

## Proton Pump Inhibitor Use Among Indian Patients with Hypertension: Prevalence, Patterns, and Possible Cardiovascular Associations — A Cross-Sectional Survey

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### ABSTRACT

**Background:** Proton pump inhibitors (PPIs) are among the most widely dispensed medications in India, frequently used without appropriate clinical supervision. Emerging evidence suggests that prolonged PPI therapy may contribute to cardiovascular risk through mechanisms including hypomagnesaemia, vitamin B12 depletion, and endothelial dysfunction. The burden of hypertension in India continues to increase, yet the intersection between chronic PPI use and blood pressure elevation remains insufficiently characterised in Indian populations.

**Objectives:** To determine the prevalence and patterns of PPI use among Indian patients with hypertension, to evaluate the association between long-term PPI exposure and hypertension diagnosis, and to examine the role of vitamin B12 deficiency as a potential mediating factor.

**Methods:** A cross-sectional, observational survey was conducted over six months using a structured, validated questionnaire distributed through an online platform (Google Forms). A total of 124 adult participants aged 18–65 years were enrolled from clinical, community, and educational settings across India. Data covered demographics, PPI use patterns (type, duration, frequency, indication), blood pressure (on-spot measurement classified by ACC/AHA 2017 criteria), vitamin B12 status, comorbidities, and cardiovascular history. Statistical

analysis included chi-square tests, Mann-Whitney U test, Kruskal-Wallis test, one-way ANOVA, and Spearman rank correlation, with normality formally assessed by the Shapiro-Wilk test.

**Results:** Of 124 participants, 86.1% reported ever using a PPI, with pantoprazole being the most common agent (46.1%). A striking prevalence gradient emerged with increasing duration and frequency of PPI use. Hypertension diagnosis was absent in those using PPIs for fewer than six months, present in 15.0% of those with 6–12 months of use, in 90.3% of 1–5 year users, and in 100% of those with more than five years of exposure ( $\chi^2=91.91$ ,  $p<0.001$ ). Daily PPI users had an 81.8% prevalence of hypertension, versus zero prevalence in occasional or as-needed users ( $\chi^2=45.95$ ,  $p<0.001$ ). Low vitamin B12 status was found in 62 participants (50%) and was strongly associated with hypertension diagnosis (OR=85.39, 95% CI: 23.7–306.9;  $p<0.001$ ). Spearman correlation confirmed a moderate positive relationship between PPI duration and systolic blood pressure ( $\rho=0.61$ ,  $p<0.001$ ).

**Conclusions:** Chronic, daily PPI use was significantly associated with hypertension diagnosis and elevated blood pressure in this Indian patient sample. Vitamin B12 deficiency emerged as a likely mediating variable. The cross-sectional design precludes causal inference, and the findings are subject to selection bias. Nevertheless, results underscore the urgent need for rational prescribing,

routine deprescribing review, and cardiovascular monitoring in long-term PPI users. Prospective cohort studies and randomised trials are warranted to confirm causality.

**Keywords:** *proton pump inhibitors; hypertension; vitamin B12; cardiovascular risk; pharmacoepidemiology; India; cross-sectional study; pantoprazole; omeprazole; self-medication*

## I. INTRODUCTION

Proton pump inhibitors (PPIs) represent a cornerstone pharmacotherapy for acid-related gastrointestinal disorders, including gastroesophageal reflux disease (GERD), peptic ulcer disease, gastritis, and Zollinger–Ellison syndrome. Since the introduction of omeprazole in the late 1980s, the class has expanded to include pantoprazole, rabeprazole, lansoprazole, and esomeprazole — all of which irreversibly inhibit the H<sup>+</sup>K<sup>+</sup>-ATPase proton pump on the secretory surface of gastric parietal cells, reducing both basal and meal-stimulated acid secretion.

In India, PPIs rank among the highest-volume prescription drug classes, with pantoprazole consistently appearing in the top five dispensed medications across both urban and rural settings. A critical concern is the widespread availability of PPIs over the counter, which has encouraged self-medication, indiscriminating long-term use, and inadequate clinical monitoring. A real-world evidence study examining partial response to standard PPI doses in India identified that a substantial proportion of patients continue PPI therapy indefinitely despite inadequate clinical indication.

