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Prevalence and Factors Associated With Proton Pump Inhibitors (PPIs) Use: A Cross-Sectional Study of PERSIAN Guilan Cohort Study

Sepide Roudgar[1] | Farahnaz Joukar[1] | Kourosh Mojtahedi[1] | Saman Maroufizadeh[2] | Mohammadreza Naghipour[1] | Fariborz Mansour-Ghanaei[1]

[1]Gastrointestinal and Liver Diseases Research Center, Guilan University of Medical Sciences, Rasht, Iran | [2]Department of Biostatistics and Epidemiology, School of Health, Guilan University of Medical Sciences, Rasht, Iran

Correspondence: Fariborz Mansour-Ghanaei (fmansourghanaei@gmail.com)

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ABSTRACT

Background and Aims: Proton pump inhibitors (PPIs) are used extensively in the treatment of patients with upper gastrointestinal disorders. In this study, we aimed to investigate the prevalence of PPI consumption and related factors in the Prospective Epidemiological Research Studies in Iran (PERSIAN) Guilan Cohort study (PGCS) population.

Methods: This was a cross-sectional study form the PGCS, and investigated 10,520 participants for PPI consumption, which were divided into two groups: users and nonusers. Demographical data, clinical characteristics, and PPI types were recorded. The data were analyzed using SPSS version 16 and GraphPad Prism version 9, and a significance level of 0.05 was considered.

Results: The prevalence of PPI use in the overall participants was 4.8%, and it was higher in females compared to males (6.1% vs. 3.3%). According to the regression analysis, being in the overweight category was associated with a 26% lower likelihood of PPI use ($p = 0.021$). Low physical activity was linked to a 1.72-fold higher odds of PPI consumption ($p < 0.001$). Individuals with reflux, multiple underlying diseases, and the use of nonsteroidal anti-inflammatory drugs (NSAIDs) had significantly higher odds ratios for PPI consumption ($p < 0.001$).

Conclusion: This study highlights the concerning trend of increasing PPI use and identifies low physical activity, reflux, multiple underlying diseases, and NSAID use associated with higher risk of PPI use. It emphasizes the need for caution in prescribing PPIs and raising awareness among both healthcare providers and patients about the potential risks and side effects.

1 | Introduction

The consumption trend of proton pump inhibitors (PPIs) has been a subject of growing interest in recent years. PPIs are widely prescribed medications used to reduce gastric acid secretion and are commonly used for the treatment of gastroesophageal reflux disease (GERD), peptic ulcers, and other acid-related disorders [1, 2]. Epidemiological studies have shed light on the widespread use of PPIs in both clinical and nonclinical settings. The prevalence of PPI consumption has been reported to be significantly high among individuals relying on these medications for long-term management of acid-related conditions. This trend has raised concerns about the potential consequences of prolonged PPI use, including adverse effects, drug interactions, and increased healthcare costs [3–5]. According to recent studies, it was discovered that half of individuals using PPIs are aged over 50. This high prevalence of nonevidence-based PPI use, combined with safety concerns, emphasizes the

Sepide Roudgar and Farahnaz Joukar contributed equally as the first author to the work.

pressing necessity to optimize the utilization of PPIs among the elderly population [6–8].

One of the challenges in establishing the true prevalence of PPI use lies in the fact that these medications are available over-the-counter (OTC) in some countries, leading to self-medication and underreporting [9, 10]. Additionally, the lack of consistent monitoring systems and standardized criteria for PPI prescription contribute to difficulties in accurately assessing the prevalence rates across different populations [11, 12]. Moreover, certain medical conditions and patient characteristics have been associated with a higher likelihood of PPI consumption. Patients with chronic conditions such as GERD, Barrett's esophagus, and gastric ulcers often require long-term PPI therapy [13–15]. However, inappropriate prescribing practices, including the use of PPIs for non-indicated conditions or at higher doses than necessary, have become a concern. This raises issues of patient safety, potential drug interactions, and the need for regular re-evaluation of the appropriateness of PPI therapy.

While PPIs play a crucial role in managing acid-related conditions, their widespread use and potential overuse present challenges in terms of epidemiology, accurate prevalence estimation, and appropriate prescribing practices. In this regard, the current study aimed to evaluate the prevalence of PPI consumption and the associated factors among the Prospective Epidemiological Research Studies in Iran (PERSIAN) Guilan Cohort study (PGCS) population.

