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"A Study To Assess The Prescribing Pattern And Risk Associated With Use Of Proton Pump Inhibitors In A Tertiary Care Teaching Hospital."

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ABSTRACT-

BACKGROUND-"TO ASSESS PRESCRIBING PATTERN AND RISK ASSOCIATED WITH USE OF PPIs."

OBJECTIVE-

1.To analyse prescribing pattern of PPIs.
2. To find and report ADR.
3. To compare different drug amongst PPIs class.
4. To find potential interactions. 5. To assess risk associated with use of PPIs.

MATERIAL AND METHODS-It is a Prospective observational study conducted at a single centre done by obtaining the data of the patients.Total 214 patients data was collected and observed from Parul sevashram Hospital. In the data collection analysis form, the data was reported and analysed using graphical, chart, figures and tabulations and summarised visually. Unpaired t-test, chi-square, and an analysis of variance (ANOVA) were used in MS-Excel's statistical analysis, and the p-value was calculated.

RESULTS-During this six month of study period, total 214 patients from various department like general medicine, surgery, orthopaedic, respiratory etc. As per exclusion and inclusion criteria age below 18 is excluded.according to data there were 99 male and 115 female participants out of 214 total. During study most of the cases are collected from medicine ward at about (52 %), surgery ward (27.7%), Gynec ward (8.9 %), pulmonary ward (2.8 %), respiratory ward (1.41%), orthopaedic ward (5.2%), from others department (1.89 %) of data were collected.

CONCLUSION-This study revealed that mostly prescribed drugs amongst PPIs class is pantoprazole. And analysis suggest that long term/ high dose PPIs users are characterised by an increaded risk of fragibity fracturs, renal impairment, thrmbocytopenia and hypersecreation of acids as a withdrawn effect. 91% of PPIs prescribed in brand name and 85% pantoprazole in combination with domperidone.The study also concluded that the use of databases such as MicroMedex and Drugs.com was useful as secondary source for reference

KEY WODS- WHO (World Health organization), PPIs(Proton Pump Inhibitors), AEBE (Auditory Brainstem evoked response), GI (Gastrointestinal), AGE(Acute Gastroenteritis).

I. INTRODUCTON

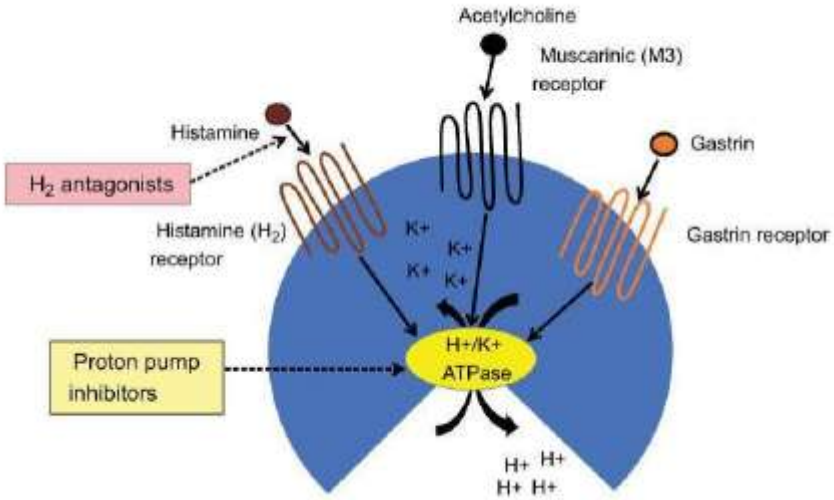
Proton pump inhibitors [PPIs] are medications that work by reducing the amount of stomach acid made by glands in the lining of stomach. PPIs are a class of medications that cause a profound and prolonged reduction of stomach acid production. They do so by irreversibly inhibiting the stomach's H+/K+ ATPase proton pump. They are the most potent inhibitors of acid secretion available. PPI have largely replaced the H2- receptor antagonists, a group of medications with similar effects but different mode of action. PPIs are among the most widely sold medications in the world. (2018) a nationwide drug utilization study on proton pump was conducted. 1,372,790 prescriptions filled over the entire study period, of which 95% were of higher – dose PPIs. Annual incidence remained stable across time (3.3-4.1 per 100 persons per year), while the annual prevalence increased from 8.5 per 100 persons to 15.5 per 100 persons. The proportion of PPIs users concurrently

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 761-778 www.ijprajournal.com ISSN: 2456-4494

using nonsteroidal anti- inflammatory drugs decreased over the study period, while the proportion concurrently using acetylsalicylic acid, oral anticoagulants, or platelet inhibitors increased. A survey of 1000 clinicians from India showed a high prevalence of GERD (39.2%), peptic ulcer disease (PUD 37.1%) and non-ulcer dyspepsia (25.2%) with nearly 50% of patients requiring prompt endoscopy [1] . According to the FDA Adverse Event Reporting System, adverse events for PPIs are responses to all drugs reported since 1989, including ADR skin reactions primarily represented by rashes, urticaria, erythema and pruritus, and anaphylactic shock. It is equivalent to 0.37% of. In this study, pantoprazole is the most common allergic molecule (2018) PPIs are generally considered to be effective and well tolerated, with only rare and mild side effects from short-term use of PPIs, but concerns and signs of possible longterm complications of PPI therapy. Is appearing. Possible side effects range from interaction with other drugs, increased risk of infection, decreased intestinal absorption of vitamins and minerals, to kidney damage and dementia investigated primarily by case-control and cohort studies[3]

PPIs AGENT: Following proton pump inhibitors are available for clinical use: • Omeprazole – (over-the-counter drug (OTC) and Rx-only in the us) • Esomeprazole – (OTC and Rx-only in the US and Australia) • Pantoprazole • Lansoprazole – (OTC and Rx-only in the US) • Rabeprazole • Dexlansoprazole MEDICAL USE: • To treat ulcers in the stomach and the part of the gut called duodenum. • To reduce acid reflux which may cause heartburn or inflammation of the gullet (oesophagitis). These conditions are sometimes called Gastro oesophageal reflux disease (GERD). • As one part of treatment to get rid of Helicobacter pylori – a bacterium found in the stomach, which can cause ulcers. • To help prevent and treat ulcers associated with Anti- inflammatory medicines called non- steroidal anti-inflammatory drugs (NSAIDs). • In a rare condition called Zollinger-Ellison syndrome. • Barrett's oesophagus • Stress gastritis and ulcer prevention in critical care

MECHANISM OF ACTION OF PPIS:



Proton siphon inhibitors act by irreversibly obstructing the hydrogen/potassium adenosine triphosphatase chemical framework (the H+/k+ ATPase, or, all the more generally, the gastric proton siphon) of the gastric parietal cells. The proton siphon is the terminal stage in gastric corrosive discharge, being straightforwardly answerable for emitting H+ particles into the gastric lumen, making it an optimal objective for repressing corrosive discharge. Focusing on the terminal advance in corrosive creation, as well as the irreversible idea of the hindrance, brings about a class of meds that are fundamentally more compelling than H2 antagonists and decrease gastric corrosive emission by up to close to 100%. Diminishing the corrosive in the stomach can help

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the mending of duodenal ulcers and decrease the aggravation from acid reflux and indigestion. Notwithstanding, stomach acids are expected to process proteins, vitamin B12, calcium, and different supplements, and too little stomach corrosive causes the condition hypochlorhydria. The PPIs are given in a dormant structure, which is naturally charged (lipophilic) and promptly crosses cell films into intracellular compartments (like the parietal cell canaliculus) with acidic conditions. In a corrosive climate, the idle medication is protonated and adjusts into its dynamic structure. As depicted over, the dynamic structure will covalently and irreversibly tie to the gastric proton siphon, deactivating it. In H. pylori annihilation, PPIs help by expanding the stomach pH, making the bacterium shift out of its coccoid structure which is impervious to the two acids and anti-toxins. PPIs likewise show a few more vulnerable unexpected impacts in destruction. HOW DO PROTON PUMP INHIBITOR WORK? Your stomach normally produce acid to help digestion of food and to kill germs(bacteria). This acid is corrosive so your body produces a natural mucous barrier which protects the lining of the stomach from being worn away(eroded). In some people this barrier may have broken down allowing the acid to damage the stomach, causing an ulcer. In others there may be a problem with muscular band at the top of the stomach (the sphincter) that keeps the stomach tightly closed. This may allow the acid to escape and irritate the gullet (oesophagus). This is called ‘acid reflux’ which can cause heartburn and inflammation of the gullet(oesophagus). PPIs stop cells in the lining of the stomach producing too much acid. This can help to prevent ulcers from forming or assist the healing process. By decreasing the amount of acid, they can also help to reduce acid reflux-related symptoms such as heartburn. They are called ‘Proton pump inhibitors’ because they work by blocking(inhibiting) a chemical system called the hydrogen-potassium adenosine triphosphatase enzyme system (other wise known as the ‘proton pump’). This chemical system is found in the cells in the stomach lining that makes stomach acid [14].