While short-term PPI use is considered safe and well-tolerated, the long-term safety profile of these agents has been subject to increasing scrutiny over the past decade. Observational and population-based studies have linked chronic PPI exposure to an array of adverse outcomes, including hypomagnesaemia, vitamin B12 deficiency, hypocalcaemia, increased susceptibility to *Clostridioides difficile* infection, chronic kidney disease, and — most pertinently for the present study — an elevated risk of hypertension and adverse cardiovascular events. The proposed mechanistic pathways connecting PPI therapy to elevated blood pressure include: (i) inhibition of dimethylarginine dimethylaminohydrolase (DDAH), leading to accumulation of asymmetric dimethylarginine (ADMA) and consequent reduction in nitric oxide bioavailability; (ii) impaired magnesium absorption causing vascular

hyperreactivity; and (iii) vitamin B12 depletion inducing hyperhomocysteinaemia, which promotes endothelial injury and arterial stiffening.

India faces a dual burden: hypertension — already a leading cause of cardiovascular morbidity and mortality — is estimated to affect approximately 28–33% of urban adults and 25–28% of rural adults, with a substantial proportion remaining undiagnosed. Concurrently, the irrational use of PPIs — particularly in patients receiving multiple cardiovascular, analgesic, and anti-inflammatory medications — creates conditions under which PPI-mediated blood pressure elevation could meaningfully contribute to cardiovascular risk. Yet, published evidence explicitly examining the association between PPI use and hypertension in Indian populations remains sparse.

The present study was therefore designed to address this gap through a cross-sectional, survey-based approach — enrolling patients with hypertension and characterising their PPI use patterns, vitamin B12 status, blood pressure measurements, and cardiovascular history — with the aim of generating hypothesis-generating data to inform future prospective investigations and clinical practice guidelines.

## II. MATERIALS AND METHODS

### 2.1 Study Design and Setting

This was a cross-sectional, observational survey-based study conducted over six months. Data were collected through a structured online questionnaire (Google Forms) distributed via social media, email, and community healthcare networks across multiple Indian states. Ethical approval and informed consent were obtained before any data collection.

### 2.2 Study Population and Eligibility

Adult participants aged 18–65 years were eligible for inclusion if they had a clinical diagnosis of hypertension or were currently receiving antihypertensive medication, or if they had documented PPI use. Participants were excluded if they were younger than 18 or older than 65 years, refused consent, or provided incomplete responses. A total of 124 participants met the eligibility criteria and were included in the final analysis.

### 2.3 Questionnaire Instrument

The structured questionnaire comprised four sections: (i) demographic and lifestyle information (age, sex, education, smoking, alcohol use, family history of cardiovascular disease); (ii) PPI usage patterns (type, indication, duration, frequency, and self-medication behaviour); (iii) hypertension status, blood pressure measurements, antihypertensive

therapy, and co-morbidities; and (iv) cardiovascular disease history and self-rated heart health. The instrument was piloted in a small group and revised for clarity prior to deployment.

#### 2.4 Blood Pressure Assessment

Participants recorded their current blood pressure numerically (e.g., 138/88 mmHg). Values were classified according to the 2017 American College of Cardiology/American Heart Association (ACC/AHA) guidelines: Normal (<120/<80 mmHg), Elevated (120–129/<80 mmHg), Stage 1 Hypertension (130–139 or 80–89 mmHg), and Stage 2 Hypertension ( $\geq 140$  or  $\geq 90$  mmHg).

#### 2.5 Statistical Analysis

Continuous variables were assessed for normality using the Shapiro-Wilk test (preferred for  $n < 2000$  due to its superior statistical power). Based on normality findings, group comparisons for blood pressure employed the Mann-Whitney U test (two groups) or Kruskal-Wallis test with post-hoc Bonferroni correction (multiple groups). One-way ANOVA was applied where all subgroups satisfied normality individually, and was cross-validated with the Kruskal-Wallis test. Associations between categorical variables and hypertension were assessed by Pearson chi-square test or Fisher's exact

test (where expected cell frequencies fell below five). Spearman rank correlation ( $\rho$ ) was used for ordinal-continuous associations (PPI duration versus blood pressure). Odds ratios (OR) with 95% confidence intervals were computed for applicable 2x2 contingency tables. A two-tailed p-value of  $< 0.05$  was considered statistically significant. All analyses were performed using Python (scipy, pandas) and cross-verified in Microsoft Excel.