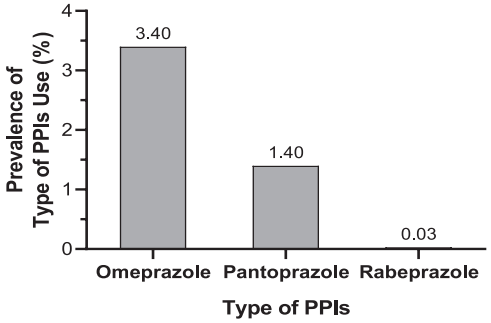

FIGURE 1 | Frequency of PPI consumption in participants.

2 | Methods and Materials

2.1 | Study Population

This cross-sectional survey is part of a cohort study conducted on 10,520 individuals in PGCS in Guilan province, Iran, between 2022 and 2023 [16, 17]. This study was approved by the Ethics Committee of the Guilan University of Medical Sciences, Rasht, Iran [IR.GUMS.REC.1401.405], and all patients gave their consent to participate in the study. Data collection through face-to-face interviews involved assessing demographical and clinical characteristics, including age, gender, marital status, education level, employment, habitat, socioeconomic status (SES), waist-to-hip ratio (WHR), physical activity, cigarette and hookah smoking, opium use, alcohol consumption, hypertension, diabetes, reflux, number of underlying diseases, use of nonsteroidal anti-inflammatory drugs (NSAIDs), and consumption of different types of PPIs. The inclusion criteria for the study included people who were taking PPIs with the physician's diagnosis and confirmed by checking the patient's accompanying medications.

Also, physical activity according to the metabolic equivalent of task (MET) was divided into three tertiles by low, moderate, and high levels of activity in a day by measuring the number of hours of walking, working, exercising, and so forth. Anthropometric indices including weight (in kg), height, hip, waist, and wrist circumference (in cm) were measured according to the National Health and Nutrition Examination Survey Manual. Body mass index (BMI) groups were defined as underweight (BMI $< 18.5\ kg/m^2$), normal weight (BMI $= 18.5–24.99\ kg/m^2$), overweight (BMI $= 25–29.9\ kg/m^2$), and obese (BMI $\geq 30\ kg/m^2$).

2.2 | Statistical Analysis

In this study, continuous variables were expressed as mean ± standard deviation (SD) and categorical variables as numbers (percentage). To compare the differences between PPI users and nonusers, *t*-tests were used for continuous variables, and the χ^2 test was used for categorical data. Logistic regression analysis was employed to examine the association of the use of PPI with related variables, calculating odds ratios (OR) and 95% confidence intervals (CIs). The ORs were adjusted for demographic

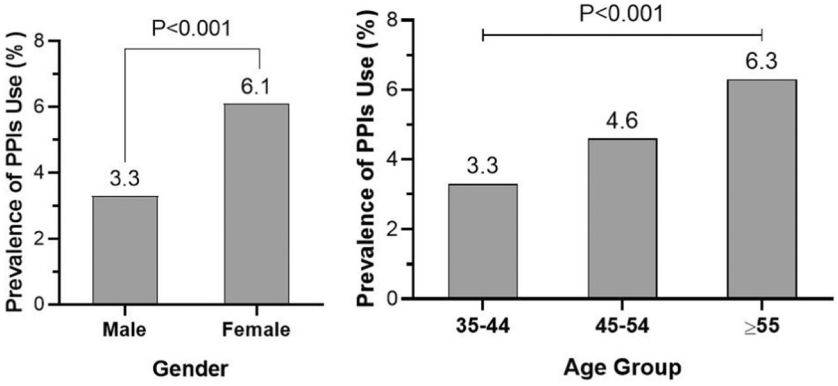

FIGURE 2 | Prevalence of PPI consumption according to gender and age in participants. The *p* value is based on the χ^2 test; a *p* value less than 0.05 was considered statistically significant.

TABLE 1 | Comparison of sociodemographic and clinical characteristics between PPI users and nonusers among participants.