THE GASTRIC H, K- ATPase:

The gastric ATPase is an individual from the P2 type ATPase. The initial step of the response is phosphorylation of the synergist subunit by MgATP, with commodity of protons, this progression is trailed by luminal potassium-subordinate dephosphorylation and potassium reabsorption. The outcome is electroneutral trade of cytoplasmic protons for exoplasmic potassium. The E1 type of the chemicals permits admittance to the particle restricting space from the cytoplasmic surface. Restricting of two ATP moieties, alongside two magnesium particles, happens in this conformity. One balances out the alpha beta direction of the initial two phosphates of the nucleotide, and the second, in nearness to the acceptor as somewhat build-up, permits move of the gamma phosphate to the synergist subunit of the protein and starts the difference in adaptation from the E1 structure to the E1P conformer with the particle locales restricting the hydronium particles. This cycle is trailed by transformation to the E2P structure, in which the protons are delivered outward and k+ ties from the luminal surface. ATP plays double part in the vehicle pattern of the gastric H, K-ATPase. ATP phosphorylates the compound and advances the change. The potassium impediment site shows mutilated octahedral math, with K+ bound overwhelmingly on the M4 helix, with ligands contributed by spine carbonyl oxygens of V338, A339, and V341, and by side chain oxygens of E820 and E795. PPIs can be partitioned into two gatherings in view of their essential design. Albeit all individuals have a subbed pyridine way, one gathering has connected to different benzimidazoles, though different has connected to a subbed imidazopyridine. All promoted PPIs (omeprazole, lansoprazole, pantoprazole) are in benzimidazole group. Proton pump inhibitors are prodrugs and their actual inhibitory form is somewhat controversial.in acidic solution, the sulfenic acid is isolated before reaction with one or more cysteines accessible from the laminar surface of the enzyme, a tetracyclic sulphonamide. The effectiveness of these drugs derives from two factors: their target, the H+/K+ ATPase which is responsible for the last step in acid secretion; therefore, their action on acid secretion is independent of the stimulants to acid secretion, of histamine, acetylcholine. The proton pump, H+/K+ ATPase is a ALPHA, BETA- heterodimeric enzyme. ALPHA: The catalytic alpha subunit has ten transmembrane segments with a cluster of intramembrane carboxylic amino acids located in the middle of the transmembrane segments TM4, TM5, TM6 and TM8. BETA: The beta subunit has one transmembrane segment with N terminus in cytoplasmic region. The extracellular domain of the beta subunit contains six or seven N – linked

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glycosylation sites which is important for the enzyme assembly, maturation and sorting.

METABOLISM OF PROTON PUMP INHIBITORS:

The PPIs are dormant in their local structure and are quickly utilized by the liver. Since PPI is a corrosive actuated prodrug, it is critical to keep the PPI plasma level high until the gastric corrosive secretes. Keeping up with high plasma level of the medication is essentially impacted by the personality of the digestion. Digestion of PPIs is subject to the cytochrome P450 framework. CYP2C19 and CYP3A4 polymorphism are significant parts for this. Omeprazole is changed over to hydroxyl and 5-O-demethyl metabolites by CYP2C19 and to the sulfone by CYP3A4. As per the metabolic pace of omeprazole, people are delegated homozygous broad metabolizer (homo EM), heterozygous broad metabolizer (hetero EM), and poor metabolizer (PM). PMs show a 3 to 10 folds higher region under the Plasmic fixation bend (AUC) than homo EM, while hetero Ems display a 2 to 3 folds higher AUC. The CYP2C19 genotype extraordinarily impacted this distinction. The most widely portrayed variation alleles for PMs are CYP2C19*2 and CYP2C19*3, which encode for non-utilitarian proteins. Omeprazole is a racemic combination of 2 enantiomers, R-omeprazole and s-omeprazole. Every enantiomer showed different liking to the CYP catalyst. R-omeprazole was more delicate to CYP2C19 while s-omeprazole was less touchy. Subsequently, s-omeprazole gave better plasma level of medication. Like omeprazole, lansoprazole likewise was widely used by CYP2C19 and CYP3A4. Significant metabolites f lansoprazole are 5-hydroxy lansoprazole and sulfone. Comparable examples of digestion were seen in pantoprazole and rabeprazole

EFFICACY OF INHIBITION OF ACID SECRETION:

These medications restrain the gastric H, K-ATPase by covalent restricting, so the span of their belongings is surprisingly lengthy from their levels in the blood. Nonetheless, PPIs can't restrain all gastric corrosive siphons with oral dosing on the grounds that not all siphons are dynamic during the hour and a half-existence of the PPI in the blood. Since PPIs have a short half-life, just 70% of the siphon compounds are hindered. It takes around 2 to 3 days to arrive at consistent state restraint of corrosive discharge. The siphon protein has a half-existence of around 54 hours in the rodent (and most likely in people). Along these lines around 20% of siphons are recently orchestrated north of a 24 hours' time frame, and there might be more prominent siphon combination around evening time than during the day. What's more, sleep time organization of PPIs won't add to hindrance of night -time corrosive forward leap, on the grounds that the medication will have vanished continuously time corrosive emission is clear. Accepting that around 70% of siphons are initiated by breakfast and that the PPI is given 30 to an hour in advance, it tends to be determined that consistent state hindrance on once-a-day dosing is around 66% of maximal corrosive result. Expanding the portion has basically no impact once ideal measurement has been reached. Expanding the portion recurrence has some impact; a morning portion and an evening portion before suppers results in around 80% hindrance of maximal corrosive result. To work on corrosive restraint, the plasma half-existence of the PPI should be expanded. One method is to supplant the benzimidazole with imidazopyridine, easing back digestion and dragging out the half-existence of the medication, as found with tenatoprazole. This PPI enjoys a benefit in smothering evening corrosive discharge, yet its sluggish actuation dulls its benefit for daytime corrosive concealment. An elective methodology was to combine a gradually ingested subordinate of omeprazole, which then, at that point, expanded the plasma half-life around 3-overlay and created a middle PH of around 5 in starting examinations.

STABILITY OF INHIBITION OF ACID SECRETION:

Inversion of restraint of ATPase can happen either by once more amalgamation or decrease of the di sulphide connection between the PPI and the protein. A reasoning for assessment of inversion of covalent restricting to the H, K-ATPase was given by estimation of the halfexistence of siphon protein biosynthesis in rodents treated for 7 days with omeprazole, which was 54 hours, and the half-season of reclamation of ATPase movement, 15 hours. Such information proposes a faster recuperation of ATPase movement and corrosive discharge than would happen if by some stroke of good luck anew biosynthesis was answerable for reclamation of ATPase action. In different trials, the half season of reclamation of corrosive emission in omeprazole treated rodents was 20 hours. An examination of the pace of rebuilding of corrosive discharge in

