

Original Article

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## Rational Use of Proton Pump Inhibitors among Patients Admitted in a Tertiary Care Hospital

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### Abstract:

**Background:** The prevalent usage of proton pump inhibitors (PPIs) is a testament to the effectiveness of this class of medications, but it also introduces risk associated with inappropriate prescriptive and consumptive practices. Because of the negative effect of incorrect usage and overdose of PPIs, it is very important for physicians to only prescribe these drugs when needed. However, recent studies showed some concerns about long-term PPIs consumption. The rational prescription of medications is vital to ensuring the optimal use of medical resources, providing effective therapy and minimizing adverse drug reactions.

**Methods:** This observational study was conducted in the department of Pharmacology and therapeutics, Sylhet M.A.G. Osmani medical college, Sylhet, in collaboration with the department of Medicine, Surgery, Gastroenterology, Obstetrics and gynaecology, Sylhet M.A.G. Osmani medical college hospital, Sylhet, from July 2022 to June 2023. The sample size for this study was 600. Usage of PPIs was considered to be appropriate on the basis NICE guidelines and recommendations by Scarpignato et al. (2016) committees on behalf of three Italian scientific societies.

**Result:** For 600 PPIs prescriptions, total 705 case sheets were reviewed. The mean age of the study patients was 42.94±17.16 years. Female were found more 359(59.8%) than male 241(40.2%). Out of 600 patients, based on the indications of PPI usage, 287 (47.8%) of prescriptions were found appropriate, whereas inappropriate prescriptions were found in 313 (52.2%) cases. Out of 287 patients who were prescribed PPIs in an appropriate indication, 175 (61%) patients were given PPIs in an appropriate dose, whereas inappropriate dose was found in 112 (39%) of patients. Again, among 175 patients who were prescribed PPIs for appropriate dose, 24 (13.7%) patients were given PPIs in an appropriate frequency, whereas inappropriate frequency was found in 151 (86.3%) of patients. Finally, 24/600 (4%) patients were prescribed in an appropriate indication with an appropriate dose and frequency, whereas inappropriate prescription were found in 576/600 (96%) patients. PPIs were used as prophylaxis for NSAIDs in highest number 147(51.2%) of patients. Oral was the most common 348(58%) route of prescribing PPIs. Omeprazole was the highest 577(96.2%) prescribed PPIs.

**Conclusion:** Based on this study result, it could be concluded that in most of the patients PPIs prescriptions were not following appropriate indications, dose and frequency recommended by reference guidelines. Like any other drugs, PPIs should be prescribed for a clear indication, the minimum dose needed for the expected effect and medication halted when no longer necessary upon re-evaluation.

**Key words:** Proton pump inhibitor, rational use, admitted patient.

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### Introduction:

Irrational use of medicines is a worldwide problem.

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There are many ways that lead to an irrational use such as prescribing the medicine that is inappropriate to clinical guidelines indication, inadequate dose, over-use of injections when oral medication can be appropriate, the use of too many medicines per patient (polypharmacy)

and inappropriate self-medication, often of prescription only medicines.<sup>1</sup> Proton pump inhibitors are a class of medications that significantly reduce stomach acid output. PPIs decrease both basal and meal stimulated gastric acid secretion by irreversibly inhibiting the gastric H<sup>+</sup>-K<sup>+</sup>-ATPase pump, also known as the proton pump.<sup>2</sup> Many drug utilization studies have reported widespread overuse of PPIs and that are outside the current prescribing guidelines.<sup>3</sup> Audits of medical inpatients in the United Kingdom (UK) revealed 54.0% incorrect use of PPI.<sup>4</sup> Another study in the USA reported that in academic and nonacademic hospitals, only 39% of PPI prescriptions followed guidelines.<sup>5</sup> In Bangladesh, a recent study conducted in Shaheed Suhrawardy medical college revealed that about 54.2% patients were inappropriately prescribed PPIs at discharge.<sup>6</sup> Another study conducted in Dhaka medical college revealed that 71.5% of patients received PPIs incorrectly on prescriptions during their discharge.<sup>7</sup> PPIs are relatively safe and less toxic in comparison to other drugs but it is not free from side effects which cannot be overlooked.<sup>8</sup> Several studies have linked long term PPI use with more serious adverse effects such as increased risk of *Clostridium difficile* infection, osteoporotic fracture including hip fracture, community acquired pneumonia, vitamin B12 deficiency, hypomagnesemia, increased cardiovascular risk, acute interstitial nephritis, chronic kidney disease, Subacute cutaneous lupus erythematosus, risk of developing gastric cancer and higher mortality.<sup>9</sup> National Institute for Health and Care Excellence (NICE) (2014) guidance recommend indications for prescribing PPIs.<sup>10</sup> Committees on behalf of three Italian scientific societies named the Italian Society of Pharmacology (SIF), the Italian Association of Hospital Gastroenterologists (AIGO) and the Italian Federation of General Practitioners (FIMMG) presented a narrative review of safety and appropriateness of PPI therapy in 13 clinical scenarios where uncertainty existed about prescription of PPIs.<sup>11</sup> These 2 guidelines were followed in this study for making decision of inappropriate use of PPI. Despite the limited prescribing advice, PPIs usage both prescription and over-the-counter is rising globally as a result

