

Use of Proton Pump Inhibitors: An Exploration of Awareness and Practice of Health Care Professionals of Tharparkar District

Pardeep Kumar¹, Swaleha Tariq Bhombal², Sawairah Mukhtiar³, Aiman Ahsan³, Uzair Abbas^{4*} and Anmol⁵

¹Department of Family Medicine, Jinnah Sindh Medical University, Karachi, Pakistan

²Department of Family Medicine, Aga Khan University Hospital, Karachi, Pakistan

³Dow International Medical College, Dow University of Health Sciences, Karachi, Pakistan

⁴Department of Physiology, Dow University of Health Sciences, Karachi, Pakistan

⁵Liaquat University Hospital, Hyderabad, Pakistan

ABSTRACT

Background: Proton Pump Inhibitors (PPIs) are commonly prescribed drugs and their inadequate prescription can have adverse outcomes. Multiple factors are responsible for inappropriate use of PPIs including self-medication, less knowledge about PPIs in medical staff, and consumer-oriented advertising.

Objective: To assess the knowledge and practices about PPI use among Physicians in Tharparkar District of Sindh province, Pakistan.

Methods: This is a cross Sectional study that was done in the rural hospitals (Basic Health Unit, Rural Health Centre, Talukka, and District Hospital) in Tharparkar District Sindh. The study took place for 6 months from October 13, 2019, to April 12, 2020. All PMC licensed Physicians working in district Tharparkar for at least 6 months were consecutively enrolled. Knowledge questions comprised of questions about PPI and their indication and side effects while practice questions such as indication, route, and duration of action were asked. All participants were classified as having adequate knowledge and adequate practice based on the correct answer to each question. The study included PMC-licensed physicians with one-year internship/ house job experience and Physicians who had worked at district Tharparkar in a rural setting for at least 6 months. Physicians who did not give consent were excluded from the study.

Results: Of 102 practitioners, the mean age of the participants was 39.57 ±9.14 years. The majority of the practitioners were males (n=82, 80.4%). Most of the practitioners (n=66, 65%) were working in district hospitals, 21 (19.6%) in rural health centers, and 15 (14.7%) in basic health units. Adequate knowledge was observed in 34 (33.3%) while adequate practice in 33 (32.4%) participants.

Conclusion: The knowledge and practices about Proton Pump Inhibitor (PPI) use were found to be unsatisfactory among Physicians working at Tharparkar.

Keywords: Health care professionals, knowledge, practices, Proton Pump Inhibitor (PPI).

INTRODUCTION

Proton Pump Inhibitors (PPIs) are a class of medications that cause a significant and sustained decrease in gastric acid production as their principal effect [1]. Proton pump inhibitors (PPIs) were developed in the late 1980s, and their introduction has greatly revolutionized medical management for illnesses related to acid disorders [2]. Numerous drugs were created to target the parietal cell to prevent acid production because it was recognized that the parietal cell secreted gastric acid. The PPIs, which target the parietal cell H⁺/K⁺ ATPase enzyme, were first launched in 1989 to treat peptic ulcer disease and GERD, the lesions healed more quickly and the symptoms were alleviated. PPIs are the most common and widely used drugs around the globe [3]. Omeprazole, a PPI, was prescribed more than 70 million times in the United States in 2016, and 1 in 10 patients with ambulatory care visits in the country in 2009 had a history of PPI usage. PPI formulations for over-the-

