

Pattern of Proton Pump Inhibitors Use among Patients within Emergency Department of Al-Hakeem General Hospital in Najaf City-Iraq

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ABSTRACT

Proton pump inhibitors (PPIs) as one of the most frequently prescribed medications for their acid-suppressing effects. Their using continuously growing annually in all over the world. With the endless expansion of their market making the wide utilization of this pharmaceutical class frequently associated with notable instances of therapeutic inappropriateness where this phenomenon positions serious questions about the appropriateness of prescription of these drugs globally. Accordingly, current study aimed to evaluate the pattern of PPI using among patients within emergency department (ED) of single Iraqi hospital. Where there were no similar studies evaluate the appropriateness of PPIs use was had been made previously. An observational, prospective cross-sectional study performed in March 2024 included 188 patients who visited ED for non-surgical complaint at Al-Hakeem General Hospital in Al-Najaf city/Iraq. Of the total cohort, 43.09% of patients received a PPI as a part of their medical regimen in ED. Omeprazole was the mainstay prescribed medication among this medical class, it used in 91.35% of patients where it given as IV doses. Of the total patients who treated with PPI in ED, 23.45% were already taking a PPI as a part of their standard medical regimen before ED visit. Among patients received PPI in ED, 39.5% were on medication with an incorrect scheduling and/or dosage. The appropriateness, dosage and regimen correctness were noted to increase with age. Result of the current study revealed the over prescription of PPI both pre and throughout ED visit with an elevated % of inappropriate use in both settings.

Keywords: Proton pump inhibitors, Emergency unit, Medication appropriateness.

I. INTRODUCTION

Proton pump inhibitors (PPI) a pharmacological class of medications act by reducing acid secretion in the stomach. They have been offered for over three decades where comprise one of the most frequently prescribed medications. Additionally, they ranked as one of the most widely used acid-suppressing medicines, till now, they remain the mainstay of the treatment of acid-related diseases¹⁻³. Previously, FDA has approved the following medicines of this class: omeprazole, pantoprazole, lansoprazole, esomeprazole, rabeprazole and dexlansoprazole, now

all are among the top 10 most prescribed drugs in USA⁴.

This class of medications is effective in treating a variety of disorders related to gastric acidity for their well-recognized safety and efficacy with high certainty of evidences supporting the association of this class with lowering the bleeding of upper GIT⁵. Globally, the main clinical indications of PPI usage are acknowledged by several scientific societies as the following: they are proven as a medication of choice of several acid-related disorders, treatment of various forms of gastroesophageal reflux disease (GERD) in addition to the treatment of GERD complications,

management of erosive esophagitis, eosinophilic esophagitis and Barrett esophagus. Prevention and treatment of gastric ulcers that associated with NSAID usage as well as peptic ulcer disease and in prophylaxis of stress ulcer in critically ill patients. Other indications of PPI include: eradication and treatment of the infections with *H. pylori* in when they used in combination with antibacterial medications, controlling of upper digestive bleeding when used as a co-therapy in endoscopic procedures besides to their benefits in the medical treatment of Zollinger-Ellison Syndrome⁶⁻⁸.

Because of the previously mentioned well distinct indications, the using of PPIs continuously growing annually in all over the world with endless expansion of this class market making the wide utilization of this pharmaceutical class, frequently associated with notable instances of therapeutic inappropriateness where this phenomenon positions serious questions about the appropriateness of prescription of these drugs globally⁹.

Since PPIs are regularly prescribed for several GIT disorders, in addition the treatment lasting for a long duration, the global market of PPI was estimated at 2020 as 2.9 billion US\$ with probability to show a compound aggregated growth rate of 4.3% during the forecast period of 2020 to 2027¹⁰.

In addition to their economic cost, the over prescription of PPI contributes also to polypharmacy. Furthermore, the over use has been increasingly linked to a number of adverse events¹¹. Adverse outcomes of treatment with PPI mainly documented to be associated with the long-term use of this medications. This could be classified either as events related or unrelated or to the inhibition of gastric acid. Allergic responses, CKD, acute interstitial nephritis, dementia, cardiovascular consequences, besides to PPI-drug interactions are an example of outcomes unrelated to inhibition of gastric acids. Regarding to acid inhibition, consequences of over use of PPI include nutrient deficiencies, pneumonia, GIT infections, small intestinal bacterial overgrowth spontaneous bacterial peritonitis, fractures as well as increase the risks of certain types of cancer¹²⁻

¹⁵. In Iraq, the pattern of PPI use in emergency settings has not been adequately studied. Accordingly, this study aimed to fill that gap by assessing the frequency as well as the appropriateness of PPI prescription in the ED of a major Iraqi hospital in Najaf City, where understanding current prescribing practice can help guide policy and improve rational drug use.