Variables	Total ($N = 10,520$)	User of PPIs *n* (%)	Nonuser of PPIs *n* (%)	*p* value
Age (Year)				< 0.001[a]
35–44	3139 (29.8)	104 (20.7)	3035 (30.3)	
45–54	3854 (36.6)	176 (35.5)	3678 (36.7)	
> 55	3527 (33.5)	222 (44.2)	330 (33.0)	
Mean ± SD	51.52 ± 8.90	53.8 ± 8.93	51.40 ± 8.89	< 0.001[b]
Gender				< 0.001[a]
Male	4887 (46.5)	161 (32.1)	4726 (47.2)	
Female	5633 (53.5)	341 (67.9)	5292 (52.8)	
Marital status				< 0.001[a]
Single	305 (2.9)	8 (1.6)	297 (3.0)	
Married	9527 (90.6)	434 (86.5)	9093 (90.8)	
Widow/widower	566 (5.4)	53 (10.6)	513 (0.1)	
Divorced	122 (1.2)	7 (1.4)	115 (1.1)	
Education level				< 0.001[a]
Illiterate	1738 (16.5)	133 (26.5)	1605 (16.0)	
1–5	3312 (31.5)	170 (33.9)	3142 (31.4)	
6–12	4832 (45.9)	173 (34.5)	4659 (46.5)	
University	638 (6.1)	26 (5.2)	612 (6.1)	
Mean ± SD	6.63 ± 4.52	5.47 ± 4.6	6.68 ± 4.51	< 0.001[b]
Employment status				< 0.001[a]
Unemployed	4781 (45.4)	305 (60.8)	44.76 (44.7)	
Employed	5739 (54.6)	197 (39.2)	5.42 (5.3)	
Habitat				0.054[a]
Urban	4613 (43.8)	241 (48.0)	4372 (43.6)	
Rural	5907 (56.2)	261 (52.0)	4546 (56.4)	
SES				0.72[a]
Low	3507 (33.3)	171 (34.1)	3336 (33.3)	
Moderate	3506 (33.3)	172 (34.3)	33334 (33.3)	
High	3507 (33.3)	159 (31.7)	3348 (33.4)	
Mean ± SD	0 ± 1.00	0.05 ± 0.99	0 ± 1	0.29[b]
BMI (kg/m^2)				0.020[a]
Underweight	141 (1.3)	3 (0.6)	138 (1.4)	
Normal	2746 (26.1)	125 (24.9)	2621 (26.2)	
Overweight	4197 (39.9)	181 (36.1)	4016 (40.1)	
Obese	3436 (32.7)	193 (38.4)	3243 (32.4)	
Mean ± SD	28.14 ± 5.09	28.72 ± 5.09	28.11 ± 5.09	0.010[b]
WHR				< 0.001[a]
Low	2765 (26.3)	90 (17.9)	2675 (26.7)	
Moderate	1637 (15.6)	56 (11.2)	1581 (15.8)	
High	6118 (58.2)	356 ± 70.9	5762 (57.5)	
Mean ± SD	0.96 ± 0.06	0.97 ± 0.06	0.6 ± 0.06	< 0.001[b]
Physical activity (MET)				< 0.001[a]
Low	3507 (33.3)	237 (47.2)	3270 (2.6)	

(Continues)

TABLE 1 | (Continued)

Variables	Total ($N = 10,520$)	User of PPIs n (%)	Nonuser of PPIs n (%)	p value
Moderate	3506 (33.3)	155 (30.9)	3351 (33.4)	
High	3507(33.3)	110 (21.9)	3397 (33.9)	
Mean ± SD	41.26 ± 8.88	38.73 ± 7.92	41.39 ± 8.91	< 0.001[b]
Cigarette smoking (Yes)	2584 (24.6)	99 (19.7)	2485 (24.8)	0.010[a]
Hookah use (Yes)	1515 (14.4)	50 (10.0)	1465 (14.6)	0.004[a]
Opium use (Yes)	726 (6.9)	17 (3.4)	709 (7.1)	0.001[a]
Alcohol consumption (Yes)	1395 (13.3)	74 (14.7)	1321 (13.2)	0.32[a]
Hypertension (Yes)	4543 (43.2)	295 (58.8)	4248 (42.4)	< 0.001[a]
Diabetes (Yes)	2531 (24.1)	169 (33.7)	2362 (23.6)	< 0.001[a]
Reflux (Yes)	1385 (13.2)	219 (43.6)	1166 (11.6)	< 0.001[a]
Underlying disease				< 0.001[a]
No	3196 (30.4)	77 (15.3)	3119 (31.9)	
One	3470 (33.0)	125 (24.9)	3345 (33.4)	
Two	2270 (21.6)	132 (26.3)	2138 (21.3)	
Three and more	1584 (15.1)	168 (33.5)	1416 (14.1)	
NSAIDs consumption (Yes)	1505 (14.3)	173 (34.5)	1332 (13.3)	< 0.001[a]