### III. RESULTS

#### 3.1 Sociodemographic Characteristics

The study enrolled 124 participants, of whom 71 (57.3%) were male and 53 (42.7%) were female. The largest age cohort was the 25–30 year group ( $n=45$ , 36.3%), followed by the 30–40 year group ( $n=26$ , 21.0%). The majority held graduate-level education (56.1%), with 21.0% post-graduate. Approximately one-third of participants (36.1%) reported active smoking (daily or occupational exposure), and 54.8% consumed alcohol to varying degrees. A family history of myocardial infarction or stroke was reported by 54.0% of participants (Table 1).

Table 1. Sociodemographic Characteristics of Study Participants (N=124)

Variable	n	Percentage (%)
<b>Age Group</b>		
Below 25 years	21	16.9
25–30 years	45	36.3
30–40 years	26	21.0
40–50 years	15	12.1
50–60 years	17	13.7
<b>Gender</b>		
Male	71	57.3
Female	53	42.7
<b>Smoking Status</b>		
Never Smoked	78	62.9
Daily Smoker	28	22.6
Occupational Exposure	18	14.5
<b>Family History of MI/Stroke</b>		
Yes	67	54.0
No	57	46.0

#### 3.2 PPI Prevalence and Usage Patterns

Of the 124 participants, 80 (64.5%) were currently taking a PPI, 28 (22.6%) had previously taken a PPI and discontinued, and 16 (12.9%) reported never having used one — yielding a lifetime PPI exposure rate of 86.1%. Pantoprazole was the most commonly used agent (46.1%), followed by omeprazole (26.8%), rabeprazole (11.1%), esomeprazole (9.3%), and lansoprazole

(3.7%). The most frequently reported primary indication was acidity (31.5%), followed by GERD (26.7%) and gastritis (11.1%). A majority of users (56.4%) had been on PPI therapy for 1–5 years, with 6.4% exceeding five years of continuous use. Daily PPI consumption was reported by 71.3% of users. Self-medication (PPI use without a current prescription) was documented in 86.1% of participants, and 43.6% reported four or more self-

medication episodes in the preceding six months (Table 2).

**Table 2. Pattern of PPI Use Among Study Participants (N=124)**

Variable	n	%
<b>PPI Use Status</b>		
Currently taking PPI	80	64.5
Previously taken (stopped)	28	22.6
Never used PPI	16	12.9
Total ever-users	108	86.1
<b>Most Common PPI Agent (n=108 users)</b>		
Pantoprazole	52	46.1
Omeprazole	30	26.8
Rabeprazole	12	11.1
<b>Duration of PPI Use</b>		
< 1 month	5	4.6
1–6 months	13	12.0
6 months–1 year	20	16.5
1–5 years	62	56.4
> 5 years	8	6.4
<b>Frequency of Use</b>		
Daily	77	71.3
Few times per week	19	16.6
Occasional / as needed	12	11.1

### 3.3 Blood Pressure Profile

The mean systolic blood pressure (SBP) across all 124 participants was  $131.18 \pm 15.95$  mmHg (median: 130.0 mmHg; range: 108–170 mmHg), and mean diastolic blood pressure (DBP) was  $83.19 \pm 9.33$  mmHg (median: 83.0 mmHg; range: 68–104 mmHg). Shapiro-Wilk testing revealed that overall SBP and DBP distributions were non-normal ( $W=0.9476$ ,  $p=0.0001$  and  $W=0.9574$ ,  $p=0.0006$ , respectively), supporting the use of non-parametric tests for most group comparisons. When classified by ACC/AHA 2017 criteria, 33.1% of participants had normal blood pressure, 6.9% were in the elevated range, 26.2% had Stage 1 hypertension, and 29.8% had Stage 2 hypertension — meaning that 56.1% of participants had blood pressure in the hypertensive range at the time of measurement. The participants with a formal diagnosis of hypertension ( $n=67$ ) had a mean SBP of  $143.45 \pm 10.74$  mmHg, compared to  $116.75 \pm 5.58$  mmHg in those without a diagnosis ( $p<0.001$ , Mann-Whitney U test).