of numerous contributing variables. In Bangladesh the scenario is similar. So, to contend overwhelming PPIs usage more studies are required to improve prescribing practices and to increase the awareness of the existing guidelines for PPIs prescribing among clinicians.

### Material and Methods:

This cross sectional study was carried out in the department of Pharmacology and therapeutics, Sylhet M.A.G. Osmani medical college, Sylhet with collaboration of department of Medicine, Surgery, Gastroenterology, Obstetrics and gynaecology of Sylhet M.A.G. Osmani medical college hospital, Sylhet from July 2022 to June 2023. From all the patients admitted in department of Medicine, Surgery, Gastroenterology, Obstetrics and gynaecology ward of Sylhet M.A.G. Osmani medical college hospital, Sylhet during study period the study sample were those fulfilling selection criteria. According to the research guideline entitled "How to investigate drug use in health facilities" published by the WHO (1993), there should be minimum encounters 600 for a cross sectional survey. So sample size was 600 for this study. Convenient sampling method was followed in this study to enroll the study subjects. Informed written consent form were signed by the participants who fulfilled the selection criteria after explaining the objectives and benefits of the study. A specially designed preformed data collection sheet was used to collect data. The patient's demographics, clinical history, medication history, laboratory investigations and other relevant data were collected from the treatment sheets and by direct patient interview according to objectives of the study. Main outcome variables of this study were indication of PPIs use, route of PPIs, dose of PPIs, frequency of PPIs, types of PPIs, use of concomitant drugs and co morbid condition of patients. So data regarding indication, dose, frequency and route of PPIs were collected and evaluated for its appropriate usage considering NICE guidelines (2014) and the systemic review by Scarpignato et al., recommendations (2016). Information about concomitant drugs used and co morbid condition of the patients were also recorded.

**Result:**

Total 705 prescriptions were reviewed from Medicine, Surgery, Gastroenterology, Obstetrics and gynaecology departments. Among those 705 prescriptions, 600 patients (85.1%) were prescribed with PPIs. Highest age group of the study patients were 21-30 years (28.5%), followed by 51-60 years (15.8%), 41-50 years (15.3%), 31-40 years (15.2%), 61-70 years (13.7%), 18-20 years (7.0%), 71-80 years (2.5%) and the lowest age group patients were 81-90 years (2%). Mean age of patients were 42.94±17.16 years. Among 600 study patients, 359 (59.8%) were female and 241 (40.2%) were male with a ratio of 0.6: 1. Other results are presented with tables (1-7).

**Table 1: Distribution of the cases by appropriateness of PPI used in terms of indications (n = 600)**

Appropriateness of PPIs indications	No. of patients	Percentage (%)
Appropriate	287	47.8
Inappropriate	313	52.2
Total	600	100.0

**Table 2: Distribution of PPI used in different departments based on the appropriate indication (n = 600)**

Department	Indication appropriateness		Total (n=600)	Test value	P-value
	Appropriate (n=287)	Inappropriate (n=313)			
Gastroenterology	57 (66.3%)	29 (33.7%)	86 (100.0%)	38.988	<0.001
Medicine	86 (59.7%)	58 (40.3%)	144 (100.0%)		
Surgery	85 (45.9%)	100 (54.1%)	185 (100.0%)		
Obstetrics and gynaecology	59 (31.9%)	126 (68.1%)	185 (100.0%)		

Chi-Square test ( $\chi^2$ ) was done to analyze the data

**Table 3: Distribution of study patient in different departments based on the appropriate dose with appropriate indications of PPIs (n = 287)**

Department	Dose appropriateness		Total (n=287)	Test value	p-value
	Appropriate (n=175)	Inappropriate (n=112)			
Gastroenterology	47 (82.5%)	10 (17.5%)	57 (100%)	14.259	0.003
Medicine	50 (58.1%)	36 (41.9%)	86 (100%)		
Surgery	47 (55.3%)	38 (44.7%)	85 (100%)		
Obstetrics and gynaecology	31 (52.5%)	28 (47.5%)	59 (100%)		

Chi-Square test ( $\chi^2$ ) was done to analyze the data.