counter use have been accessible since 2003 for the temporary relief of persistent heartburn [4]. A 14-year follow-up analysis of PPI consumption trends revealed that PPI administration has increased and become more common over the years [5]. PPI is a type of drug that irreversibly blocks the enzyme H⁺/K⁺ ATPase, this enzyme serves as the final step of acid secretion into the stomach. They covalently bind to one or more of the cysteine residues of the H⁺/K⁺-ATPase proton pumps, rendering the pumps nonfunctional until new ones are synthesized [6]. Indications of PPIs are Peptic Ulcer Disease (PUD) including gastric and duodenal ulcers, eradication of *Helicobacter pylori* (frequently in conjunction with antibacterial), Dyspepsia, Gastroesophageal reflux disease (GERD), and the prevention and treatment of ulcers linked to NSAIDs. (1) PPIs are supposed to be relatively safe and beneficial [7]. Studies in different healthcare setups report that PPIs are frequently prescribed for inappropriate indications. In hospitalized patients, PPIs are frequently prescribed without indication and are also continued even after being discharged [8]. A study conducted in a tertiary care hospital in Switzerland concluded unjustified prescription

*Corresponding author: Uzair Abbas, Department of Physiology, Dow University of Health Sciences, Karachi, Pakistan, E-mail: uzair.abbas@duhs.edu.pk

Received: February 02, 2023; Revised: April 19, 2023; Accepted: April 28, 2023

DOI: <https://doi.org/10.37184/lnjpc.2707-3521.5.32>

of PPIs in 72% of patients and only 11% had a justified indication with appropriate dose [9]. Practitioners are prescribing PPIs for prolonged, and sometimes for a lifetime which is leading to the growing concern for the potential adverse effects [10]. Short-time usage of PPIs has side effects like headache, rash, dizziness, and gastrointestinal symptoms including nausea, abdominal pain, flatulence, constipation, and diarrhea [11]. There are multiple side effects due to long-term usage of PPIs, in recent studies, researchers advised that PPIs should be used for a short period of time and at a minimum effective dose [12], as infections, impaired absorption of nutrients like vitamin B12, iron, and calcium, dementia, kidney diseases, hepatocellular carcinoma, musculoskeletal problems, and hyper-gastrinemia related side effects are emerging as possible consequences of long-term use [13, 14]. A study conducted among patients admitted in a tertiary care hospital in Karachi Pakistan showed 66.2% of patients were receiving PPI without any specific indication while only 33.8% of patients were receiving PPI with appropriate indications suggesting overuse of PPIs among admitted patients [15]. Studies on the knowledge, attitudes, and practices of physicians regarding the appropriate use of PPIs are relatively insufficient in Pakistan, especially in rural areas of Sindh, so this study was conducted to know the knowledge and practice of PPI use by physicians of Tharparkar district of Pakistan.

MATERIALS AND METHODS

This is a cross-sectional study that took place in rural hospitals (Basic Health Unit, Rural Health Centre, Talukka, and District Hospital) in Tharparkar, Sindh. A purposive sampling technique was used. The Sample size was calculated by the WHO sample size calculator and came out to be 102. From the literature, we found the proportion of prescribing PPI was 15.2% [16]. The confidence interval was 95% and the margin of error was 7%.

The study included PMC licensed Internal medicine physicians with one-year internship/housejob experience and Physicians who had worked at district Tharparkar in a rural setting for at least 6 months. Whereas Physicians who did not give consent were excluded from the study. The study was approved by the Ethical Review Committee of the Aga Khan University Hospital. It was followed by written informed consent taken from the participants. The study involved giving out a self-made questionnaire in paper form, which comprised 3 sections A, B, and C. It was self-administered to reduce the chance of bias and after its completion, the participants were given reading materials for further enhancement of knowledge.

- 1) **Section A: Demographic details:** Age, gender, qualification, specialty, hospital, years since medical graduation, and years of clinical experience.