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people proposed that the half time was 24 hours following omeprazole restraint, though after pantoprazole it was 46 hours. Just pantoprazole seems to have a pace of recuperation viable with reclamation of corrosive emission due altogether to siphon turnover. COMPARING THE EFFICACY OF PPIs: Suppressing gastric acid secretion enhances healing of acid related diseases. Good healing of reflux esophagitis is achieved when the intragastric PH is greater than 4 for 16 hours per day, and peptic ulcer is optimally healed when the intragastric PH is greater than 3 for 16 hours per day. The best in vivo parameters to use in comparing PPIs with each other are the intragastric PH and total acid output. Generally, all PPIs provide good gastric acid suppression, but because they are used at different doses (omeprazole 20mg, lansoprazole 30mg, pantoprazole 40mg, rabeprazole 20mg, esomeprazole 40mg, and tenatoprazole 40mg). One study compared rabeprazole (20mg), lansoprazole (30mg), pantoprazole (40mg), and omeprazole (20-mg capsule vs 20-mg multiple unit pellet system tablet). Rabeprazole had the highest first day median 24 hours PH. Another study compared gastric acid inhibition following the administration (30 minutes before breakfast) of rabeprazole (20mg), esomeprazole (40mg), omeprazole (20mg), lansoprazole (30mg), and pantoprazole (40mg) for consecutive days. At the end of the day period, intragastric PH greater than 4 was maintained longer with esomeprazole, and more patients had a PH greater than 4 for more than 12 hours. Esomeprazole (40mg) gives good acid suppression (PH > 4 for 16.8h/d). When lansoprazole (30mg) was compared with omeprazole (20mg), both taken orally on a daily basis, lansoprazole maintained the PH >3 for a significantly greater time and produced a higher median 24 hours PH [46,47]. Pantoprazole (40mg) has also been compared with omeprazole (20mg); the result showed a significantly higher day time and 24 hours PH with pantoprazole. When the efficacy of each PPI is compared based on same dose, omeprazole, lansoprazole, and pantoprazole seem to produce similar acid suppression Panatoprazole (40mg) provided better night-time acid suppression than other PPIs. A significant difference was observed between tenatoprazole and esomeprazole during the nocturnal period; the mean PH was 4.64 with tenatoprazole vs 3.61 with omeprazole, and the mean percentage of time with PH greater than 4 was significantly higher for tenatoprazole. This difference is due to prolonged half-life of tenatoprazole in the blood. More GERD patients (93.7% - 94.1%) were healed at week 8 with the use of 40 mg of esomeprazole than with 20 mg of omeprazole (84.2% - 86.9%). When 40mg of esomeprazole was compared with 40mg of pantoprazole, both gave good healing rates. PPIs have been used successfully in triple therapy regimens with clarithromycin and amoxicillin for the eradication of H. pylori. There was no significant difference between different PPI – based regimens.

PHARMACOKINETICS ANND PHARMACODYNAMICS OF PPI:

Pharmacodynamic: Obviously, the amount of PPI bound to the protein is straightforwardly connected to the hindrance of gastric corrosive emission. In any case, it is extremely challenging to quantify the amount of PPI restricting in vivo, so we really want one more boundary subbing the amount of PPI restricting. The plasma level of the medication was not direct to the inhibitory movement. It was, nonetheless, saw that the gastric antisecretory impact was connected with the complete portion and AUC. Notwithstanding, this connection between the inhibitory movement and the AUC was not displayed at higher measurements of the medication. However, the connection among AUC and the restraint was not direct at higher measurements of the medication because of short half existence of the medication and the restricted openness of the compound to the medication, essentially AUC showed the adequacy of the medication with great dependability. All PPIs have around 1 hour of the disposal half-life, yet the chance to greatest plasma focus was broadly digressed from 1 to 5 hours by drug definition and food impact. Pharmacokinetic: After the clinical viability of omeprazole 20mg was very much contemplated, other PPIs were contrasted with omeprazole. For instance, lansoprazole 30mg was contrasted with omeprazole 20mg. one review showed somewhat worked on corrosive concealment by lansoprazole 30mg while another review showed no critical contrasts. Lansoprazole 30mg was not better than omeprazole 40mg. S - omeprazole enjoys a benefit on digestion as its plasma fixation is higher than that of omeprazole. AUC of s-omeprazole was a lot higher than that of omeprazole. consequently someprazole, named as esomeprazole, gave improved intragastric PH profile true to form. The metabolic benefit of esomeprazole expands the plasma fixation, bringing about higher AUC, but its short half-life (60-an hour and a half) is as yet the main point of

International Journal of Pharmaceutical Research and Applications
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interest in drug viability. Esomeprazole 40mg bd has additionally been demonstrated to be better than pantoprazole 40mg bd and lansoprazole 30mg bd in keeping up with intragastric PH at 4.0 or lower. Two times every day dosing of esomeprazole gives essentially more noteworthy corrosive concealment than once day by day dosing and may, in this way, be a sensible thought for patients requiring more prominent corrosive concealment for GERD. Rabeprazole extended release (ER) 50mg formulation was developed to provide prolonged gastric acid suppression and potentially improved clinical outcomes in GERD patients. Modified release or ER of PPIs apparently has longer effective plasma concentration. This provides a better chance to block the gastric H+, K+- ATPase activity, which allows better intragastric PH control. There have been some concerns about the safety of PPIs. The food and drug administration (FDA) has warned against the use of certain PPIs by patients on clopidogrel. However, a randomized controlled trial that compared clopidogrel alone with the combination of clopidogrel and omeprazole found no increase in adverse cardiovascular outcomes and a reduction in the rate of adverse gastrointestinal outcomes attributable to omeprazole [15] .

ADVERSE EFFECTS-

In general, proton pump inhibitors are well tolerated, and the incidence of short- term adverse effects is relatively low. The range and occurrence of adverse effects are similar for all of the PPIs, though they have been reported more frequently with omeprazole. This may be due to its longer availability and, hence, clinical experience. Common adverse effects include Headache, nausea, diarrhoea, abdominal pain, fatigue and Dizziness [5] . Infrequent adverse effects include rash, itching, flatulence, constipation, anxiety, and depression. Also, frequently, PPI use may be associated with occurrence of myopathies, including the serious reaction rhabdomyolysis[6] . Long term use of PPIs requires assessment of the balance of the benefits and risks of the therapy [7][8][9] . Although various adverse events are associated with long-term use of PPIs in some major reports, the review rated the overall quality of evidence in these studies as "low" or "very low."[8]. They explain inadequate evidence of the contingency established between PPI therapy and many of the proposed associations due to poor study design and effect size estimates. They recommend that PPIs be used at the lowest effective doses in individuals with proven indications, but in individuals who do not respond to initial empirical treatment, dose increases and continuous chronic treatment are recommended. [9] .

II. MATERIALS AND METHODS

STUDY DESIGN

Prospective observational study

ETHICAL CONSIDERATION

The study was submitted to Parul University Institutional Ethics Committee for Human Research for approval. The study was carried out among the patients with ongoing treatment of PPI in IPD. The main purpose of the study was well explained to the patients. An informed consent was maintained confidentially. After peer interviewing and reviewing, the study was approved by the ethics committee

STUDY DURATION

6 months [October 2021– March 2022]

STUDY SITE

Parul Sevashram Hospital, Parul University, Vadodara, Gujarat, India

NO. OF SAMPLE COLLECTED

214 patients

STUDY CRITERIA

1. INCLUSION CRITERIA

- Patients with age group of ≥ 18 years.
- Patients of either gender.
- Patients with ongoing treatment of PPIs.

2. EXCLUSION CRITERIA

- Patients on Chemotherapy.
- Pregnant and lactating woman.
- Patients who are not willing to participate in the study
- Outdoor patient is excluded

DESIGNING OF PATIENT DATA FORM

Data of the patients receiving PPI class of drug will be collected and recorded in the data collection form. The data collected will include: Demographic details of the patients Name, Age, Sex, Department, Weight, Date of admission, date of discharge, reason for admission, medical history,

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 761-778 www.ijprajournal.com ISSN: 2456-4494

medication history, diagnosis, prescription, other information, etc.

DATA ANALYSIS

In the data collection analysis form data will be reported and analysed using graphical, chart, figures and tabulations were used to summarize the data visually.

STATISTICAL ANALYSIS

Patient's demographic data, treatment chart data represented graphically in MS – excel and represented in percentage and were noted down in a specially designed data collection form

III. RESULTS AND DISCUSSION

TABLE:1. AGE WISE DISTRIBUTION

AGE WISE DISTRIBUTION	NUMBER OF PATIENT	PERCENTAGE (%)
18-25	22	10
26-35	47	22
36-45	50	23
46-55	48	23
56-65	32	15
ABOVE 65…	15	7