**Table 4: Distribution of study patients in different departments based on the appropriate frequency (dose interval) with appropriate dose of PPIs (n =175)**

Department	Appropriate frequency		Total (n=175)	Test value	p-value
	Appropriate (n=24)	Inappropriate (n=151)			
Gastroenterology	11 (23.4%)	36 (76.6%)	47 (100%)	10.508	0.015
Medicine	9 (18.0%)	41 (82.0%)	50 (100%)		
Surgery	4 (8.5%)	43 (91.5%)	47 (100%)		
Obstetrics and gynaecology	0 (0%)	31 (100%)	31 (100%)		

Chi-square test ( $\chi^2$ ) was done to analyze the data

**Table 5: Distribution of study patient in different departments based on the overall appropriateness (indication, dose and frequency) of PPI prescription (n =600)**

Department	Overall Appropriateness		Total (n=600)	Test value	p-value
	Appropriate (n=24)	Inappropriate (n=576)			
Gastroenterology	11 (12.8%)	75 (87.2%)	86 (100%)	28.541	<0.001
Medicine	9 (6.3%)	135 (93.7%)	144 (100%)		
Surgery	4 (2.2%)	181 (97.8%)	185 (100%)		
Obstetrics and gynaecology	0 (0%)	185 (100%)	185 (100%)		

Chi-square test ( $\chi^2$ ) was done to analyze the data.

**Table 6: Distribution of the study patients by route of PPIs administration (n=600)**

Route of administration	No. of patients	Percentage (%)
Oral	348	58.0
Intravenous	252	42.0
Total	600	100.0

**Table 7: Distribution of study patients based on the PPIs used by generic name (n=600)**

Name of PPI used	No. of patients	Percentage (%)
Omeprazole	577	96.2
Rabeprazole	8	1.3
Esomeprazole	7	1.2
Pantoprazole	5	0.8
Lansoprazole	3	0.5
Dexlansoprazole	0	0
Total	600	100

**Discussion:**

In this study total 705 case sheets were reviewed, 210 from Medicine, 200 from Surgery, 195 from Obstetrics and gynaecology and 100 from Gastroenterology department. Out of 705 cases 600 (85.1%) cases were found to be on PPIs. Of these 600 patients, 185 (30.83%) were inpatients of Obstetrics and gynaecology ward, 185 (30.83%) were inpatients of Surgery ward, 86 (14.34%) were inpatients of Gastroenterology ward and 144 (24%) were inpatients of Medicine ward. Nousheen et al. observed that out of 214 patients reviewed 100 (46.72%) were on PPIs which is much lower than our finding.<sup>12</sup> Mean age of our study population was 42.94±17.16 years ranging from 18 to 90 years. Similar results were reported by Basyal et al. where they found mean age of their study patients were 41.99±17.58 years ranging from 18 to 86 years.<sup>13</sup> Female patients were 359 (59.8%) and male patients were 241 (40.2%) with a ratio of 0.6:1 in this study. Similar finding was found in the study conducted by Anindita et al. where they showed majority 53 (58.24%) of their patients were female as compared to male patients 38 (41.76%).<sup>14</sup>

This study showed out of 600 patients who were prescribed PPIs, majority 313 (52.2%) were prescribed PPIs without a valid indication

whereas 287 (47.8%) of patients were given PPIs with an appropriate indication (Table-1). Similar result was also observed by Chia et al. where majority of patients 258/477(54.1%) were prescribed PPIs without valid indications.<sup>15</sup> But unlike this study, Lenoir et al. observed 70/97(72%) and Ladd et al. observed 155/204(76%) inappropriate indications use of PPIs prescription, which was higher than our study.<sup>16,17</sup> The rate of inappropriate indication use of PPI was highest 126(68.1%) in Obstetrics and gynaecology department and lowest 29(33.7%) in Gastroenterology department (Table-2).