- 2) **Section B: Knowledge questions about PPI and their indications, and side effects.** The total number of questions was 06. The response type is a few words or sentences. Each correct answer was scored '1' and the incorrect answer was scored '0' respectively, hence scoring less than 04 (*i.e.* $4/6 = 66.7\%$) was marked as having inadequate knowledge about PPI. The 6 questions were: mechanism of action of PPI, Part of Gastrointestinal affected by PPI, most common indication, superiority among anti-secretory agents, malabsorption of nutrients due to PPI, and cost-hierarchy of anti-secretory agents.
- 3) **Section C: Questions regarding the practice of PPI, indication, route, and duration of action.** There were 8 questions in total: PPI prescribed by Physician, reading of package insert before prescribing, perceived indications for PPI prescription, preferred PPI by a physician, preferred route of administration, duration of the prescription, an adverse effect seen, and co-prescription of PPI with other drugs. Here, only Q#3 was used to determine the adequacy of practice out of the 8 total questions, whereas the remaining 7 were about prescription preference. Q#3 assessed prescribing PPI according to the approved indication for PPI use. A '1' mark was given for the correct indication selected; the total score was 8. A minimum of 5 out of 8 scores (*i.e.* $5/8 = 62.5\%$) is marked as adequate practice.

DATA ANALYSIS

The SPSS version 19 was used for data entry and analysis. The mean and standard deviation of age and years since medical graduation was calculated. Proportions were reported for gender, qualification, and hospital. Frequencies of all knowledge and practice questions were calculated. Lastly, results were stratified based on effect modifiers such as age, gender, years of clinical experience, and qualification.

RESULTS

A total of 102 participants were included in this study. Table 1 shows the demographic characteristics of the

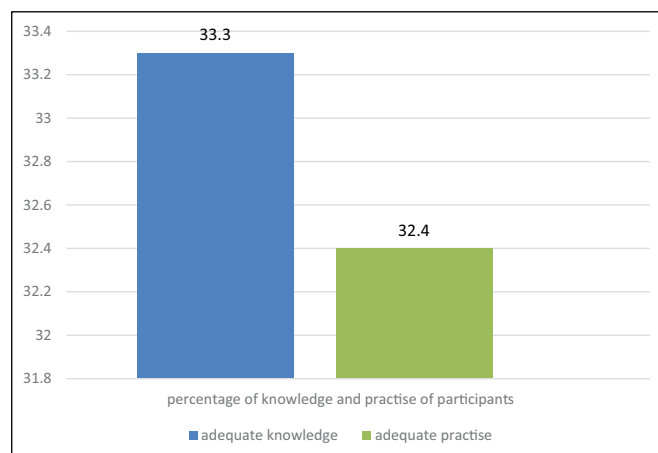


Fig. (1): Knowledge and practice level of the participants (n=102).

study population. 55% of participants were less than 40 years of age and 45% were more than 40 years of age. The majority of the participants were males (80%). Half of the participants (50%) had their graduation for 15 years and half of them had more than 15 years of education. The majority (53%) had more than 1 year of clinical experience (Fig. 1).

Table 1: Demographic profile of participants (n=102).

Variable	Frequency	Percent (%)	Mean ± SD
Age			
<40 years	56	54.9	39.57 ± 9.14
>40 years	46	45.1	
Gender			
Male	82	80.4	-
Female	20	19.6	
Years since graduation			
<15 years	51	50	15.33 ± 8.56
>15 years	51	50	
Qualification			
MBBS + 1-year house-job	84	82.4	-
Post-graduation	18	17.6	
Clinical experience			
<13 years	48	47.1	13.74 ± 8.02
>13 years	54	52.9	
Working in hospital			
Basic health unit	15	14.7	-
Rural health center	21	19.6	
District hospital	66	65	

Regarding the knowledge of PPIs as mentioned in Table 2, the majority of the participants were aware of the mechanism of action of PPIs (78%). The most common indication for prescribing PPIs was functional dyspepsia (48%) followed by GERD (25%). The majority (89%) of them knew that PPIs have superior anti-secretory properties.

Table 2: Knowledge of PPIs (n=102).