II. METHODS AND MATERIALS

The current study was an observational, prospective cross-sectional study performed in March 2024 at the emergency department of Al-Hakeem General Hospital, a hospital with 282 bed that belong to Al-Najaf Health Directorate in Al-Najaf city/Iraq. This study was approved by the Scientific Committee of Researches at Al-Najaf Health Directorate (Approval NO. 3360 dated January 23, 2024). Informed Consent was obtained from all participants before data collection. The total ED visits in this hospital during this month was about 11500 patients. Sample size was calculated as 188. According to the ED personnel and the number of patients seen during day time shift, thus it was estimated that the necessary sample size could be achieved over one weeks, five days weekly from Sunday to Thursday (17th-21th of March 2024). Patients elder than 18 years of age who visited ED during day time shift seeking medical care for their non-surgical complaint were involved into the study while exclusion criteria contained within patients who admitted to the ED from the outpatient hospital clinics and those with non-complete medical records. Pediatric, surgical and obstetric-gynecological patients were not included also. Microsoft Office Excel 2010 database was used for both revision and recording of clinical data, that included the following: patients' gender, age, past medical history, number of patients used PPI before as well as during ED visits, medication history or drug treatment before ED visit. Regarding patient used PPI before their ED visit, number of patients used PPI and the indication of use was calculated, whether used them according to medical prescription or not. Number of patients received the correct doses and regimens and using appropriateness was evaluated. PPI

inappropriateness as PPI prescribed either without indications, or with indications but with incorrect dosages and/or regimens. Reasons for ED visit or chief complaint also obtained. Treatment during ED visit also obtained and if the prescribed dose and regimens of PPI in ED was correct or not in addition to PPI inappropriateness as well as drug interactions with in ED visit also documented.

III. RESULTS AND DISCUSSION

Initially, 621 patients were observed for eligibility criteria. Out of them, 188 patients meet the criteria to be included in the study. From the total 188 patients, there were 123 (65.43%) males and 65 (34.57%) were females. Table 1 shows the demographic characters of the included patients.

TABLE 1: DEMOGRAPHIC CHAAECTERS OF PATIENTS VISITING EMERGENCY EPARTMENT (ED)

Variable	Category	Patients	
		NO.	%
Gender	Male	123	65.43
	Female	65	34.57
Age	18-24	29	15.43
	25-50	58	30.85
	51-75	63	33.51
	≥75	38	20.21
Comorbidities	HTN	71	37.77
	IHD	55	29.26
	DM	63	33.51
	GIT disease	21	11.17
	CKD	32	17.02
	Other	29	15.43
	NO Medication Used	36	19.15

Past Medication History	1-4 Drugs	85	45.21
	Polypharmacy	67	35.64
Current Medication Prescribed in ED	1-2 Drugs	78	41.49
	3-5 Drugs	58	30.85
	6-9 Drugs	29	15.43
	More than 10 Drugs	23	12.23
TOTAL		188	100.00

HTN: hypertension, IHD: ischemic heart disease, DM: diabetes mellitus, GIT: gastrointestinal tract, others: includes endocrine disease, cancers, etc....

Treatment before ED visits

Nearly one third (32.45%) of the patients were already using PPI before arriving ED where these findings align with global trends, where PPI are among the most overused and overprescribed medications often used without proper clinical justification. In this study, 77.05% of patients used this class of medication according to medical prescription. Eighty-five (54.21%) of the 188 patients were taking 1-4 drug before their visit to the ED and 23.2% of them were taking a PPI, while 67 patient (35.64) were taking more than 5 drugs (polypharmacy) and 56.72% of them were taking PPI. In both groups, omeprazole was the most prevalent used medication where it used by 62.29% of patients. Pantoprazole, esomeprazole and lansoprazole were used by 14.75%, 13.11% and 9.83% respectively. Only 53.19% of patients who currently on prescribed PPI treatment received the correct dose and regimen, thus 59.02% of patients were taking a PPI inappropriately. Interestingly, age was found to correlate with better prescribing practice where patients aged ≥75 years had the lowest rates of inappropriate use with the highest percentage of of correct dosage and regimen adherence. Anywhere 47.37% of patients older than 75 years were reported to be on PPI before ED visit, correct dosage regimen was reported among 64.29% of them. The % of PPI inappropriateness was the lowest among patients of this age group while the highest % of PPI

inappropriateness was documented in patients between 18-24 years.

Among patients on prescribed PPI, 22 (46.8%) used their medication by incorrect scheduling and/or dosage, nine had a higher dose, six had a lower dose, two had a higher frequency and five patients had both cases received PPI for GERD treatment, treatment of gastroduodenal ulcer with PPI were documented in 8.19% of patients and in 9.83% of cases on PPI, they

a larger dose with a higher frequency than required. Table 2 showed the use of PPI before ED visit

Regarding the clinical indications related to pre-ED use of PPI, 29.5% of patients take PPI as *H. pylori* eradication therapy, prophylaxis of NSAID induced ulcer documented in 13.11% of the users, 18.03% of used as a prophylaxis of GI ulcers due to GIT surgery while 21.31% of patients used PPI for unrecognized indications.