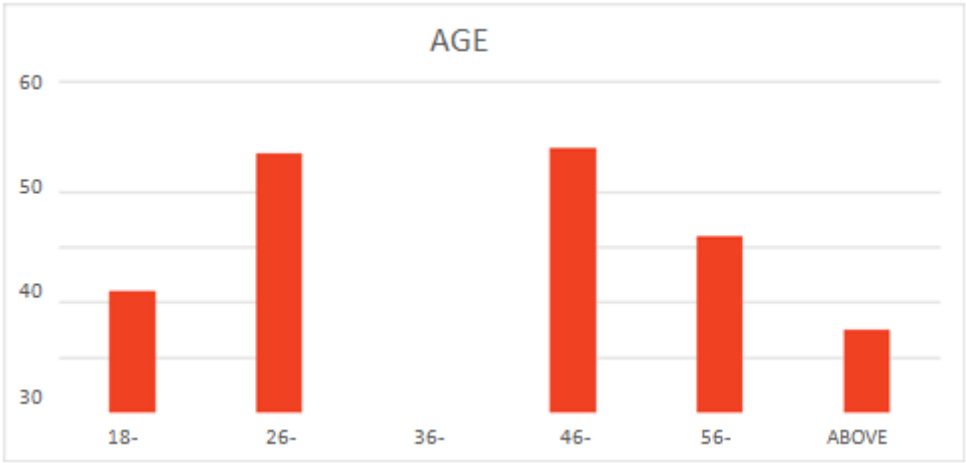


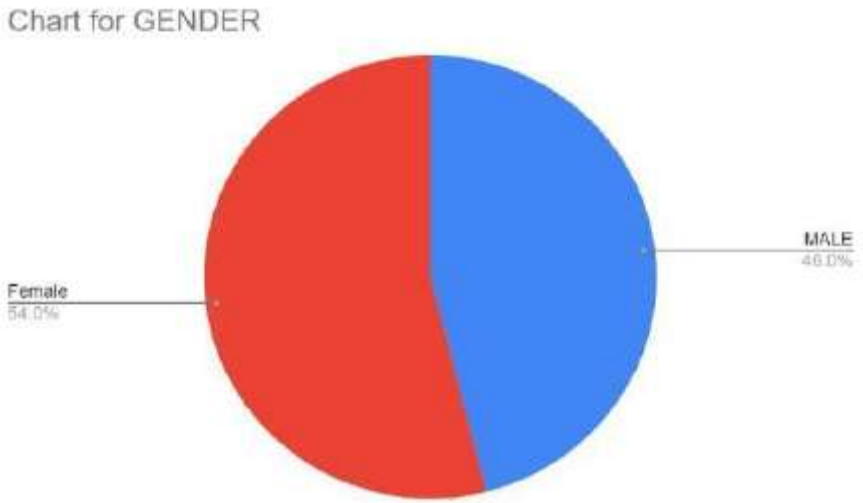
FIGURE: 1. HISTOGRAM CHART OF AGE RATIO.

As shown in table 1. During the study out of 214 Patient's, 10(%) of patient's were between the age of 18-25 years, 22(%) of patient's were between the age of 26-35 years, 23(%)of patient's were between the age of 36-45 years, 23(%) of patient's were between the age of 46-55 year, 15(%) of patient's were between the age of 56-65 years AND, 7(%) of patients were from age group above 65 years.

TABLE 2. GENDER WISE DISTRIBUTION

GENDER	SAMPLE COLLECTED	PERCENTAGE (%)
MALE	99	46
FEMALE	115	54
TOTAL	214	100

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 761-778 www.ijprajournal.com ISSN: 2456-4494



FUGURE 2. GENDER WISE DISTRIBUTION

The above table suggest the participant distribution as per their gender on, evaluation it was observed that most of the patients were female about 56% and male of about 46%.

TABLE:3. DEPARTMENT WISE DISTRIBUTION

DEPARTMENT	SAMPLE COLLECTED	PERCENTAGE (%)
MEDICINE	111	52.11
SURGERY	59	27.7
GYNEC	19	8.9
PULMONARY	6	2.8
RESPIRATORY	4	1.41
ORTHO	11	5.2
EMERGENCY	1	0.47
SKIN WARD	1	0.47
PSYCHIATRIC	1	0.47
COVID SPECIAL	1	0.47
TOTAL	214	100

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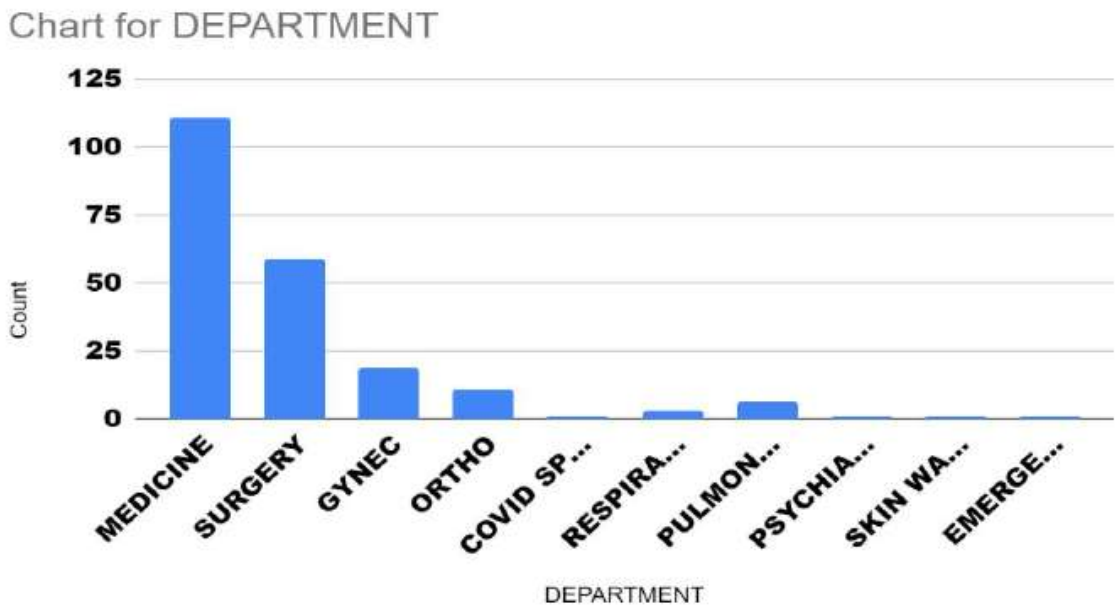

FIGURE: 3. DEPARTMET WISE DISTRIBUTION

During our study most of the cases are collected from medicine ward at about (52 %), surgery ward (27.7%), Gynec ward (8.9 %), pulmonary ward (2.8 %), respiratory ward (1.41%), orthopaedic ward (5.2%), from others department (1.89 %) of data were collected.

TABLE:4. ROUTE WISE PRESCRIBING PATTERN

ROA	PANTOPRAZOLE	RABEPRAZOLE	OMEPRAZOLE
ORAL	109 (44.92%)	15 (6.42%)	10 (4%)
IV	90 (37.08%)	13 (5.58%)	5 (2%)
TOTAL	199(82%)	28(12%)	15(6%)

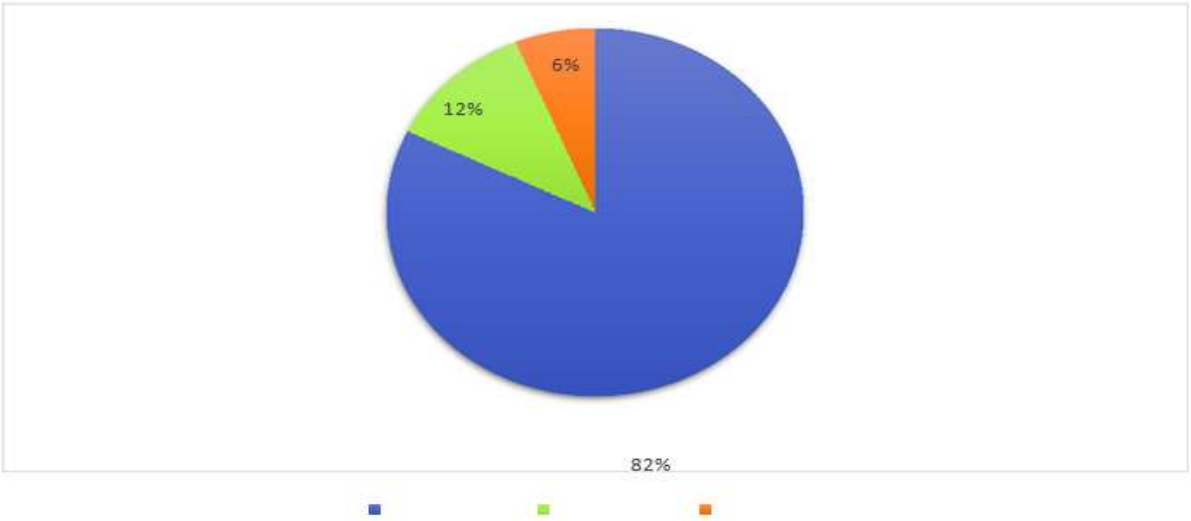

FIGURE: 4. PATTERN OF PRESCRIPTION.