Variable	Frequency	Percent (%)
Mechanism of action of PPIs		
Inhibit the H ⁺ /K ⁺ ATPase pump	80	78.4
Inhibit gastrin release	18	17.6
Don't know	4	4
PPIs affect which part of the GIT		
Stomach	96	94.1
Esophagus	5	4.9
Liver	1	1
Small intestine	-	-
The most common indication for PPIs		
Functional dyspepsia	49	48
Eradication of H.pylori	15	14.7
GERD	25	25
Upper GI bleeding	2	2
Gastritis	11	10.8
Superior anti-secretory agent		
PPIs	91	89.2
Histamine H2 receptor antagonist (H2RA)	5	4.9
	-	-

Variable	Frequency	Percent (%)
Antacid	6	6
PPIs decrease the absorption of		
Vitamin B12	41	40.2
Iron	11	10.8
Calcium	8	8
Magnesium	4	3.9
All of the above	38	37.3
Cheaper anti-secretory agents		
PPIs	29	28.4
H2RA	3	2.9
Antacid	70	69

Regarding the practices for prescribing as mentioned in Table 3, the majority of the participants (90%) prescribe PPIs. The most common conditions for prescribing included Gastric ulcer, GERD, Dyspepsia, Duodenal ulcer, Eradication of H Pylori, and prevention and treatment of NSAID-induced gastritis. Diarrhea and nausea/vomiting were the most common adverse effects seen by them.

Table 3: Practice regarding PPIs (n=102).

Variable	Frequency	Percent (%)
Do you prescribe PPIs		
Yes	92	90.2
No	10	9.8
Do you read the package insert before prescribing		
Yes	33	32.4
No	28	27.5
Sometimes	41	40
For which of the following condition you prescribed PPI (multiple answers can be selected)		
Gastric ulcer	74	72.5
Duodenal ulcer	56	54.9
Eradication of H.pylori	59	58
Severe peptic ulcer bleeding (following endoscopic treatment)	45	44.1
Dyspepsia	52	51
GERD	69	67.6
Prevention and treatment of NSAID-associated ulcer	41	40.2
Zollinger Ellison Syndrome	17	16.7
PPIs generation of drugs preferably prescribed		
Omeprazole	69	67.6
Esomeprazole	24	23.5
Pantoprazole	-	-
Lansoprazole	9	9
The most common route of administration preferred		
Oral	99	97.1
Intravenous (IV)	3	2.9
Intramuscular (IM)	-	-
For how long do you prescribe PPIs		
<1 week	1	1
1-2 weeks	21	20.6
2-4 weeks	74	73
4-6 weeks	6	5.9
6-12 months	-	-
Any adverse effects noticed		
Rash/Hypersensitivity	1	1

Variable	Frequency	Percent (%)
Nausea/Vomiting	21	20.6
Diarrhea	74	73
None	6	5.9
With which drugs PPIs were prescribed		
NSAIDS	71	69.6
Aspirin	18	17.6
Clopidogrel	13	13

DISCUSSION

Previously there had been research in urban areas regarding physician's knowledge and practice of PPIs but there are lesser studies done in a rural setting, whereas it is well known that a greater population resides in rural areas in Pakistan. This study was done with the help of a self-generated questionnaire given to licensed physicians that included questions regarding knowledge and clinical use of PPIs.

Regarding clinical use, our study concluded that the participants with adequate practice with PPI were 32.4%. Among various studies done across the world, one study by Eid *et al.* was done with 400 PPI prescriptions to check how many physicians were compliant with the guidelines. It was concluded that 39% were compliant and the remaining 61% were guideline non-compliant. It was further known that most of the compliant population were from academic hospitals [17]. Hence proving, that the data collection and study of knowledge and practice in rural hospitals is of extreme importance. Moreover, there was an observational cohort study by Burdsall *et al.* depicted that 79.7% were prescribed PPI of which 52% of the patient had no appropriate diagnosis for PPI use [18]. Furthermore, a retrospective study showed that the overall prevalence of potentially inappropriate prescription (PIP) in the study population (n=166,108) was 34% of which (11%) were proton pump inhibitors given at maximum therapeutic dose for > 8 weeks [19]. A retrospective cross-sectional study depicted that 216 (54%) cases were on PPI medication and their indications included acute gastritis (4%), GERD (5%), preoperative medication (11%), and along with NSAIDS (24%) but a vast majority (56%) of PPI prescriptions had no clear indication [20]. This enormous number leaves a huge question mark as to why was PPI given without any indication.

