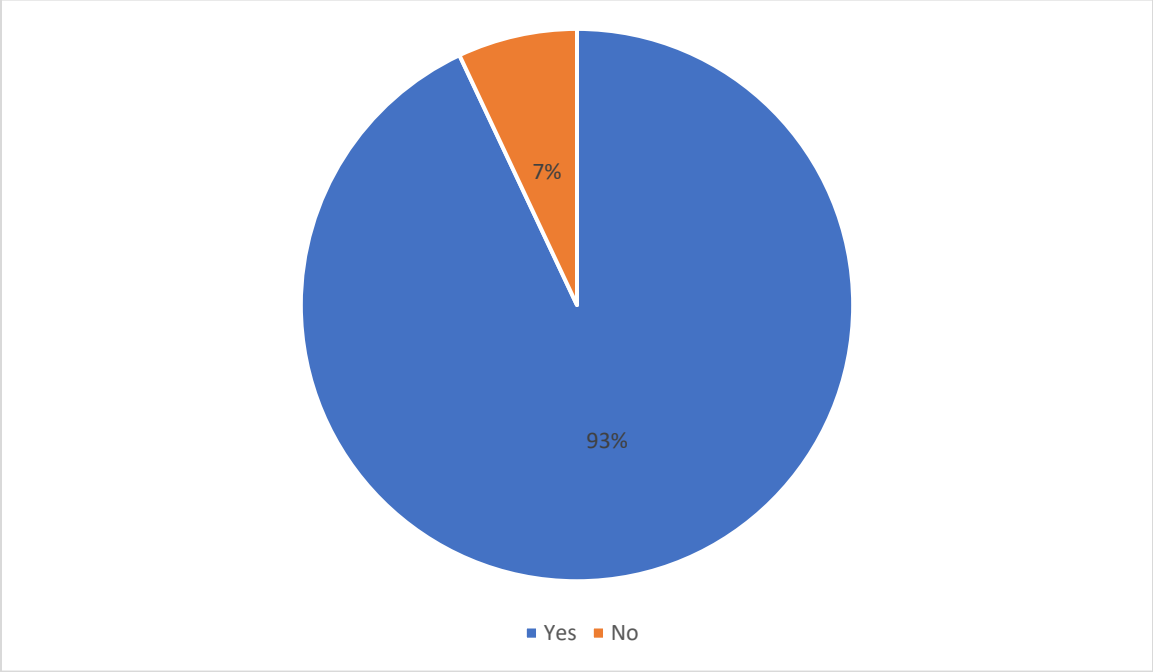

Fig 08: Knowledge about PPI

As indicated by this survey, 93% of respondents understand PPI medications, while 7% of the population is unaware.