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 761-778 www.ijprajournal.com ISSN: 2456-4494

As shown in table:4. In route of administration a total no of PPIs prescribed 242 through orally and IV were, pantoprazole (n=199, in percent total 82%) medication were prescribed and analysed out of which 44.91% were prescribed orally and 37.08% were prescribed intravenous route (IV).
Rabeprazole (n=28, in percent total 12%) medications were prescribed and analysed out of which 6.42% were prescribed orally and 5.57% were prescribed intravenous route (IV).
Omeprazole (n=15, in percent total 6%) medications were prescribed and analysed out of which 4% were prescribed orally and 2% were prescribed intravenous route (IV).
Lansoprazole, esomeprazole and dexlansoprazole were not prescribed.

TABLE:5. PRESCRIPTION AS PER BRAND & GENERIC NAME

INDICATION	No. Of prescription	PERCENTAGE (%)
PPIs Prescribed in brand name	195	91
PPIs Prescribed in generic name	19	9

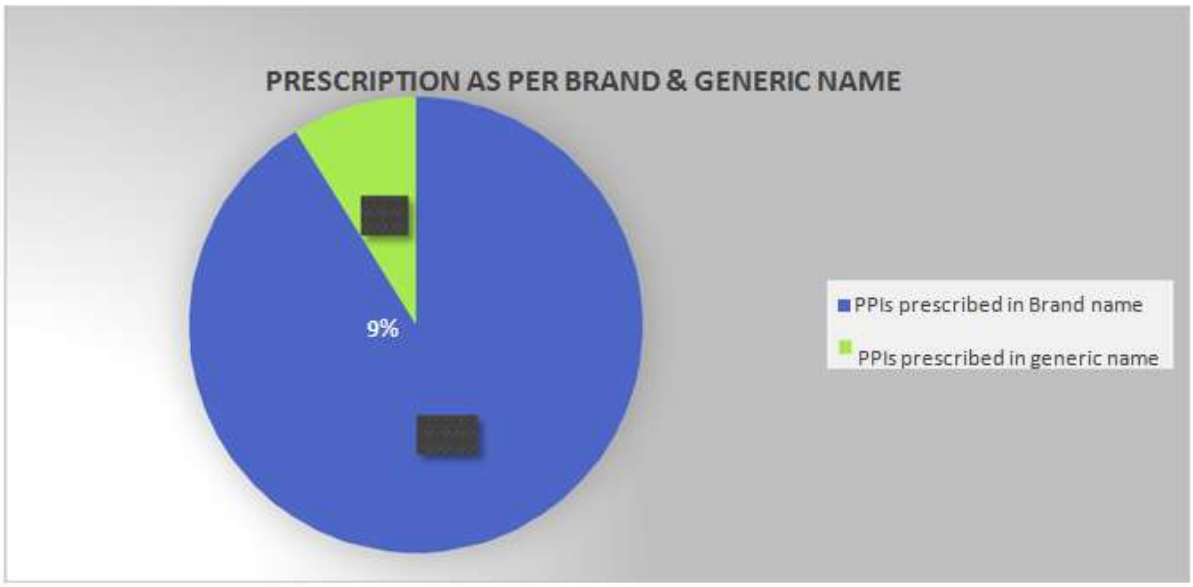

FIGURE: 5. PRESCRIPTION AS PER BRAND & GENERIC NAME

As shown in table 2 in the study of pattern of prescription total (n=214) drugs were prescribed. out of this brand name (91%) [195] were used in most of the cases an only (9%) [15] of generic name were prescribed and revealed in FIGURE. 5.

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 761-778 www.ijprajournal.com ISSN: 2456-4494

TABLE:6. PRESCRIBING PATTERN BASED ON THERAPY.

DUAL THERAPY	No. of cases	Percentage (%)
Pantoprazole + Omeprazole	1	0.73
Rabeprazole + Pantoprazole	7	3.27
MONO THERAPY	206	96

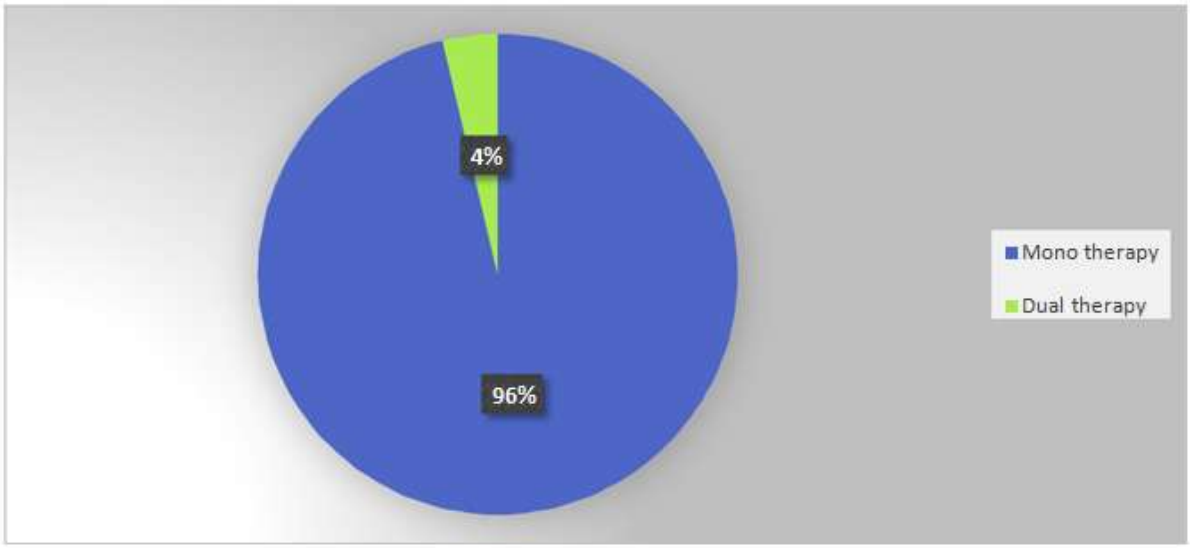

FIGURE: 6. PRESCRIBING PATTERN BASED ON THERAPY.

On the basis of prescription pattern of PPIs therapy out of 214 samples 206 (96%) where prescribed as monotherapy and 8 (4%) where prescribed as dual therapy, including (pantoprazole + omeprazole 0.73% and rabeprazole + pantoprazole 3.27%).

TABLE:7. ADR OBSERVED IN PATIENTs.

Total no. of sample	Total ADR Found.
214	05

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 761-778 www.ijprajournal.com ISSN: 2456-4494