Note: p value of less than 0.05 was considered statistically significant.
Abbreviations: BMI, body mass index; NSAIDs, nonsteroidal anti-inflammatory drugs; SD, standard deviation; SES, socioeconomic status; WHR, waist-to-hip ratio.
[a]χ^2 test.
[b]Independent t-test.

and clinical variables. The statistical analysis was performed using SPSS for Windows, version 16.0 (SPSS Inc., Chicago, Illinois, the United States). All statistical tests were two-sided, and a p value of < 0.05 was considered statistically significant.

3 | Results

The average age of the 10,520 participants was 51.52 ± 8.90 years, and 3527 (33.5%) were aged 55 years or older. About 5633 (53.5%) were female, 9527 (90.6%) were married, 5739 (54.6%) were employed, and 4613 (43.8%) resided in urban areas. The average education level and BMI among the participants were 6.63 ± 4.52 years and 28.14 ± 5.09 kg/m^2, respectively. A total of 2584 (24.6%) were smokers, 1515 (14.4%) used hookah, 726 (6.9%) used opium, and 1395 individuals (13.3%) consumed alcohol. There were 4543 (43.2%) with hypertension, 2531 (24.1%) with diabetes, and 1385 (13.2%) with reflux. Furthermore, 3470 (33.0%) had one comorbid condition, 2270 (21.6%) had two comorbid conditions, 1584 (15.1%) had three or more comorbid conditions, and 1505 (14.3%) used NSAIDs.

The prevalence of PPIs in all participants was 4.8%, and omeprazole was the most prevalent compared to other PPIs (Figure 1). Overall, there was a trend toward a higher rate of PPI consumption among females compared to males (6.1% vs. 3.3%, $p < 0.001$), as well as those over 55 years old (Figure 2). As observed in Table 1, PPI users had a higher proportion of females. The PPI users had a higher age, lower education level, higher BMI, higher WHR, and lower physical activity compared to nonusers ($p < 0.05$). Among PPI users, married and employed people, as well as cigarette, hookah, and opium users, had a lower prevalence of PPI use than nonusers ($p < 0.05$). The proportion of people with high blood pressure, diabetes, reflux, the number of comorbidities, and the amount of NSAID use was higher in PPI users compared to nonusers ($p < 0.001$) (Table 1).

In the group of PPI users, there are factors such as older age, being a female, being a widow, lower education level, unemployment, obesity, higher WHR, less physical activity, not smoking, not using hookah and opium, high blood pressure, diabetes, reflux, and a high number of underlying diseases as well as the use of NSAIDs had a direct association to the high prevalence of PPI use ($p < 0.05$) (Table 2). According to the regression on PPI use (Table 3), individuals in the overweight category had a 26% lower possibility of consuming PPIs ($p = 0.021$). Also, subjects with low levels of physical activity were 1.72 times more likely to be taking PPIs ($p < 0.001$). Patients with reflux, three or more underlying diseases, and NSAIDs consumption had significantly higher OR of PPI use, 5.41, 2.27, and 2.26, respectively ($p < 0.001$).

4 | Discussion

The prevalence of PPI consumption, a class of medications commonly prescribed for acid-related gastrointestinal disorders, has risen significantly in recent years, which is attributed to multiple factors, including the growing incidence of GERD, increased recognition of its associated symptoms, and the availability of PPIs as OTC medications. Understanding the prevalence of PPI use and the related influential factors is crucial for optimizing patient care and mitigating potential

TABLE 2 | Association between the use of PPIs and the demographic and clinical characteristics of participants using the χ^2 test.