4.5. Cause of taking PPI

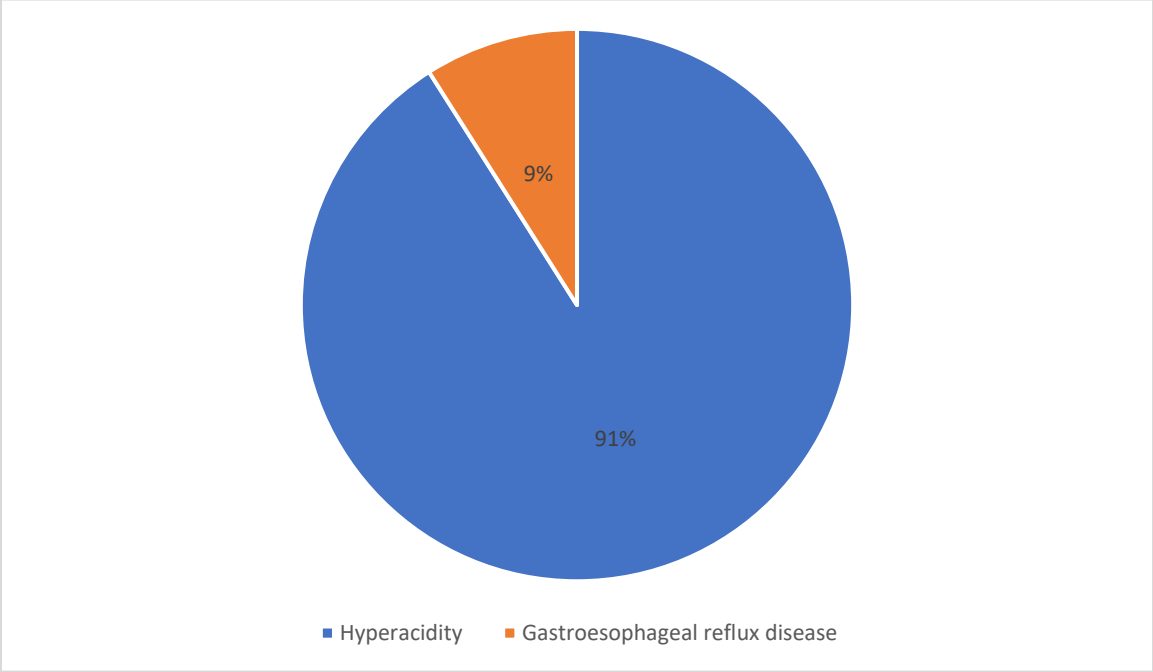

Fig 09: Cause of taking PPI

In this survey, I discovered that 91% of respondents take PPIs for hyperacidity, while 9% take them for gastroesophageal reflux disease (GERD).

4.6. Most used drug

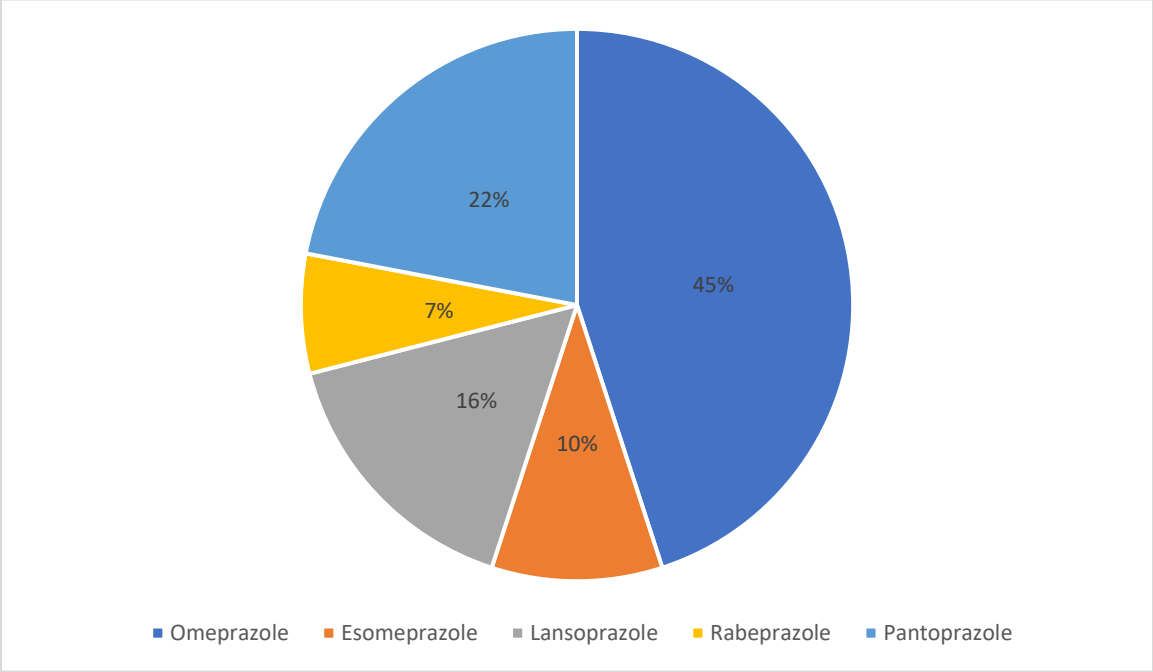

Fig 10: Mostly used drug

As indicated by this survey, omeprazole is the most frequently prescribed medication, with a 45% prevalence. Esomeprazole is employed as a 10% PPI. Rabeprazole is administered to 7% of the population. Pantoprazole is administered to 22% of individuals. Omeprazole is the most frequently prescribed proton pump inhibitor.