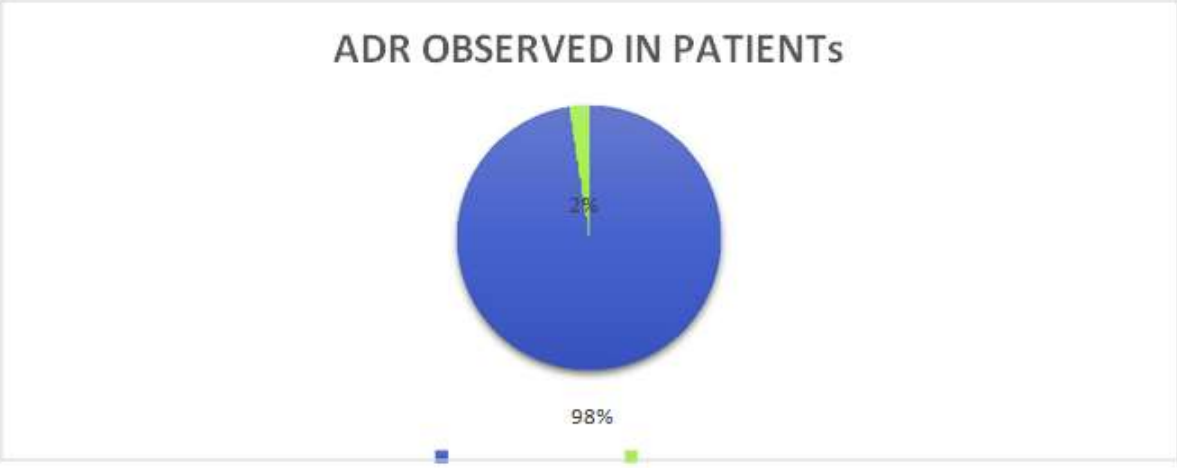

FIGURE: 7. ADR OBSERVED IN PATIENTs

TABLE:7.1. ADR OBSERVED IN PATIENTs

SEVERE CONSTIPATION	VOMITING	ANAL FISSURE	RENAL IMPAIRMENT
2	1	1	1

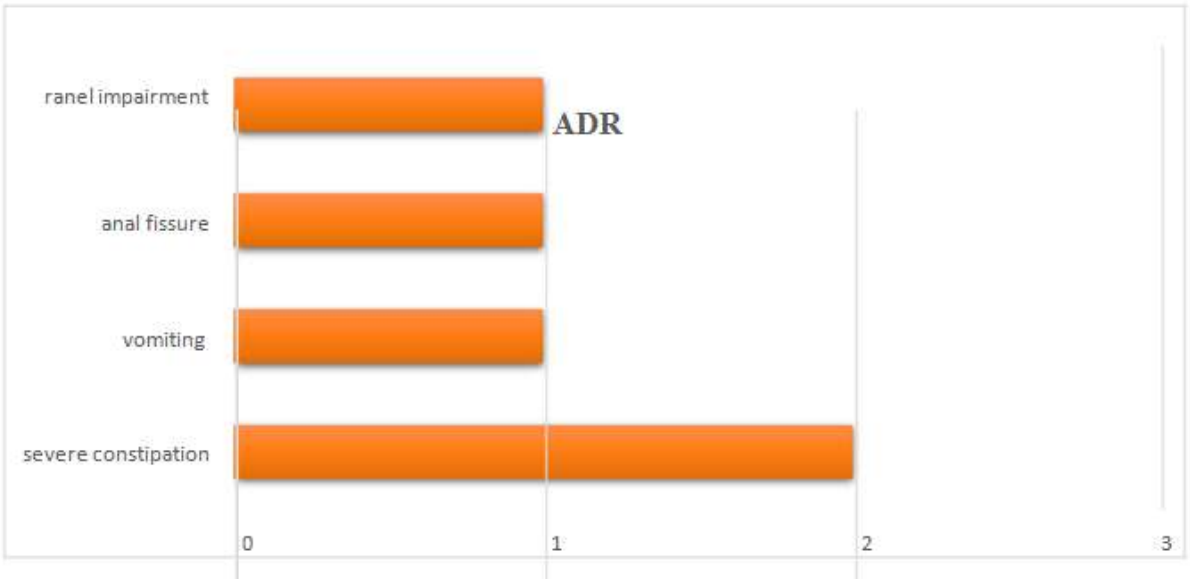

FIGURE: 7.1. ADR OBSERVED IN PATIENTs

Out of 214 patients who are on PPIs therapy, 5 patients had PPIs related ADR. A total of 5 cases were reported in IPD (In-patient department), most commonly reported ADR were severe constipation, vomiting, renal impairment, and anal fissure and suspected drug was pantoprazole. Causality assessment was done using Naranjo scale and according to score, the ADR were classified as definite/highly probable and probable.

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 761-778 www.ijprajournal.com ISSN: 2456-4494

TABLE:8. POTENTIAL INTERACTION FOUND.

TOTAL NO. OF SAMPLE	INTRACTION FOUND	Percentage (%)
214	31	13%

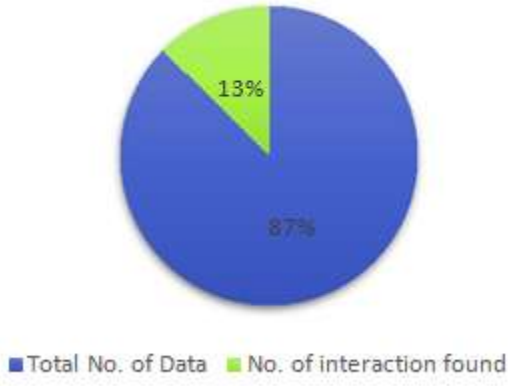

FIGURE: 8. POTENTIAL INTERACTION FOUND.

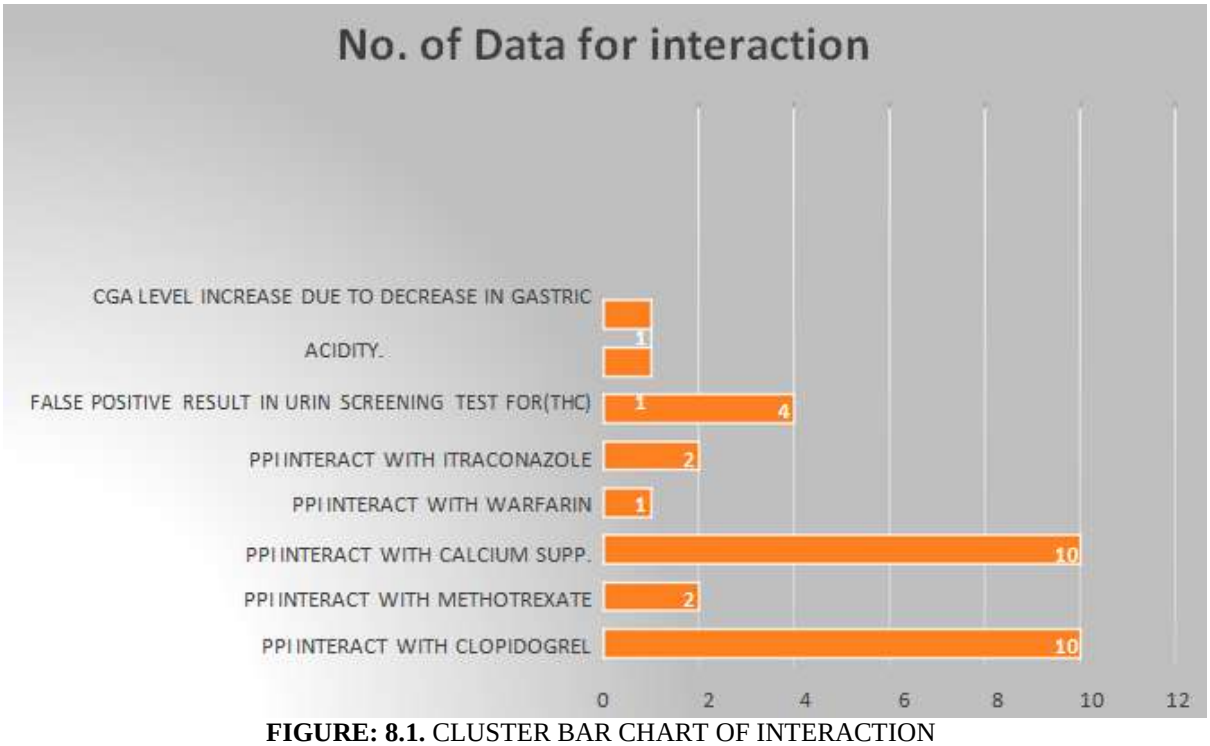

FIGURE: 8.1. CLUSTER BAR CHART OF INTERACTION

As Shown in table 8. In the study of potential interaction total(n=214) sample were observed, out of which (n=31,13%) of potential interaction were found. Most of the interaction were found with Clopidogrel as well as with calcium supplements, also interactions found with antifungal like Itraconazole and Fluconazole as well as interaction leading to false positive result in urine screening test for THC. However, CGA level also increased due to decreases in gastric acid level shown in figure (8.1).

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 761-778 www.ijprajournal.com ISSN: 2456-4494

TABLE:9. COMPARED DRUGS AMONGST PPIs CLASS.

PPIs	Total no. of prescribed	Percentage (%)
PANTOPRAZOLE	194	91%
RABEPRAZOLE	16	7%
OMEPRAZOLE	4	2%
Total No. of sample:	214	100%

FIGURE: 9. PIE CHART OF COMPARED DRUG AMONGST PPIs CLASS.

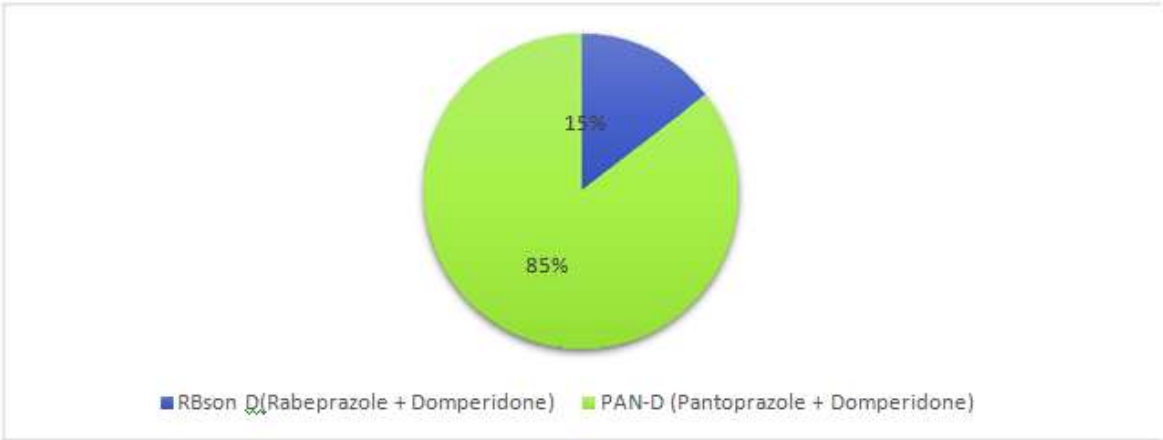

FIGURE: 9.1. COMBINATION PRESCRIBED.