TABLE II: USED OF PROTON PUMP INHIBITORS (PPI) BEFORE EMERGENCY DEPARTMENT VISIT

Variable	Category	Patients NO.	Used PPI Before ED Visit		Used PPI By Physician Prescription Before ED Visit		PPI Used in Correct Dose and Regimen Before ED Visit		Inappropriate use of PPI	
			NO.	%	NO.	%	No	%	No	%
Gender	Male	123	42	34.15	34	80.95	18	52.94	24	57.14
	Female	65	19	29.23	13	68.42	7	53.85	12	63.16
Age	18-24	29	3	10.34	1	33.33	0	0.00	3	100.00
	25-50	58	14	24.14	9	64.29	3	33.33	11	78.57
	51-75	63	26	41.27	23	88.46	13	56.52	13	50.00
	≥75	38	18	47.37	14	77.78	9	64.29	9	50.00
Past Medication History	NO Medication Used	36	0	0.00	0	0.00	0	0.00	0	0.00
	1-4 Drugs	85	23	27.06	15	65.22	12	80.00	11	47.83
	Polypharmacy	67	38	56.72	16	42.11	13	81.25	25	65.79
Total		188	61	32.45	47	77.05	25	53.19	36	59.02

Treatment throughout ED Visit

Throughout their ED visits, a total of 81 (43.09%) of 188 patients received a PPI as a part of their medical regimen in ED. 78 patients (41.49% of the total) were managed with 1-2 pharmacological agent, 21 (26.92 %) of them received a PPI while 78.26% of patients who managed with more than ten drugs received PPI in ED. Again, omeprazole is the mainstay prescribed medication among this medical class where it used in 91.35% of patients. The remaining 8.64% of patients received esomeprazole. Both agents prescribed to given by IV route of administration. Of the 81 patients who treated with PPI in ED, 19 (23.45%) were already taking a PPI as a part of their standard medical regimen before ED visit. Among patients received PPI in ED,

32 (39.5%) of them were on incorrect scheduling and/or dosage, 11 had incorrect dose and 21 had a higher frequency than required. Table 2 showed the use of PPI during ED visit.

The appropriateness, dosage and regimen correctness were noted to increase with age where 92.86% of patients older than 75 years reported to receive PPI in a correct dosage and regimen and only 7.14% of patient with in this age group used PPI inappropriately.

Drug interactions were documented by evaluating of patients' medical records, it seemed that total 16 (19.75%) of 81 patients who received PPI within ED had PPI drug interaction where the higher % observed among female patients. Individuals between 51-75

years and those on 6-9 drugs in ED had higher frequency of drug interactions. The vast majority of PPI related drug interactions were related to omeprazole use, mainly when it concomitantly used with clopidogrel.

One hundred sixty-three (86.70%) of all included 188 patients were discharged to home, 14 (7.44%) were admitted for more than one day in ED while 11 (5.85%) were admitted to various department of the hospital to received more advanced medical care. Treatment with PPI was maintained in 9 (36%) of all admitted patients as IV route with omeprazole.

TABLE III: USING OF PROTON PUMP INHIBITORS (PPI) DURING EMERGENCY DEPARTMENT VISIT

Variable	Category	NO.	Received PPI in ED		Correct Dose and Regimen of PPI in ED		Inappropriate Use of PPI in ED		PPI Drug-Drug Interactions	
			NO.	%	NO.	%	NO	%	NO	%
Gender	Male	123	64	52.03	38	59.38	26	40.63	11	17.19
	Female	65	17	26.15	11	64.71	6	35.29	5	29.41
Age	18-24	29	14	48.28	10	71.43	4	28.57	0	0.00
	25-50	58	27	46.55	12	44.44	15	55.56	2	7.41
	51-75	63	26	41.27	14	53.85	12	46.15	4	15.38
	≥75	38	14	36.84	13	92.86	1	7.14	10	71.43
Current Medication Prescribed in ED	1-2 Drugs	78	21	26.92	3	14.29	18	85.71	0	0.00
	3-5 Drugs	58	24	41.38	13	54.17	11	45.83	1	4.17
	6-9 Drugs	29	18	62.07	16	88.89	2	11.11	7	38.89
	More than 10 Drugs	23	18	78.26	17	94.44	1	5.56	8	44.44
Total		188	81	43.09	49	60.49	32	39.51	16	19.75

This study has the novelty of studying how PPI, the widely used medical class are prescribed in ED of a major Iraqi hospital. Where this study highlights the prevalent use with the frequent inappropriateness of PPI prescription in this setting.