4.7. Use of Alternative Medication

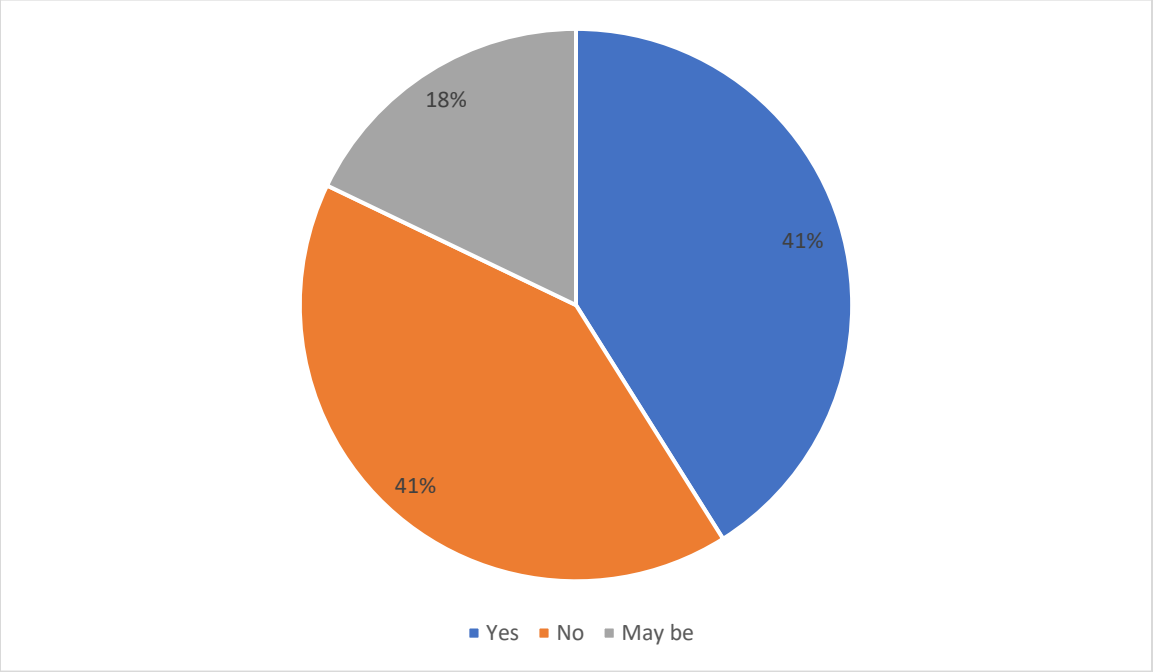

Fig 11: Use of Alternative Medication

In this survey, 41% of respondents are currently utilizing alternative medications, while 41% still need to implement alternative treatments. A mere 18% of individuals need clarification about undertaking any alternative.