As per table (9), most commonly prescribed drugs amongst PPIs class were pantoprazole at about 194(91%) from 241 sample size, Rabeprazole at about 7% and omeprazole at about 2% while compared amongst PPIs drug class, some of the drugs were prescribed in combination like pantoprazole +domperidone at about 85% and, Rabeprazole+ domperidone at about 15 % as shown in figure (9.1).

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 761-778 www.ijprajournal.com ISSN: 2456-4494

TABLE: 10. RISK-ASSOCIATED WITH USE OF PPIs.

RISK-ASSOCIATED WITH USE OF PPIs	NO. OF CASES (214)	PERCENTAGE (100%)
AFTER CHRONIC USE OF PPIs, SUDDEN STOP OF PPIs CAN CAUSE HYPERSECRETION	2	0.93%
LONG TERM USE OF PPIs CAN WORSEN CONDITION OF ANAL FISSURE	1	0.47%
LONG TERM USE OF PPIs MAY LEADS TO ANAL FISSURE	1	0.47%
LONG TERM USE OF PPIs MAY INCREASE THE INCIDENCE RATE OF BONE FRACTURE	3	1.40%
LONG TERM USE OF PPIs MAY LEADS TO THROMBOCYTOPENIA	3	1.40%
LONG TERM USE OF PPIs CAN WORSEN CONDITION OF THROMBOCYTOPENIA	2	0.93%
LONG TERM USE OF PPIs CAN CAUSE RENAL IMPAIRMENT	8	3.69%
TOTAL RISK ASSOCIATED	**31**	**9.30%**

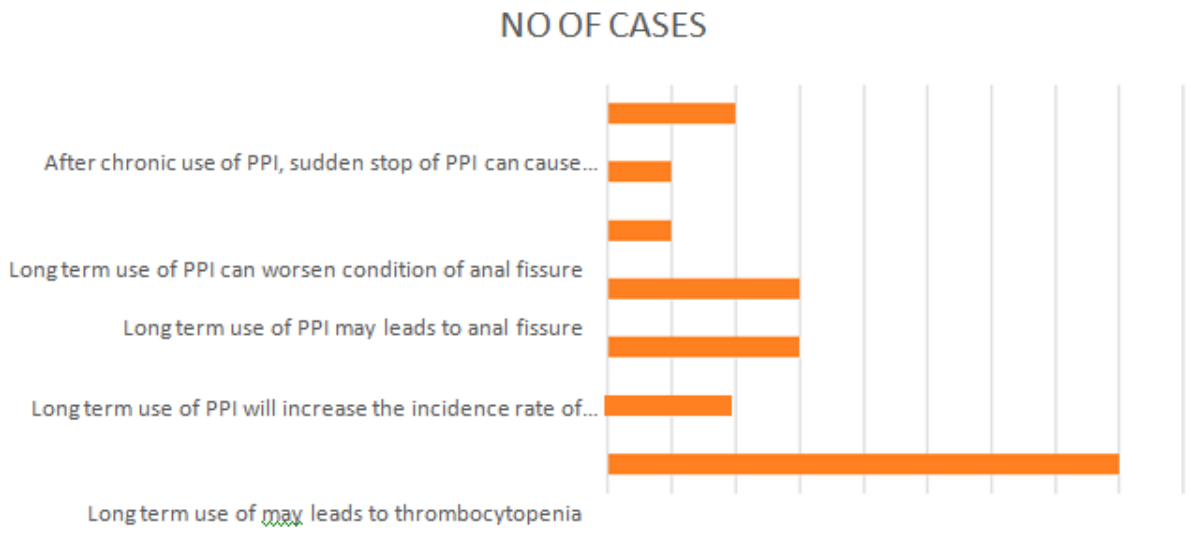

FIGURE: 10. RISK-ASSOCIATED WITH USE OF PPIs.

As shown in TABLE[10] out of 214 cases no. Of risk-associated with PPIs is 31 in PERCENT 9.30%. Out of which most of them were concerned with long term use of Proton Pump Inhibitors.

IV. DISCUSSION

In a prospective study conducted for six months in various wards, such as General Medicine, surgery, Gynecology, Orthopedic and respiratory. About 214 patients were included of various age groups above 18. Our study Aimed to assess prescribing pattern and risk associated with

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 761-778 www.ijprajournal.com ISSN: 2456-4494

use of PPIs. Based on Micromedex database found out potentiol interactions and adverse drug reactions of drugs. This database is selected as Micromedex, A well known source that provide easy access to large amountof data.

During the study out of 214 Patient's, out of which 10(%) of patient's were between the age of 18-25 years, 22(%) of patient's were between the age of 26-35 years, 23(%) of patient's were between the age of 36-45 years, 23(%) of patient's were between the age of 46-55 year, 15(%) of patient's were between the age of 56-65 years AND, 7(%) of patients were from age group above 65 years. On basic of gender wise distribution 46% were male patients, and 56% were female patients.

Oskar O. Halfdanarson et.al.,[25] suggested that annual prevalence increase from 8.5 per 100% to 15.5 per 100%. So, prevalence increased with patient age and was higher among women than men.

From above 100% of data, 2% adverse drug reaction was found. Most commonly reported ADR were severe constipation, vomiting, renal impairment, and anal fissure and suspected drug was pantoprazole. **Casciaro M. et.al.,**[26] study suggested that pantoprazole 50.7% was the most frequently used drug followed by omeprazole 34.2%. Till now there is no preventability assessment and severity assessment on the ADRs for PPIs alone. This was the study which assessed the severity and preventability of ADRs among PPIs.

On basis of route of administration 55.33% are given orally and 44.67% is given Intravenously for immediate onset of action, were 91% are prescribed as in brand name and 9% are prescribed as in generic name. **Andrew J. Gawron et.al.,**[35] study suggested that from 329.2 million patients from 2006 to 2010. Of these, 53% were prescribed as brand name and 47% were prescribed as generic name.

In our study 13% of potential interaction with proton pump inhibitors were addressed mostly with clopidogrel as well as calcium supplement. On comparing drugs amongst PPIs class where, 91% of prescribed drug is pantoprazole, 7% of rabeprazole and 2% is omeprazole. **Dr. Archana et.al.,**[36] study suggested that pantoprazole 50.15% were the PPI most commonly prescribed. And there are certain studies **BijayaBasyal et.al.,**[37] suggested similar to our result.

Also some drugs prescribed in combination such as pantoprazole + domperidone in larger portion about 85% and rabeprazole + domperidone about 15%. Analysis based on risk associated with PPIs during study are mainly concerned with the disease condition such as kidney disease, anemia, bone related disorders and gastrointestinal disease due to long term use .

V. SUMMARY AND CONCLUSION

This study revealed that mostly prescribed drugs amongst PPIs class is pantoprazole. And analysis suggest that long term/ high dose PPIs users are characterised by an increaded risk of fragibity fracturs, renal impairment, thrmbocytopenia and hypersecreation of acids as a withdrawn effect. 91% of PPIs prescribed in brand name and 85% pantoprazole in combination with domperidone. PPIs use may be associated with various micronutrient deficiencies. These developments of deficiencies is likely and highly corelated with aditional patient risk factors. Rather than being singly attributed to PPIs use. Further study into the long term effects and clinical implications of PPIs related micronutrient deficiency is warranted.

The study also concluded that the use of databases such as MicroMedex and Drugs.com was useful as secondary source for reference

REFERENCES-

[1]. Klok RM, Postma MJ, Van Hout BA, Brouwers JR. Meta-analysis: comparing the efficacy of proton pump inhibitors in short-term use. Alimentary pharmacology & therapeutics. 2003 May;17(10):1237-45.

[2]. Wedemeyer RS, Blume H. Pharmacokinetic drug interaction profiles of proton pump inhibitors: an update. Drug safety. 2014 Apr;37(4):201-11.

[3]. Scarpignato C, Gatta L, Zullo A, Blandizzi C. Effective and safe proton pump inhibitor therapy in acid-related diseases–A position paper addressing benefits andpotential harms of acid suppression. BMC medicine. 2016 Dec;14(1):1-35.