Our study found that only 33.3% of physicians had sufficient knowledge of PPI. Likewise, a study conducted in Emergency care set up in India stated that knowledge about PPI-related adverse effects among physicians was low and ranged from 10% to 44% [21]. Similarly, research that was conducted in Pakistan concluded that only 49% of the physicians had a licensed clinical indication whereas 51% had no definite indications, and of which 34% were bought over the counter (OTC) [22]. Another cross-sectional survey of the appropriateness of PPI prescription was conducted in Karachi among the inpatient population, The study showed that

among 288 patients admitted during the survey period, intravenous(IV) PPIs were given in 86 patients and among them only 19 (22.9%) patients were justified for receiving IV PPI. Meanwhile, the remaining 65 patients (75.5%) were inappropriately given [23].

Among various PPIs, Omeprazole is the most frequently used OTC drug and is usually self-medicated [24]. In our study, the majority of the participants reported gastric ulcer as the most common reason for prescribing PPI, followed by GERD, eradication of H. pylori, and duodenal ulcer. In 2 similar studies, it was reported that acute gastritis and stomach protection were the most common indication followed by stress ulcer prophylaxis, GERD, and the use of NSAIDS [25, 26]. Our study depicts that 73% of the participants had been prescribed PPI for 2-4 weeks, comparatively longer than a previous study that prescribed it for 1-2 weeks. (25) Safety of PPIs is also essential and is well documented; some studies confirmed that it could be limited to taken once daily [27, 28]. Furthermore, it is also stated that it is safe to take PPIs for a short term up to 14–28 days without referring to a specialized physician albeit more research should be done to affirm it. Prescribing medicines without adequate knowledge and practice is ethically and socially hazardous. This indicates that a large proportion of physicians are still prescribing PPIs inappropriately, which can lead to potential harm to patients. The overuse of PPIs is a growing concern worldwide, and efforts should be made to promote the rational use of PPIs. Hence there is a need for educational programs and training for rural physicians to enhance their knowledge and understanding of PPIs. Physicians should be encouraged to follow evidence-based guidelines and make informed decisions based on the patient's condition and history to minimize the risks associated with PPIs.

The study identified several gaps in the knowledge and practice of PPIs among rural physicians in Pakistan. Further research is needed to explore the reasons behind inappropriate prescribing practices, develop effective interventions to promote the rational use of PPIs and investigate the long-term effects of PPI therapy.

Study limitations- our study was linked to one district of Pakistan and doesn't represent the knowledge and practice of the province. As the literacy rate is increasing with time, knowledge and practice may see a potential rise in number.

CONCLUSION

The findings of this study concluded that knowledge and practices about PPI among physicians working at Tharparkar were found to be unsatisfactory. Hence, dire work is needed to promote awareness and avoid PPI misuse. It is suggested that several fundamental keystones like carrying out periodic training about PPI rational use and emphasizing the pharmacist's role in stopping PPI sales without prescription are pivotal.

In addition, it is also crucial to offer special courses to medical, pharmaceutical, and nursing students, which emphasize the specific behavior of rational PPI use.

ETHICS APPROVAL

This study was approved by the Ethical Review Committee of the Aga Khan University Karachi. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the Helsinki Declaration.

CONSENT FOR PUBLICATION

Written informed consent was taken from the participants.

AVAILABILITY OF DATA

The datasets are available with the corresponding author.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

We acknowledge all the medical practitioners of tharparkar district for their participation in the study."

AUTHORS' CONTRIBUTION

All the authors contributed equally to the publication of this article.