4.8. Adverse effect

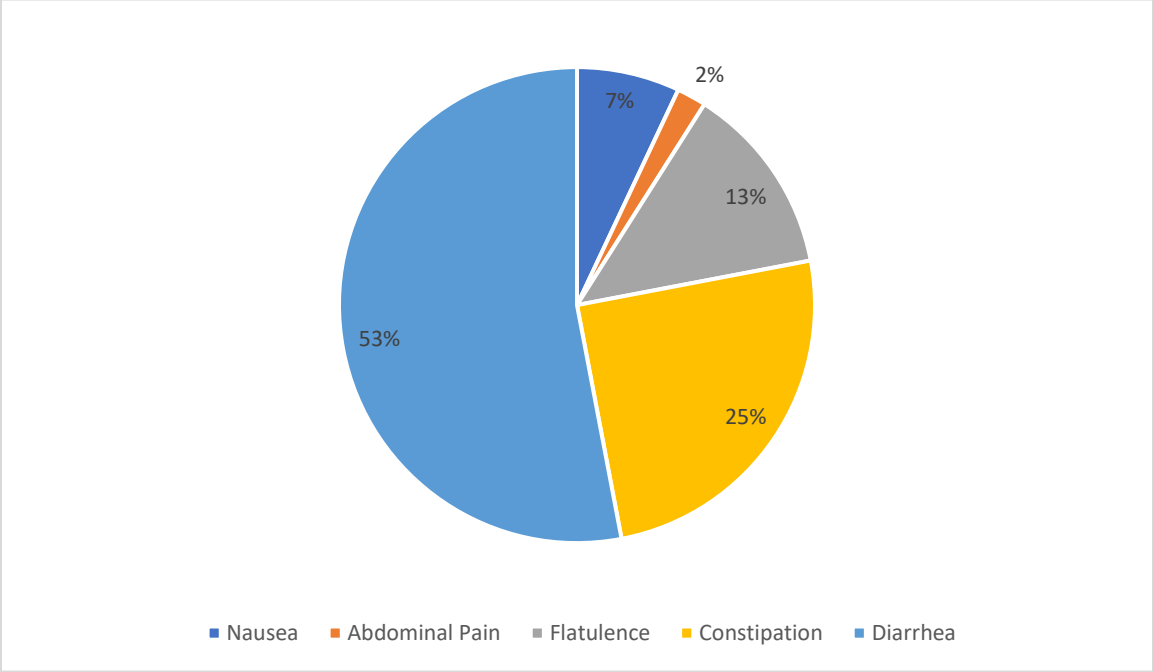

Fig 12: Adverse effect

Diarrhea is an adverse effect of PPI drugs that affects 53% of respondents in this survey. Constipation is experienced by 25% of the population. Abdominal discomfort is experienced by 2% of the population. Nausea is experienced by 7% of individuals.

