



# Epidemiological Study Assessing the Overuse of Proton Pump Inhibitors in Lebanese Population

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Received: 01 May 2020  
Accepted: 09 Sep. 2020

## ABSTRACT

### BACKGROUND

Proton pump inhibitors (PPIs) are the most potent gastric agents for most acid-related disorders. Their effectiveness has led to their overutilization, leading to potential risks on patients and significant economic implications.

The aim of this study was to determine the frequency of PPI overuse in Lebanon. Hence, the economic impact of this overutilization, if proven to be present, can be inferred.

### METHODS

An epidemiological descriptive cross-sectional study was conducted in pharmacies all around Lebanese governorates over a 1-year period, using questionnaires handed out to 1000 participants coming to buy PPIs. Subjects taking PPIs for inappropriate indications or in inappropriate dosages or durations were considered abusing PPIs. PPIs are indicated for multiple gastric disorders and for prophylaxis of gastrointestinal injury when taking gastro-toxic medications.

### RESULTS

71.4% of subjects were overusing PPIs. Approximately 25 million US dollars were being wasted annually. Three categories of overuse were inferred (indication, dosage, and duration). Gastro protection was the most common reason for taking PPIs. Demographic variables and doctors' prescriptions did not influence PPI overuse.

### CONCLUSION

PPIs are massively overused in Lebanon, leading to a huge burden on the health care system. Adhering to evidence-based guidelines and educational programs is highly recommended to enhance the quality and efficiency of prescriptions.

### KEYWORDS:

Protons pump inhibitors, Inappropriate prescribing, Patients, Risk, Pharmacies.

Please cite this paper as:

Hoteit M, Mattar E, Allaw R, Abou Rached A. Epidemiological Study Assessing the Overuse of Proton Pump Inhibitors in Lebanese Population. *Middle East J Dig Dis* 2020;12:265-270. doi: 10.34172/mejdd.2020.192.

## INTRODUCTION

Proton pump inhibitors (PPIs) are currently favored over other gastric acid-suppressive medications because of their high efficacy, good tolerance, safety profile, and affordable costs with both original and generic preparations. Thus, they have been adopted worldwide among primary care providers and their presence is ubiquitous within the armamentarium of the modern gastroenterologist.<sup>1</sup>

However, the effectiveness of PPIs has led to their overutilization in



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multiple treatment arenas.<sup>2</sup> In many countries, PPIs have been among the top ten best-selling medicines for several years.<sup>3</sup> In Lebanon, approximately 36 million dollars were spent on PPIs in 2018.<sup>4</sup>

A growing number of publications worldwide show concerns about the appropriate use of PPIs, proving that they are being overprescribed globally.<sup>3</sup> Such an ample overuse of PPIs raises concerns about high costs and potential side effects due to long term treatment.

In Lebanon, no similar data is available regarding this issue. Therefore, our study aims to determine the frequency of patients overusing PPIs in Lebanon to further clarify the picture of unnecessary prescriptions. Moreover, we suspect that this practice leads to preventable and significant cost expenditure and may place patients at an increased risk for potential adverse events due to non-indicated PPI therapy if the latter was proved to be present.

## MATERIALS AND METHODS

### Subjects and data collection

An epidemiological descriptive cross-sectional study was carried out over a 1-year period from October 2017 to October 2018. A total of 1000 participants aged above 18 years, with no specific race or sex, coming to buy PPIs from pharmacies were randomly selected and asked to fill a questionnaire about their PPI use with the help of the pharmacists in charge. Questionnaires, which included 15 questions alternating between open and closed questions, were used to collect demographics (age, sex, level of education, place of residency) and clinical variables (the type of PPI used, indication of use, duration of treatment, dosage, and concomitant use of gastro-toxic drugs). They were distributed to a total of 50 pharmacies dispersed all over the six Lebanese governorates. The number of participants for each governorate was chosen to be proportional to the size of the population in each governorate to get a truly representative sample of the Lebanese population. The participants signed a consent form to approve, giving us confidential information and allowing us to use it in our study.