Currently, this study established that PPI prescribing was higher in male patients than female. Similar finding regarding users' gender documented previously¹⁶.

Formerly, the present study showed that omeprazole was the most commonly used and prescribed drug both in pre and during ED visit. Similar finding regarding omeprazole were documented previously¹⁷⁻¹⁹. While pantoprazole previously documented as the most

widely used in USA for example²⁰. In 2020, a Chinese study carried in outpatients setting indicated that omeprazole was the most broadly used PPI and the PPIs were inappropriately prescribed in half of patients²¹. While our results showed higher percentage of inappropriate prescription in both pre and during ED visit (59.02% and 85.71% respectively) with much higher percentage among PPI prescribed during ED visit. Our finding gives an image of extensive prescription of PPI at excessive high a dose for even unrecognized indications. Where this class of medications was reported as one of misused drugs both at the community and hospital level, similar findings reported formerly in spite of side effects and numerous drug interactions that could developed by excessive

and prolong use²¹⁻²⁴. Studies in primary care and emergency settings suggest that PPIs are frequently prescribed for inappropriate indications or for indications where their use offers little benefit²⁵.

Regarding the clinical indications related to pre-ED use of PPI, current study revealed that the eradication of *H. pylori* is coming in the top where it documented in 29.5% of patients followed by use for prophylaxis of NSAID induced ulcer in 13.11% of the patients, while GERD treatment is coming in the 3ed degree. These results are in contrast of that documented by previous studies where GERD treatment and NASID prophylaxis were more predominant²⁶.

Results regarding prehospital usage of PPI specified that 32.45% of the participants were on PPI prior to their ED visit. By comparing to the results of previous studies such as Lenoir., et al study that carried out in 2019 that showed that 54% of patients were on PPI preadmission. This finding was much higher than that documented in our current study. Same study showed that 29% of patients had treatment with PPI initiated at hospital²⁵, this finding was much lower than that documented in our current study, where our results showed that 43.09% of patient in were on PPI during ED visit. Our results were also higher than observed in other previous study²⁷.

An elevated rate of PPI prescription was documented in our results where there were 77.05% of patients on PPI pre-ED visits used these medications by medical prescription where the remaining percent used them as an OTC or by non-prescription manner. Correspondingly, a previous study showed using PPI as an OTC medications to control GERD symptoms (Sheikh et al., 2014). PPIs have been available as an OTC medication since 2003, and previous data reported a significant amount of off-label PPI use²⁸.

Hospital prescription rates of PPI as one of anti-ulcer medication increased over the last decades²⁹. This explains the high percent pf PPI use that appear in our data results where PPI used for 43.09% of ED visitor patients.

Despite of their widely used as prescribed drugs worldwide, more than half of the prescriptions

indications of PPI were unjustified and the misused of this therapeutic class has substantial consequences such as additional health expenditure²⁶. Additionally, the outcomes of the current study revealed over with inappropriate use and prescriptions of PPI among included patients, these results are parallel with findings of previous studies that also showed frequent inappropriate over prescription of PPI with excessive (16,17,27-29).

Current results indicated that the treatment with PPI was maintained in 9 (36%) of patients who discharged from ED to other hospital settings. Where hospital admitted patients received IV form of PPI (omeprazole). Previous studied documented that patients with frequent hospitalization usually receiving PPIs, often inappropriately³⁰, and patients were maintained on these medications following discharge in the everyday medication schedule even when introducing this treatment during the ED visit, that could be explained by the possibility of development of rebound acid hypersecretion later to cessation of PPI therapy that in turn leading to the recurrence of gastric symptoms and thus to drug dependency, hence, PPI overuse raises, this in addition to using PPI as an OTC medication for relieving GERD symptoms in about 32% of population as documented by previous study²⁵.

Currently, our data showed the possibility of PPI related drug interactions were reported among 19.75% of patients who received PPI during the current ED visit. There is an increase in the rate of possible D-D interactions with both increases patients age and the number of received medications within ED visit where the highest percent (71.43%, 44.44%) observed among patients older than 75 year and those who admitted with more than ten medications respectively. Similar finding was reported by previously where there were concerns about the potential risks especially in the elderly patients who affected by multiple comorbidities and taking multiple medications. Although using of PPI treatment in a short course pattern, such as those prescribed during ED visit, have not been linked to an adverse events or drug interactions. Regarding the cardiovascular risk, the concomitant use of clopidogrel and PPIs has been specifically investigated in several studies as

clopidogrel and PPIs are both metabolized by the cytochrome P450 isoenzyme 2C19, leading to drug–drug interaction due to competition at the binding site³¹.

IV. CONCLUSION

According to the data, there were over prescription of PPI both pre and throughout ED visit with an elevated percent of inappropriate use in both settings.

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