Variables	User of PPIs		*p* value[a]
	n/*N*	(%)	
Age (Year)			< 0.001
35–44	104/3039	3.3	
45–54	176/384	4.6	
> 55	222/3527	6.3	
Gender			< 0.001
Male	161/4887	3.3	
Female	341/5623	6.1	
Marital status			< 0.001
Single	8/305	2.6	
Married	434/9527	4.6	
Widow/widower	53/566	9.4	
Divorced	7/122	5.7	
Education level			< 0.001
Illiterate	133/1738	7.7	
1–5	170/3312	5.1	
6–12	173/4832	3.6	
University	26/638	4.1	
Employment status			< 0.001
Unemployed	305/4781	6.4	
Employed	197/5739	3.4	
Habitat			0.054
Urban	241/4613	5.2	
Rural	261/5907	4.4	
SES			0.72
Low	171/3507	4.9	
Moderate	172/3506	4.9	
High	159 (3507)	4.5	
BMI (kg/m^2)			0.020
Underweight	3/141	2.1	
Normal	125/2746	4.6	
Overweight	181/4197	4.3	
Obese	193/3436	5.6	
WHR			< 0.001
Low	90/2765	3.3	
Moderate	56/1637	3.4	
High	356/6118	5.8	
Physical activity			< 0.001
Low	237/3507	6.8	
Moderate	155/3506	4.4	
High	110/3507	3.1	
Cigarette smoking			0.010
No	403/7936	5.1	
Yes	99/2584	3.8	
Hookah use			0.004
No	452/9005	5.0	
Yes	50/1515	3.3	
Opium use			0.001
No	485/9794	5.0	
Yes	17/726	2.3	
Alcohol consumption			0.32
No	428/9125	4.7	
Yes	74/1395	5.3	
Hypertension			< 0.001
No	207/5977	3.5	
Yes	295/4543	6.5	
Diabetes			< 0.001
No	333/7989	4.2	
Yes	169/2531	6.7	
Reflux			< 0.001
No	283/9135	3.1	
Yes	219/1385	15.8	
Underlying disease			< 0.001
No	77/3196	2.4	
One	125/3470	3.6	
Two	132/2270	5.8	
Three or more	168/1584	10.6	
NSAIDs consumption			< 0.001
No	329/9015	3.6	
Yes	173/1505	11.5	

Note: p value of less than 0.05 was considered statistically significant.
Abbreviations: BMI, body mass index; *n*, number of PPI users in each category; *N*, total number of individuals in each category; NSAIDs, nonsteroidal anti-inflammatory drugs; SES, socioeconomic status; WHR, waist-to-hip ratio.
[a]χ^2 test.

adverse effects [11, 18]. In this study, the prevalence of PPI use in the PGCS population was 4.8%. It has been reported that the prevalence of PPI use is higher in other countries, such as Switzerland (23.0%) and Denmark (7.4%), compared to the findings of our study [8, 19]. The availability of generic PPI medications has increased their use without a prescription due to their lower cost, leading to increased consumption of these drugs [20].

Furthermore, studies have shown that PPI use is highly prevalent among the elderly population [21, 22]. Our findings are consistent with these results, demonstrating a higher use of PPIs in the older age group. Possible factors contributing to this phenomenon include the presence of multiple concurrent health conditions, heightened susceptibility to acid-related gastrointestinal disorders, the use of multiple medications,

TABLE 3 | Association between the use of PPIs and the demographic and clinical characteristics of participants using logistic regression.