REFERENCES

- Association BM. British National Formulary Basingstoke, UK: Pharmaceutical Press; 59th Revised Edition March 2010.
- Wolfe MM. Proton pump inhibitors: Overview of use and adverse effects in the treatment of acid related disorders. Available from: <https://www.uptodate.com/contents/proton-pump-inhibitors-overview-of-use-and-adverse-effects-in-the-treatment-of-acid-related-disorders>
- Vakil N. Prescribing proton pump inhibitors. *Drugs* 2012; 72(4): 437-45. DOI: <https://doi.org/10.2165/11599320-000000000-00000>
- Hayes KN, Nakhla NR, Tadrous M. Further evidence to monitor long-term proton pump inhibitor use. *JAMA Netw Open* 2019; 2(11): e1916184. DOI: <https://doi.org/10.1001/jamanetworkopen.2019.16184>
- Torres-Bondía F, de Batlle J, Galván L, Buti M, Barbé F, Piñol-Ripoll G. Evolution of the consumption trend of proton pump inhibitors in the Lleida Health Region between 2002 and 2015. *BMC Public Health* 2022; 22(1): 818. DOI: <https://doi.org/10.1186/s12889-022-13217-6>
- El Rouby N, Lima JJ, Johnson JA. Proton pump inhibitors: from CYP2C19 pharmacogenetics to precision medicine. *Expert Opin Drug Metab Toxicol* 2018; 14(4): 447-60. DOI: <https://doi.org/10.1080/17425255.2018.1461835>
- Kinoshita Y, Ishimura N, Ishihara S. Advantages and disadvantages of long-term proton pump inhibitor use. *J Neurogastroenterol Motil* 2018; 24(2): 182-96. DOI: <https://doi.org/10.5056/jnm18001>
- Dharmarajan TS. The use and misuse of proton pump inhibitors: an opportunity for deprescribing. *J Am Med Dir Assoc* 2021; 22(1): 15-22. DOI: <https://doi.org/10.1016/j.jamda.2020.09.046>
- Lenoir C, El Biali M, Luthy C, Groscurin O, Desmeules JA, Rollason V. Snapshot of proton pump inhibitors prescriptions in a tertiary care hospital in Switzerland: less is more? *Int J Clin Pharm* 2019; 41(6): 1634-41. DOI: <https://doi.org/10.1007/s11096-019-00929-w>
- Scarpignato C, Gatta L, Zullo A, Blandizzi C, Scarpignato C, Blandizzi C, *et al.* Effective and safe proton pump inhibitor therapy in acid-related diseases – A position paper addressing benefits and potential harms of acid suppression. *BMC Med* 2016; 14(1): 179. DOI: <https://doi.org/10.1186/s12916-016-0718-z>
- Haastrup PF, Thompson W, Søndergaard J, Jarbøl DE. Side effects of long-term proton pump inhibitor use: a review. *Basic Clin Pharmacol Toxicol* 2018; 123(2): 114-21. DOI: <https://doi.org/10.1111/bcpt.13023>
- Song HJ, Jiang X, Henry L, Nguyen MH, Park H. Proton pump inhibitors and risk of liver cancer and mortality in patients with chronic liver disease: a systematic review and meta-analysis. *Eur J Clin Pharmacol* 2020; 76(6): 851-66. DOI: <https://doi.org/10.1007/s00228-020-02854-8>
- Yibirin M, De Oliveira D, Valera R, Plitt AE, Lutgen S. Adverse effects associated with proton pump inhibitor use. *Cureus* 2021; 13(1): e12759. DOI: <https://doi.org/10.7759/cureus.12759>
- Castellana C, Pecere S, Furnari M, *et al.* Side effects of long-term use of proton pump inhibitors: practical considerations. *Pol Arch Intern Med* 2021; 131: 541-9. doi:10.20452/pamw.15997