[4]. Sachas G, Shin JM, Howden CW. Review article: the clinical pharmacology of proton inhibitors. Aliment Pharmacol Ther. 2006;23(2):2-8.

[5]. Rossi S. Australian medicines handbook. 2006.

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 761-778 www.ijprajournal.com ISSN: 2456-4494

[6]. Clark DW, Strandell J. Myopathy including polymyositis: a likely class adverse effect of proton pump inhibitors. European journal of clinical pharmacology. 2006 Jun;62(6):473-9.
[7]. Corleto VD, Festa S, Di Giulio E, Annibale B. Proton pump inhibitor therapy and potential long-term harm. Current opinion in endocrinology, diabetes and obesity. 2014 Feb 1;21(1):3-8.
[8]. Freedberg DE, Kim LS, Yang YX. The risks and benefits of long-term use of proton pump inhibitors: expert review and best practice advice from the American Gastroenterological Association. Gastroenterology. 2017 Mar 1;152(4):706-15. De Bruyne P, Ito S. Toxicity of long-term use of proton pump inhibitors in children. Archives of disease in childhood. 2018 Jan 1;103(1):78-82
[9]. Vaezi MF, Yang YX, Howden CW. Complications of proton pump inhibitor therapy. Gastroenterology. 2017 Jul 1;153(1):35-48.
[10]. Ito T, Jensen RT. Association of long-term proton pump inhibitor therapy with bone fractures and effects on absorption of calcium, vitamin B12, iron, and magnesium. Current gastroenterology reports. 2010 Dec;12(6):448-57.
[11]. Abtahi S, Driessen JH, Burden AM, Souverein PC, van den Bergh JP, van Staa TP, Boonen A, de Vries F. Concomitant use of oral glucocorticoids and proton pump inhibitors and risk of osteoporotic fractures among patients with rheumatoid arthritis: a population-based cohort study. Annals of the Rheumatic Diseases. 2021 Apr 1;80(4):423-31.
[12]. Kwok CS, Yeong JK, Loke YK. Meta-analysis: risk of fractures with acid-suppressing medication. Bone. 2011 Apr 1;48(4):768-76.
[13]. Gronich N, Lavi I, Lejbkowicz F, Pinchev M, Rennert G. Association of CYP2C19 polymorphism with proton pump inhibitors effectiveness and with fractures in real- life: retrospective cohort study. Clinical Pharmacology & Therapeutics. 2022 Feb 5.
[14]. Maret-Ouda J, Markar SR, Lagergren J. Gastroesophageal reflux disease: a review. Jama. 2020 Dec 22;324(24):2536-47.
[15]. Cheung KS, Chan EW, Wong AY, Chen L, Wong IC, Leung WK. Long-term proton pump inhibitors and risk of gastric cancer development after treatment for Helicobacter pylori: a population-based study. Gut. 2018 Jan 1;67(1):28-35.
[16]. Cheung KS, Chan EW, Wong AY, Chen L, Wong IC, Leung WK. Long-term proton pump inhibitors and risk of gastric cancer development after treatment for H. pylori: A population-based study. Digestive Disease Week, American Gastroenterological Association, Chicago, USA. 2017.
[17]. Leontiadis GI, Veldhuyzen Van Zanten S, Hookey L, Armstrong D, Jones N, Moayyedi P. Canadian Association of Gastroenterology statement on the putative link between proton pump inhibitor treatment and gastric cancer after Helicobacter pylori eradication. Journal of the Canadian Association of Gastroenterology. 2018Dec 3;1(4):155-8.
[18]. Cheung KS, Leung WK. Long-term use of proton-pump inhibitors and risk of gastric cancer: a review of the current evidence. Therapeutic advances in gastroenterology. 2019 Mar;12:1756284819834511.
[19]. Shin JM, Kim N. Pharmacokinetics and pharmacodynamics of the proton pump inhibitors. Journal of neurogastroenterology and motility. 2013 Jan;19(1):25.
[20]. Kamran Q, Mund MD, Ali HA, Barkat MQ. Pathophysiology and Clinical Applications of Gastro-Esophageal Reflux Disease. Archives of Clinical and Biomedical Research. 2017;1(5):242-54.
[21]. Najm WI. Peptic ulcer disease. Primary Care: Clinics in Office Practice. 2011 Sep 1;38(3):383-94.
[22]. Kumar A, Kumar D, Kumar R, Prasad J, Kumar M, Joshi P, Fulzele P. Peptic Ulcersand their Complications. Journal of Drug Delivery and Therapeutics. 2020 Jun 15;10(3-s):256-61.
[23]. Al-aajem BM. Association of Helicobacter pylori infection and vitamin B12 deficiency. GSC Biological and Pharmaceutical Sciences. 2019 Nov 30;9(2):143- 6.
[24]. Lanas A, Chan FK. Peptic ulcer disease. The Lancet. 2017 Aug 5;390(10094):613-24.

[25]. Hálfdánarson ÓÖ, Pottegård A, Björnsson ES, Lund SH, Ogmundsdottir MH, Steingrímsson E, Ogmundsdottir HM, Zoega H. Proton-pump inhibitors among adults: a nationwide drug-utilization study. Therapeutic advances in gastroenterology. 2018 May 29; 11:1756284818777943.

[26]. Casciaro M, Navarra M, Inferrera G, Liotta M, Gangemi S, Minciullo PL. PPI adverse drugs reactions: a retrospective study. Clinical and Molecular Allergy. 2019 Dec;17(1):1-5.

[27]. Eusebi LH, Rabitti S, Artesiani ML, Gelli D, Montagnani M, Zagari RM, Bazzoli F. Proton pump inhibitors: risks of long-term use. Journal of gastroenterology and hepatology. 2017 Jul;32(7):1295-302. Serbin MA, Guzauskas GF, Veenstra DL. Clopidogrel-proton pump inhibitor drug-drug interaction and risk of adverse clinical outcomes among PCI-treated ACS patients: a meta-analysis. Journal of managed care & specialty pharmacy. 2016 Aug;22(8):939-47.

[28]. Durand C, Willett KC, Desilets AR. Proton pump inhibitor use in hospitalized patients: is overutilization becoming a problem?. Clinical Medicine Insights: Gastroenterology. 2012 Jan;5:CGast-S9588.

[29]. Sachar H, Vaidya K, Laine L. Intermittent vs continuous proton pump inhibitor therapy for high-risk bleeding ulcers: a systematic review and meta-analysis.JAMA internal medicine. 2014 Nov 1;174(11):1755-62.

[30]. Scarpignato C, Gatta L, Zullo A, Blandizzi C. Effective and safe proton pump inhibitor therapy in acid-related diseases–A position paper addressing benefits andpotential harms of acid suppression. BMC medicine. 2016 Dec;14(1):1-35.

[31]. Özdemir SK, Bavbek S. Hypersensitivity reactions to proton-pump inhibitors: Clinical presentation, diagnosis, and management. InAllergy & Asthma Proceedings 2020 Mar 1 (Vol. 41, No. 2).

[32]. Kepil Özdemir S, Yılmaz I, Aydın Ö, Büyüköztürk S, Gelincik A, Demirtürk M, Erdoğdu D, Cömert Ş, Erdoğan TU, Karakaya G, Kalyoncu AF. Immediate-type hypersensitivity reactions to proton pump inhibitors: usefulness of skin tests in thediagnosis and assessment of cross-reactivity. Allergy. 2013 Aug;68(8):1008-14.

[33]. Ariel H, Cooke JP. Cardiovascular risk of proton pump inhibitors. Methodist DeBakey cardiovascular journal. 2019 Jul;15(3):214.

[34]. Gawron AJ, Feinglass J, Pandolfino JE, Tan BK, Bove MJ, Shintani-Smith S. Brand name and generic proton pump inhibitor prescriptions in the United States: insights from the national ambulatory medical care survey (2006–2010). Gastroenterology Research and Practice. 2015 Feb 5;2015.

[35]. Daudu OU, Ajiboye M, Ajala S, Buru ME. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) e-ISSN: 2279-0853, p-ISSN: 2279-0861. Volume 16, Issue 5 Ver. VI (May. 2017), PP 34-35 www. iosrjournals. org.

[36]. Basyal B, Marasine NR, Sankhi S, Lamichhane R, Uprety BN. Prescribing pattern of proton pump inhibitors among patients visiting the outpatient general medicine clinic in a tertiary care teaching hospital in Nepal. Journal of Health Research. 2021 Jun