4.8. Use as OTC drug

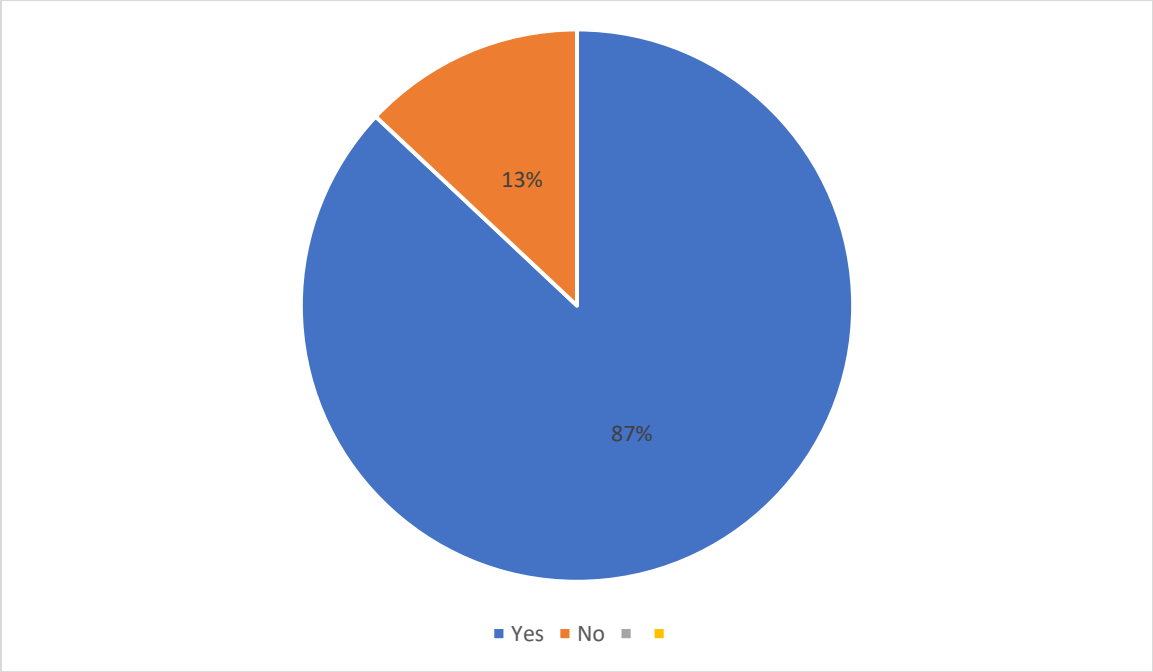

Fig 13: Use as OTC drug

In this survey, 87% of respondents reported using PPIs as over-the-counter medications without a prescription. Only 13% of individuals utilize this prescribed medication.

4.9. Follow up doctor

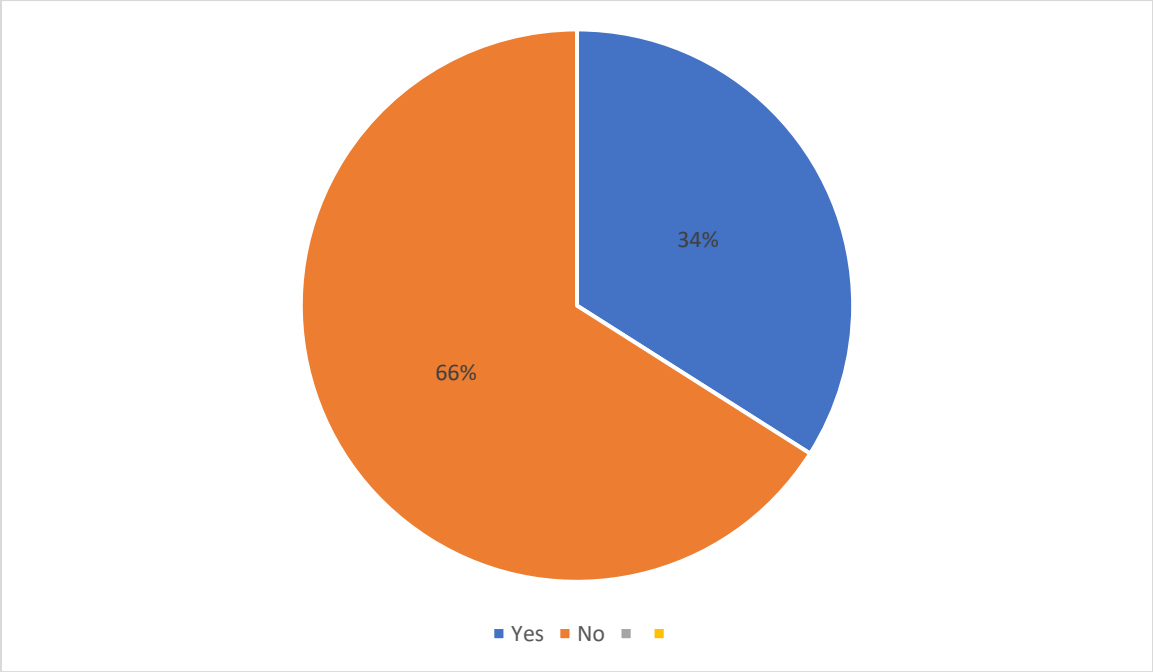

Fig 14: Follow up doctor

In this survey, 66% of respondents must follow up with their physician regarding using over-the-counter medications. People adhere to their physicians' instructions in 34% of cases.