Our study again showed out of 287 patients, who were prescribed PPIs for appropriate indication, 175 (61%) patients were given PPIs in an appropriate dose, whereas inappropriate dose was found in 112 (39%) of patients (Table-3). However, in study reported by Lenoir et al. 63% patients and by Kelly et al. 68% patients of justified indications usage of PPI did not have an appropriate dose, which were much higher than our findings.<sup>16,18</sup> Furthermore in our study, out of 175 patients who were prescribed PPIs for an appropriate dose, 24 (13.7%) patients were given PPIs in an appropriate frequency and inappropriate frequency were found in 151 (86.3%) patients (Table-4). This finding was higher than the study by Okoro et al. where they observed 33.3% inappropriate frequency use of PPI.<sup>19</sup>

Overall in this study, among 600 patients who were prescribed PPIs, only 24 (4%) patients were prescribed with an appropriate indication, dose and frequency following guideline. So rest 576 (96%) patients were prescribed inappropriately in terms of indication, dose and frequency (Table-5). Similar study was done by Okoro et al. where they evaluated appropriateness of PPI in terms of indication, dose, duration and frequency. They found inappropriate PPI prescription in 201/220(91.4%) in their study which is close to our observations.<sup>19</sup>

In this study, out of 287 patients, who were prescribed PPIs for an appropriate indication, most of the patients 147 (51.2%) were given PPIs as prophylaxis for NSAID induced ulcer. Almost similar finding (68.4%) of prescribing

PPIs commonly to reduce the risk of gastric ulceration associated with NSAID was found in another study.<sup>20</sup>

Majority 348/600 (58%) patients were prescribed with PPI through oral route in this study and rest 252/600(42.0%) patients were prescribed in intravenous route (Table-6). This is found to be consistent with the study by Nousheen et al. where majority of patients 150/214(70%) were given PPIs by oral route.<sup>3</sup>

In this study, among 600 patients, highest 577 (96.2%) patients were prescribed with Omeprazole (Table-7). Similar results were shown by other studies where Omeprazole was given in 152/153(99.35%) of prescriptions.<sup>14</sup> But other studies found Pantoprazole as the highest 150/152(98.70%) prescribed generic of PPI.<sup>3,21</sup> The reason for high prescription of Omeprazole in our study is that, this is the only PPI which is supplied in our hospital in both oral and intravenous preparation.

Though similar two studies were conducted in Bangladesh previously but those studies were done in Medicine department only with small sample size (107 and 117 only).<sup>6,7</sup> In those studies only indication appropriateness were assessed. But this study were done in Medicine, Surgery, Gastroenterology, Obstetrics and gynaecology departments with larger sample. Furthermore, in this study not only indications appropriateness but also route, dose and frequency appropriateness of PPI were also assessed.

### **Conclusion:**

Based on this study result, it could be concluded that in most of the patients, PPIs prescriptions were not following appropriate indications, dose and frequency recommended by reference guidelines. Like any other drugs, PPIs should be prescribed for only a clear indication, the minimum dose needed for the expected effect and medication halted when no longer necessary upon re-evaluation.

### **Limitations of The Study:**

There were some limitations noticed during conducting this study, those were:

- Short duration of the study period. So evaluation of large sample size could not be possible.
- This study involving only one tertiary care hospital in Bangladesh may not represent other clinical setting in the country.
- Patients outside the mentioned department of Sylhet M.A.G. Osmani medical college hospital were not included in this study.
- Effects of inappropriate use of PPIs such as short term and long term drugs adverse effects, adverse drug reaction, drug interaction and financial burden of overused drug were not analyzed due to limited time frame.

### **Recommendations:**

To ensure rational prescribing of PPIs and to conduct further study in future following are the recommendations:

- Development of national or institutional specific guidelines regarding the rational use of PPIs.
- Identification of factors causing inappropriate PPI use is necessary.
- It is necessary to conduct a research on evaluation of burden of inappropriate PPI usage.
- Further education of appropriate PPI usage to the prescriber is time demanding.

### **Conflict of Interest:**

The authors stated that there is no conflict of interest in this study.

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No specific funding was received for this study.

### **Ethical Consideration:**

The study was conducted after approval from institutional ethical review committee. The confidentiality and anonymity of the participants were maintained.

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