### Data analysis:

PPIs are indicated for multiple gastrointestinal (GI) disorders and should be administered in an appropriate

dosage and for an adequate duration. We have relied on evidence-based guidelines to specify PPI indication along with the duration of use and dosage for each. Hence, we have considered the following listed disorders as indications for PPI use in our study: reflux disease,<sup>1</sup> peptic ulcer disease,<sup>1</sup> *Helicobacter pylori* (*H. pylori*) infection in combination with antibiotics,<sup>1</sup> dyspepsia,<sup>1</sup> hiatal hernia,<sup>5</sup> Barret esophagus,<sup>5</sup> erosive esophagitis,<sup>1</sup> treatment and prophylaxis of non-steroidal anti-inflammatory drugs (NSAIDs),<sup>1,6</sup> and acetylsalicylic acid<sup>6</sup> associated GI injury, and prophylaxis of GI injury for patients taking corticosteroids in case of a history of upper GI bleeding (GIB).<sup>7</sup>

The data were analyzed using a statistical software that was developed using Microsoft visual studio 2015. The percentage of PPI abusers from our total sample size (n = 1000) was calculated, as well as the percentage of overuse according to different parameters (e.g., age, sex, level of education, place of residency). Furthermore, the overuse was classified into three categories (overuse of indication, dosage, and duration).

The statistical software IBM SPSS statistics, version 21.0 was used. Categorical variables were summarized by frequency and percentage, and the one-way ANOVA test was applied to prove a significant association between two categorical variables. A *p* value of less than 0.05 was considered statistically significant.

## RESULTS

### Baseline characteristics

A total of 1000 participants taking PPIs were included in this study. The mean age was 55 years (minimum: 18 – maximum: 98), and the sex ratio (male/female) was 0.91 (Table 1). The level of education was less than a high school diploma in 42.4%, high school diploma in 21.3%, and university degrees and higher studies in 36.3% (Table 1). The number of participants for every governorate is represented in table 1, and it was proportional to the true population in each governorate. Omeprazole was the most widely used drug, accounting for 42.6% of the total PPI prescriptions. More than half of our study population was taking PPIs for gastroprotection (53.7%) (Table 2). Only 10.8% were taking PPIs as an auto-prescription or following the advice of a certain person, while 89.2%

**Table 1: Baseline characteristics and the overuse distribution in number and percentage**

Variables	Group	Total	Abuse	Abuse % Per group	Abuse % in overusing sample	p values
Age Group	< 20	15	8	53.33%	1.12%	0.872
	20-30	94	66	70.21%	9.24%	
	30-40	129	85	65.89%	11.90%	
	40-50	134	105	78.36%	14.71%	
	50-60	180	146	81.11%	20.45%	
	60-70	178	127	71.35%	17.79%	
	70-80	145	89	61.38%	12.46%	
	80-90	110	77	70.00%	10.78%	
	> 90	15	11	73.33%	1.54%	
Sex	Female	527	389	73.81%	54.48%	0.086
	Male	473	325	68.71%	45.52%	
Location	Baalabek-Hermel & Bequaa	190	129	67.89%	18.07%	0.403
	Beirut	80	57	71.25%	7.98%	
	Mount Lebanon	340	250	73.53%	35.01%	
	Nabatieh	70	56	80.00%	7.84%	
	North Lebanon & Akkar	220	152	69.09%	21.29%	
	South Lebanon	100	70	70.00%	9.80%	
Education	Less than a high school diploma	424	289	68.16%	40.48%	0.195
	High school diploma	213	155	72.77%	21.71%	
	Higher studies & university diploma	363	270	74.38%	37.82%	
Prescribed by physicians	Yes	714	633	88.66%	88.66%	-
	No	286	259	90.56%	36.27%	

**Table 2: Reasons mentioned by subjects for taking proton pump inhibitors and the distribution of overuse in each**

Reasons	Total	Abuse	Abuse % per reason	Abuse % per total overusing sample
Dyspepsia	91	73	80.22%	10.22%
Epigastric pain	72	67	93.06%	9.38%
Gastro protection	537	414	77.09%	57.98%
Peptic ulcer disease	113	78	69.03%	10.92%
Reflux	117	29	24.79%	4.06%
Other*	70	53	75.71%	7.42%

\* Other reasons: abdominal pain, Barrett esophagus, dysphagia, erosive esophagitis, gastric cancer, gastroenteritis, H. pylori infection, hemorrhoids, hiatal hernia, irritable bowel syndrome, liver cirrhosis, polypharmacy, post-hospital discharge, and post-sleeve gastrectomy.

took PPIs following a doctor's prescription (Table 1). Gastroenterologists and cardiologists were the two most common specialists to prescribe PPIs, accounting for 37% and 26% of the doctors' prescriptions, respectively.