4.10. Effect on health & life style

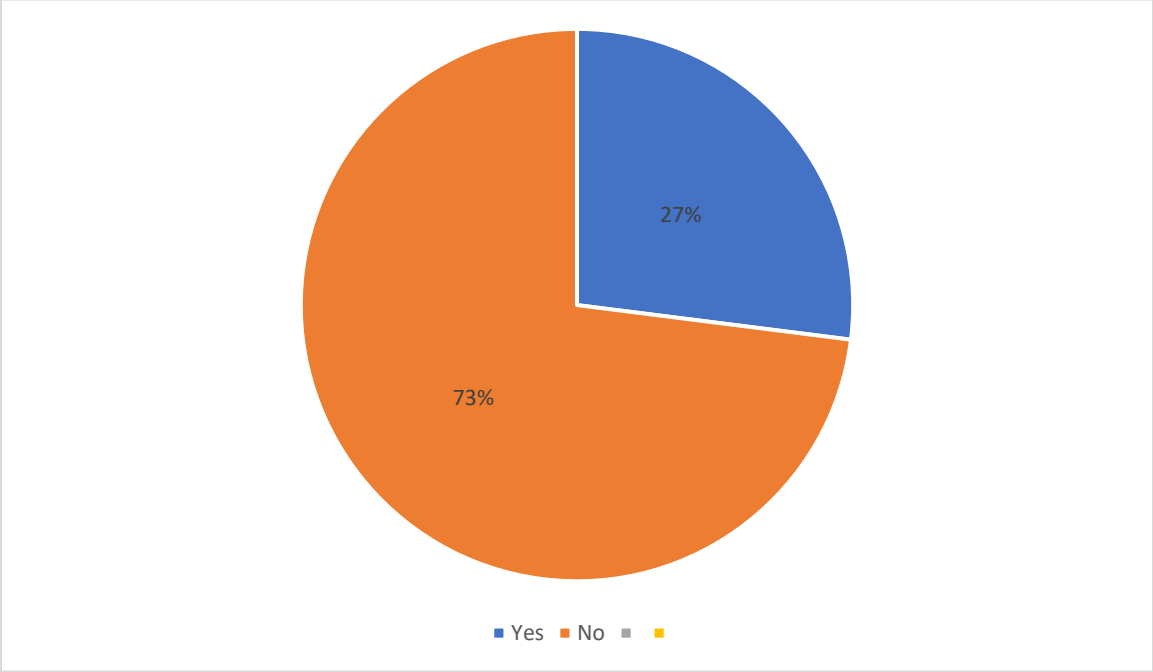

Fig 15: Effect on health & life style

This survey indicates that 27% of respondents believe that the irrational use of PPI medications can impact their health and lifestyle. According to 73% of respondents, there is no issue.