	Simple logistic regression		Multiple logistic regression	
Variables	**OR (95% CI)**	***p* value**	**OR (95% CI)**	***p* value**
Age (Year)				
35–44	1		1	
45–54	1.40 (1.09–1.79)	0.008	1.21 (0.93–1.57)	0.15
> 55	1.96 (1.54–2.49)	< 0.001	1.18 (0.09–1.55)	0.24
Gender		< 0.001		0.068
Male	1		1	
Female	1.89 (1.56–2.29)		1.54 (0.97–2.46)	
Marital status				
Single	1		1	
Married	1.77 (0.87–3.60)	0.11	1.36 (0.65–2.83)	0.42
Widow/widower	3.84 (1.80–8.18)	0.001	1.55 (0.70–3.44)	0.28
Divorced	2.26 (0.80–6.37)	0.12	1.84 (0.63–5.36)	0.26
Education level				
University	1		1	
6–12	0.87 (0.57–1.33)	0.53	1.02 (0.65–1.61)	0.93
1–5	1.27 (0.84–1.94)	0.26	1.35 (0.84–2.18)	0.21
Illiterate	1.95 (1.27–3.00)	0.002	1.53 (0.92–2.55)	0.099
Employment status		< 0.001		0.97
Unemployed	1		1	
Employed	0.52 (0.43–0.63)		1.00 (0.77–1.28)	
Habitat		0.055		0.072
Rural	1		1	
Urban	1.19 (1.00–1.43)		1.20 (0.98–1.46)	
SES				
High	1		1	
Moderate	1.09 (0.87–1.35)	0.46	0.86 (0.67–1.10)	0.24
Low	1.08 (0.87–1.35)	0.50	0.86 (0.66–1.11)	0.22
BMI (kg/m^2)				
Normal	1		1	
Underweight	0.46 (0.14–1.45)	0.18	0.54 (0.17–1.76)	0.31
Overweight	0.95 (0.75–1.19)	0.63	0.74 (0.57–0.95)	0.021
Obese	1.25 (0.99–1.57)	0.060	0.76 (0.58–1.00)	0.052
WHR				
Low	1		1	
Moderate	1.05 (0.75–1.48)	0.77	0.91 (0.63–1.31)	0.62
High	1.84 (1.45–2.32)	< 0.001	0.86 (0.54–1.36)	0.52
Physical activity				
High	1		1	
Moderate	1.43 (1.11–1.83)	0.005	1.20 (0.92–1.57)	0.19
Low	2.24 (1.78–2.82)	< 0.001	1.72 (1.32–2.24)	< 0.001
Cigarette smoking		0.010		0.66
No	1		1	

(Continues)

TABLE 3 | (Continued)

Variables	Simple logistic regression		Multiple logistic regression	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Yes	0.74 (0.59–0.93)		1.08 (0.77–1.51)	
Hookah use				
No	1	0.004	1	0.80
Yes	0.65 (0.48–0.87)		0.95 (0.66–1.38)	
Opium use	1	0.002	1	0.19
No				
Yes	0.46 (0.28–0.75)		0.70 (0.42–1.19)	
Alcohol consumption		0.32		0.19
No	1		1	
Yes	1.14 (0.88–1.47)		1.22 (0.90–1.65)	
Hypertension		< 0.001		—[a]
No	1		1	
Yes	1.94 (1.61–2.32)		—[a]	
Diabetes		< 0.001		—[a]
No	1		1	
Yes	1.64 (1.36–1.99)		—[a]	
Reflux		< 0.001		< 0.001
No	1		1	
Yes	5.87 (4.87–7.08)		5.41 (4.46–6.58)	
Underlying disease				
No	1		1	
One	1.51 (1.13–2.02)	0.005	1.22 (0.91–1.64)	0.19
Two	2.50 (1.88–3.33)	< 0.001	1.55 (1.14–2.10)	0.005
Three or more	4.81 (3.64–6.34)	< 0.001	2.27 (1.66–3.10)	< 0.001
NSAIDs consumption		< 0.001		< 0.001
No	1		1	
Yes	3.43 (2.83–4.16)		2.26 (1.82–2.82)	

Note: A *p* value of less than 0.05 was considered statistically significant.
Abbreviations: aOR, adjusted odds ratio; BMI, body mass index; CI, confidence interval; NSAIDs, nonsteroidal anti-inflammatory drugs; OR, crude odds ratio, SES, socioeconomic status; WHR, waist-to-hip ratio.
[a]This variable was considered in the underlying disease group.

and inadequate efforts to discontinue unnecessary prescriptions [4]. Consistent with our findings, other studies have indicated a higher prevalence of PPI use in females compared to males [19, 23]. However, in some studies, there was no difference between men and women in the prevalence of PPIs [8, 21].