- Samar R, Ali SA, Samar V, Mushtaq MZ, Humayun A. SHORT COMMUNICATION-Inappropriate use of proton pump inhibitor for stress ulcer prophylaxis in a tertiary care hospital in Karachi, Pakistan. *Pak J Pharm Sci* 2021; 34(6): 2253-5.
- Alnabulsi RK, Jambi RO, Dhabab N, Alsubahi T, Basheikh M, Kamel FO, *et al.* Physician's practice toward and knowledge about proton pump inhibitor prescription in Jeddah, Saudi Arabia. *Int Ann Med*. 2018; 2: 8. DOI: <https://doi.org/10.24087/IAM.2018.2.6.517>
- Eid SM, Boueiz A, Paranj S, Mativo C, Landis R, Abougergi MS. Patterns and predictors of proton pump inhibitor overuse among academic and non-academic hospitalists. *Int Med* 2010; 49(23): 2561-8. DOI: <https://doi.org/10.2169/internalmedicine.49.4064>
- Patterson Burdsall D, Flores HC, Krueger J, Garretson S, Gorbien MJ, Iacch A, *et al.* Use of proton pump inhibitors with lack of diagnostic indications in 22 Midwestern US skilled nursing facilities. *J Am Med Dir Assoc* 2013; 14(6): 429-32 DOI: <https://doi.org/10.1016/j.jamda.2013.01.021>
- Bradley MC, Fahey T, Cahir C, Bennett K, O'Reilly D, Parsons C, *et al.* Potentially inappropriate prescribing and cost outcomes for older people: a cross-sectional study using the Northern Ireland enhanced prescribing database. *Eur J Clin Pharmacol* 2012; 68(10): 1425-33. DOI: <https://doi.org/10.1007/s00228-012-1249-y>
- Patil R, Aithal S, Hooli TV, Hv V. Drug utilisation study of proton pumps inhibitors in inpatients of a tertiary care hospital: a cross-sectional study. *Natl J Integr Res Med* 2015; 6: 62-5.
- Padhy BM, Bhadauria HS, Gupta YK. Attitude and knowledge of Indian emergency care residents towards use of proton pump inhibitors. *Int Sch Res Notices* 2014; 2014: 968430. DOI: <https://doi.org/10.1155%2F2014%2F968430>
- Shafi S, Soomro R, Abbas S. Proton pump inhibitors - over-prescribed in a rural community? *Pak J Med Sci* 2011; 27(2): 300-2.
- Naqvi SHA, Saqib SM, Khan WA, Syed IAA. Rising use of proton pump inhibitors: a Karachi perspective. *Sci Int (Lahore)* 2014; 26(5): 1941-4.
- Chen J, Yuan YC, Leontiadis GI, Howden CW. Recent safety concerns with proton pump inhibitors. *J Clin Gastroenterol* 2012; 46(2): 93-114. DOI: <https://doi.org/10.1097/mcg.0b013e3182333820>
- Alhossan A, Alrabiah Z, Alghadeer S, Bablghaith S, Wajid S, Al-Arifi M. Attitude and knowledge of Saudi community pharmacists towards use of proton pump inhibitors. *Saudi Pharm J* 2019; 27(2): 225-8. DOI: <https://doi.org/10.1016/j.jpsps.2018.11.002>

26. Nawas GT, Nawas T, Malaeb D, Helou SE, Hallit S. Assessing the appropriate use of proton pump inhibitors amongst the outpatient Lebanese population. *Int J Curr Microbiol App Sci* 2016; 5(10): 767-77. DOI: <http://dx.doi.org/10.20546/ijcmas.2016.510.083>
27. Gawron AJ, Pandolfino JE, Miskevics S, Lavela SL. Proton pump inhibitor prescriptions and subsequent use in US veterans diagnosed with gastroesophageal reflux disease. *J Gen Intern Med* 2013; 28(7): 930-7. DOI: <https://doi.org/10.1007/s11606-013-2345-0>
28. Boardman HF, Heeley G. The role of the pharmacist in the selection and use of over-the-counter proton-pump inhibitors. *Int J Clin Pharm*. 2015; 37(5): 709-16. DOI: <https://doi.org/10.1007/s11096-015-0150-z>