#### Overuse percentage and distribution according to different characteristics

The total overuse was calculated to be 71.4% of the patients taking PPI. 59.2%, 22.1%, and 18.7% of the patients were taking PPIs with overuse of indication, overuse of duration, and overuse of dosage, respectively. The latter was further subdivided into two categories (Table 3). No significant difference in the overuse distribution was found between sexes ( $p = 0.086$ ), age groups ( $p = 0.872$ ),

levels of education ( $p = 0.195$ ), and governorates ( $p = 0.403$ ) (Table 1). We found that patients abusing PPIs following a physician's prescription and auto-medication were 70.96% and 75%, respectively (Table 1). The overuse of PPI was similar among gastroenterologists and other specialties, as the overuse percentage, in each of these two groups, accounted for 69.79% and 71.66%, respectively. There was no indication for PPI use as gastroprotection in 77% of cases (Table 2).

#### Estimation of potential costs of PPI overuse in Lebanon

In Lebanon, approximately 36 million dollars were spent on PPIs in 2018. Our study showed 71.4% of overuse. Hence, an estimate of 25 million dollars is being wasted yearly in Lebanon on PPIs.

#### DISCUSSION

In recent years, there has been a significant increase worldwide in the number of publications covering the topic of overuse of PPIs in both the inpatient and outpatient settings proving that PPIs are being overprescribed globally.<sup>3</sup>

Our study surveyed participants from all over the six Lebanese governorates to assess the frequency of PPIs overuse in the outpatient setting in Lebanon. The results showed that 71.4% of the study population are overusing PPIs. For instance, a PubMed literature search on 'proton pump inhibitor overuse' showed that the ballpark figure for inappropriate PPI use ranged from 40% to 81%, with a mean of 63%.<sup>8</sup> In our study sample, most of the participants were taking PPIs for gastroprotection. According to an expert consensus,<sup>6</sup> PPIs are the preferred drugs for the treatment and prophylaxis of NSAIDs- and acetylsalicylic acid-associated GI injury, taking into account the patients' risk factors and medical illnesses. The approach suggested in this consensus was applied in our study. As a result, we found out that among the 537 participants taking PPIs for gastroprotection, 414 participants (77%) were abusing them. Similarly, a study done by Rotman and colleagues assessing PPI use in the ambulatory setting in the United States found that 62.9% of PPI users had no documented GI diagnosis/complaints or other appropriate indications.<sup>9</sup> Another study done by Ntaios and co-workers showed that PPIs were taken by 25.4% of hospital inpatients in a Greek tertiary hospital, but as

**Table 3: Overuse categories**

Overuse category	Percentage	
Overuse of indication	59.2%	
Overuse of duration	22.1%	
Overuse of dosage	Overuse of dosage in reflux disease	4.2%
	Overuse of dosage in other than reflux disease	14.5%

many as 81.2% of them had no indications and had no instructions concerning the duration of treatment after discharge.<sup>10</sup> Lack of instructions (preferably written) on the duration of treatment could lead to overuse of duration. In our study, 22.1% were taking PPIs for justified reasons but for a longer duration than indicated. It is unknown whether these patients failed to follow-up with their physicians, or if the latter failed to re-evaluate the need for continued therapy. A study done by Reimer and Bytzer showed that only 27% of subjects receiving PPIs in a long-term basis had a diagnosis justifying the need for this long-term therapy.<sup>11</sup>

The use of above-standard doses of PPIs (usually a double dose) for initial treatment of upper GI tract symptoms is ubiquitous. However, Targownik and others showed that initial symptomatic pharmacotherapy with a double dose of PPIs in Canadian outpatients was not superior to the treatment with a standard dose in reducing resource utilization in a 1-year follow up.<sup>12</sup> Furthermore, there was no difference in the efficacy of using a higher dose of PPI, but an increased cost. The standard dose of PPIs for any indication is determined by the FDA/NICE guidelines. In our study, 18.7% of PPI users were taking PPIs in a dose higher than indicated, which leads to increased expenditure. In a study conducted on the Icelandic population in an outpatient setting, it was noticed that patients were increasingly treated with higher-dose PPIs and for durations longer than recommended by clinical guidelines.<sup>13</sup> In the case of patients taking PPIs for reflux disease where the long-term treatment should be individualized (continuous vs. intermittent vs. on-demand/ high dose vs. low dose),<sup>14</sup> many patients with gastroesophageal reflux disease (GERD) take too high doses of PPIs in the long term, whereas it is possible to reduce a double dose to a standard dose in 80% of the cases, and a standard dose to a half dose in 58% of the cases.<sup>15</sup> Although current guidelines recommend step down and on-demand