Moreover, in the present study, as the level of education increased, the use of PPIs decreased. This may be due to the increase in the awareness of educated people about the use of these drugs and their side effects, and other studies also confirm this relationship [9, 24]. In our study, the prevalence of PPI use was higher among obese individuals, which may be attributed to the influence of obesity on symptoms related to GERD, such as heartburn and acid reflux [25]. Consistent with our findings, other studies have also reported a high prevalence of gastrointestinal symptoms and elevated PPI consumption in obese populations [11, 26, 27].

There was a possibility of high consumption of PPI in people with low physical activity, which is confirmed by Czwornog et al.'s study [28]. However, some investigations, showing conflicting results, point to an exacerbation of gastroesophageal reflux during physical exercises [29, 30]. According to Mendes-Filho et al., engaging in high-intensity physical activity may increase the likelihood of experiencing gastroesophageal reflux episodes. In contrast, light or short sessions of physical activity do not appear to have any impact on reflux occurrences [31]. As well, in this study, PPI consumption is more prevalent in widow/widowers, while some other studies have shown that GERD and PPI consumption are more prevalent in married people [11, 32]. The increased prevalence of PPI use among widows/widowers may be due to higher levels of stress and reduced social support, which can exacerbate gastrointestinal conditions and lead to increased reliance on PPIs for symptom management. The high prevalence of PPI consumption among

unemployed individuals with lower incomes in this study aligns with the findings of Boxel et al., which indicated an association between sociodemographic factors such as low income and chronic PPI use [33].

Moreover, in the present study, cigarette smoking, hookah use, and opium consumption were less prevalent among PPI users. Controversially, other findings reported that smoking and alcohol consumption increase GERD and consumption of PPIs [26, 34]. Similar to other studies [35, 36], our results also showed that the patients with hypertension, diabetes, and underlying diseases and the patients using NSAIDs had a high consumption of PPI, so having more than three underlying diseases and using NSAIDs were associated with a higher possibility of taking PPIs. Also, we observed that individuals with reflux symptoms had the highest prevalence and association with the use of PPIs, which is due to the use of PPIs to alleviate digestive symptoms [32]. In this study, a myriad of pivotal demographic and clinical variables were investigated in PPI users in a large population. One of the limitations of this study is the failure to examine the specific reasons for PPI use and the duration of its administration. Also, due to the cross-sectional nature of this research, we were not able to examine the side effects caused by the use of PPIs.

5 | Conclusion

This study highlighted the increasing prevalence of PPI use and identified specific demographic and clinical variables such as low physical activity, reflux, more underlying diseases, and NSAID use influencing the probabilities of consuming more. The findings contributed to optimizing patient care by identifying high-risk groups and highlighted the importance of patient education and shared decision-making regarding PPI prescriptions.

Author Contributions

Sepide Roudgar: investigation, writing – original draft, writing – review and editing, validation, methodology, data curation. **Farahnaz Joukar:** investigation, writing – original draft, writing – review and editing, methodology, validation, software, formal analysis, data curation. **Kourosh Mojtahedi:** investigation, methodology, writing – review and editing, software, data curation, formal analysis. **Saman Maroufizadeh:** investigation, writing – review and editing, validation, software, formal analysis, data curation. **Mohammadreza Naghipour:** investigation, writing – review and editing, validation, software, formal analysis, data curation. **Fariborz Mansour-Ghanaei:** data curation, supervision, writing – review and editing, validation, methodology, investigation.

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Ethics Statement

This study was approved by the ethics committee of the Guilan University of Medical Sciences, Rasht, Iran [ethics code: IR.GUMS.REC.1401.405]. The methods were carried out in agreement with the principles and propositions established in the Declaration of Helsinki for all human or animal subjects.

This cross-sectional survey is part of the Prospective Epidemiological Research Studies in Iran (PERSIAN) Guilan Cohort study (PGCS). The PGCS design was approved by the ethics committees at the Ministry of Health and Medical Education, the Digestive Diseases Research Institute (Tehran University of Medical Sciences), and also Guilan University of Medical Sciences (P/3/132/215).

Consent

All individuals gave their informed consent to participate in the study.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The authors confirm that the data supporting the findings of this study are available within the article and are available from the corresponding author upon request.

Transparency Statement

The lead author Fariborz Mansour-Ghanaei affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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