4.11. Safe for use

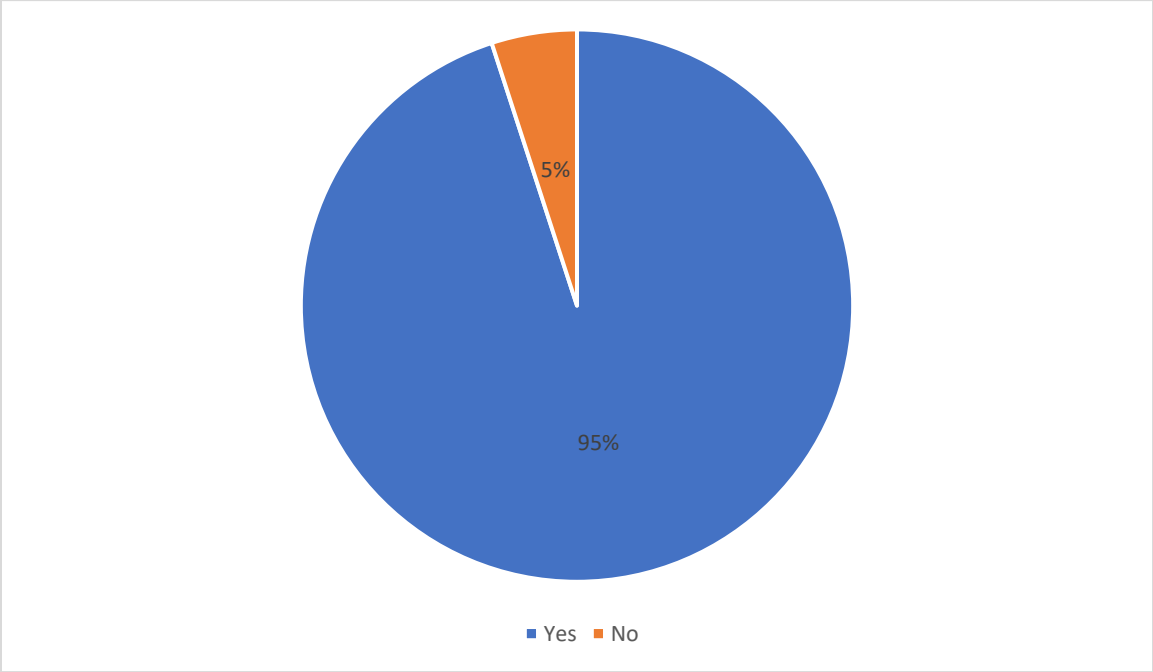

Fig 16: Safe for use

In this survey, 95% of respondents believe that PPIs are secure. Five percent of individuals believe that it is not suitable for use.

4.12. Satisfied with of PPI Medicine price

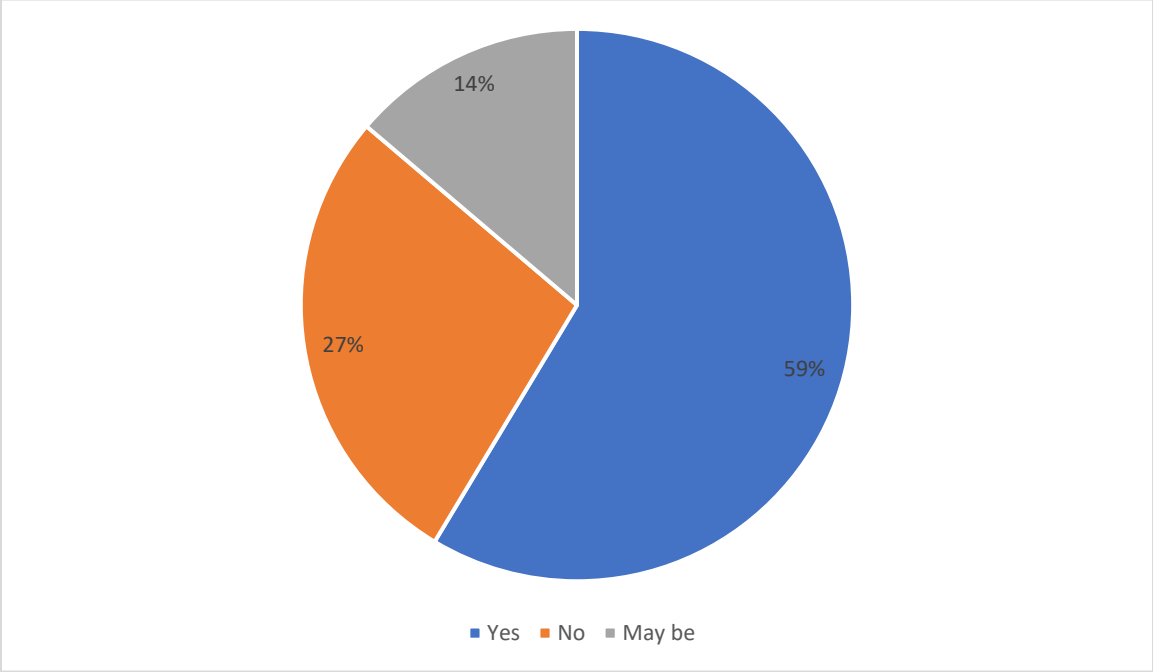

Fig 17: Satisfied with of PPI Medicine price

In this survey, 59% of respondents believe that the cost of PPI medication is cost-effective. While 27% of individuals think that the price is excessive, only 14% are not assumed to be aware of the price.