strategies of treatment in selected subjects with GERD, some patients, as well as clinicians, seem to be reluctant to accept such instructions. Besides, certain individuals tend to continue pharmacotherapy with PPIs despite no evidence of pathology. For example, in a study by Gawron and colleagues, as many as 45% of 90 patients evaluated for “refractory GERD” kept taking PPIs after exclusion of any form of reflux.<sup>16</sup> Our study results were concordant with these findings as it showed that 25% of patients taking PPIs for GERD were overusing the dose.

#### **Dependencies between demographic variables and overuse**

No correlation exists between the overuse and each of the age, sex, levels of education, and place of residence. We can conclude that there is widespread overuse of PPI all over Lebanon, and this overuse is not confined to a specific location, age group, or socioeconomic class. Interestingly, our study showed that PPIs were prescribed by physicians in 89.2%, but with 71% being inaccurate prescriptions, even among gastroenterologists. A study done in China demonstrated the lack of a satisfactory level of knowledge among the medical staff concerning the rational use of PPIs.<sup>17</sup> Similar studies are unavailable in Lebanon, but they are highly needed because of the lack of awareness of medical staff could be regarded as a potential cause of PPIs abuse in the country.

#### **The economic impact of PPI overuse in Lebanon**

In Lebanon, approximately 36 million dollars were spent on PPIs in 2018. Because the sample size chosen is large and diverse, it can be considered as a representative of the Lebanese population; the results can thus be generalized. Assuming that 71.4% of PPI users in Lebanon are abusing it, approximately 25 million dollars are being wasted yearly in Lebanon. Such amount of money wasted yearly on PPIs is considered huge in a financially struggling country, in which health care services are not available for all. Adhering to evidence-based indications for PPI use is the best way to avoid such losses. Our study is just an example of the economic losses in Lebanon that is resulted from inappropriate uses of drugs. It can be considered as an eye-opener and a pioneer to lead and encourage other studies to be conducted on other drugs

that are probably being overused in Lebanon such as NSAIDs, antiplatelet drugs, antibiotics, and others, which in their turn also lead to a deleterious economic impact on the health care system in Lebanon.

#### **Strengths**

Our study was a study with a large population, and the sample was representative. In addition, the patients were randomly selected with no selection bias. Furthermore, it proved that PPIs are being overused in Lebanon. Also, it identified economic losses and huge expenses on the health care system in Lebanon resulting from inappropriate uses of drugs.

#### **Limitations**

This study is limited by a few factors. We relied on the subjects' subjective answers to questionnaires, not on medical records. In addition, it had missing data as the questionnaire did not include all patients' risk factors for GI injury (like smoking, alcohol intake, etc), and we lacked official endoscopy and/or pathology reports to confirm certain diagnoses (peptic ulcer disease, erosive esophagitis, *H. pylori* infection, and Barret's esophagus).

#### **CONCLUSIONS**

Our findings elucidate the frequency of PPI overprescription in the outpatient setting in Lebanon, leading to huge expenses on the health care system and the potential risk of adverse effects. PPIs are indeed irreplaceable drugs in the management of acid-related disorders, but like any drug therapy, they are not risk-free. PPIs overuse in the outpatient setting is initiated by prescription for undocumented diagnoses. Non-adherence to step-down therapy or reassessment per guidelines allows the maintenance of both proper and improper PPI administrations.

Based on the results of our study, an action needs to be taken to put an end to this overuse. Physicians should adhere to evidence-based indications, and patients should also be educated and followed up by their physicians to re-evaluate the need for continued therapy. Once these measures are underway, they will help enhance the quality and efficiency of prescriptions. Thus, favorable clinical and economic outcomes will be attained.

**ACKNOWLEDGMENTS**

No funding was provided for this work.

**ETHICAL APPROVAL**

The study obtained ethics approval from the ethics committee of Sainte Therese Hospital. This committee is chaired by Dr Hikmet Husseiny, a member of the National Lebanese Ethics Committee. All the participants signed a consent form prior to filling the questionnaire.

**CONFLICT OF INTEREST**

The authors declare no conflict of interest related to this work.

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