4.13. Intake Medication

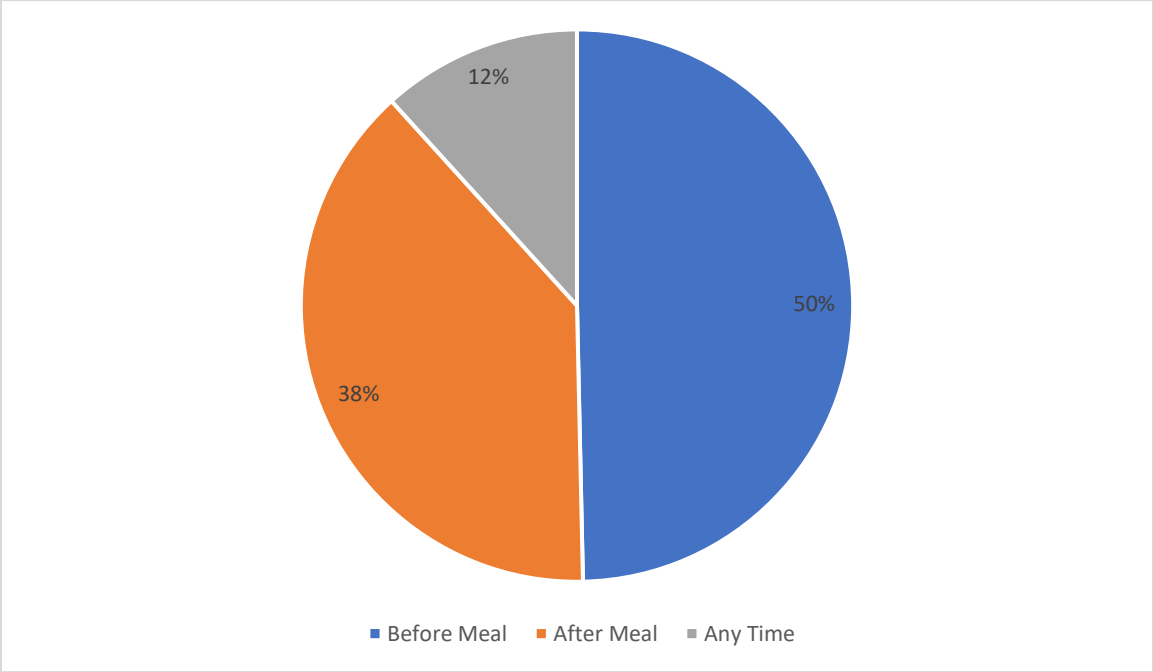

Fig 18: Intake Medication

According to the survey, 50% of patients consume their medication before a meal, 38% take their PPI medication after their meal, and only 12% consume it at any given moment.

Conclusion

5. Conclusion

Acid-related disorders, including dyspepsia, peptic ulcer disease, and GERD, are frequently treated with proton pump inhibitors (PPIs). Nevertheless, there is increasing apprehension regarding the irrational utilization of PPIs, particularly in low- and middle-income countries such as Bangladesh. The unreasonable use of PPIs in Bangladesh is influenced by a variety of factors, including a lack of awareness among the general population and healthcare providers regarding the appropriate use of PPIs, the prescription of PPIs without a proper diagnosis and evaluation of the underlying condition, and the availability of PPIs over-the-counter without a prescription. The irrational use of PPIs on patients' medical conditions has the potential to result in the long-term adverse effects of osteoporosis and renal damage, as well as an increased risk of infections and drug interactions. The general population and healthcare providers must increase their awareness of the appropriate use of PPIs to address the issue of irrational use in Bangladesh. Additionally, enforcing regulations regarding the sale and availability of PPIs is imperative.

Reference

6. Reference

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