### 3.4 Association Between PPI Use and Hypertension

All 67 clinically diagnosed hypertensive cases were found within the PPI user group, while none of the 16 participants who had never used PPIs had a hypertension diagnosis ( $\chi^2(1)=19.17$ ,  $p<0.001$ ). The odds ratio was computationally undefined owing to complete separation of the groups, indicating an extreme magnitude of association. Duration-stratified analysis revealed a compelling monotonic gradient (Table 3): hypertension was absent among those with fewer than six months of PPI exposure, present in 15.0% of those with 6–12 months of use, in 90.3% of 1–5 year users, and in 100% of those using PPIs for more than five years ( $\chi^2(5)=91.91$ ,  $p<0.001$ ). An analogous pattern was evident with use frequency: daily users had an 81.8% hypertension prevalence, compared to 21.1% for those using PPIs a few times per week and zero for occasional or as-needed users ( $\chi^2(3)=45.95$ ,  $p<0.001$ ). Spearman rank correlation between PPI duration and SBP confirmed a moderate-to-strong positive association ( $\rho=0.61$ ,  $p<0.001$ ). In contrast, PPI type did not independently predict hypertension diagnosis ( $\chi^2(4)=1.27$ ,  $p=0.866$ ).

**Table 3. PPI Duration vs. Diagnosed Hypertension — Prevalence Gradient**

PPI Duration	HTN: Yes	HTN: No	Total	HTN %
Never used PPI	0	16	16	0.0%

< 1 month	0	5	5	0.0%
1–6 months	0	13	13	0.0%
6 months–1 year	3	17	20	15.0%
1–5 years	56	6	62	90.3%
> 5 years	8	0	8	100.0%

$$\chi^2(5) = 91.91, p < 0.001$$

### 3.5 Vitamin B12 Status and Its Association with Hypertension

Exactly half of the participants (n=62, 50.0%) reported low vitamin B12 status. The association between low B12 and diagnosed hypertension was the strongest statistical finding in this dataset: 58 of 62 (93.5%) participants with low B12 had diagnosed hypertension, compared to only 9 of 62 (14.5%) among those with normal B12 levels ( $\chi^2(1)=74.81$ ,  $p<0.001$ ; OR=85.39, 95% CI: 23.7–306.9). Furthermore, among participants with low B12, mean SBP was significantly higher than in those with normal B12 values (Mann-Whitney U,  $p<0.001$ ). These findings are consistent with the proposed mechanistic pathway wherein PPI-induced B12 malabsorption raises plasma homocysteine, promoting endothelial dysfunction and elevated vascular resistance.

### 3.6 Gender and Age Group Analyses

Male participants had a significantly higher prevalence of hypertension (66.2%) compared to females (36.7%), with an OR of 3.23 ( $\chi^2(1)=6.78$ ,  $p=0.003$ ). Kruskal-Wallis analysis across five age groups demonstrated a significant age-related increase in SBP (H=29.47,  $p<0.001$ ). Post-hoc pairwise comparisons with Bonferroni correction ( $\alpha=0.005$ ) identified the most significant SBP elevation in the 40–50 and 50–60 year groups relative to the under-30 cohort. Notably, the 25–30 year group — the largest in this sample — already demonstrated a meaningful proportion of hypertension, consistent with the widely reported earlier onset of cardiovascular risk factors among South Asians.

## IV. DISCUSSION

This cross-sectional survey of 124 Indian adults provides several observations of pharmacoepidemiological relevance. The 86.1% lifetime PPI exposure rate within this sample is substantially higher than estimates derived from general population surveys, and likely reflects the clinical and community settings from which participants were recruited — environments where acid-related disorders and cardiovascular comorbidities are over-represented. While this figure

should not be generalised to the Indian population at large, it does highlight the extent of PPI penetration in settings where hypertensive patients receive care.

The most striking finding was the duration-dependent gradient between PPI exposure and hypertension diagnosis. The threshold at six months of continuous use — below which no hypertension was recorded and above which prevalence rose sharply — aligns with mechanistic evidence that DDAH inhibition, magnesium depletion, and vitamin B12 deficiency each require sustained PPI exposure before reaching clinically meaningful thresholds. Magnesium deficiency, in particular, impairs vascular smooth muscle relaxation and has been shown to elevate peripheral vascular resistance — an effect that typically becomes biochemically measurable only after several months of continuous PPI therapy.

The association between low vitamin B12 and hypertension, though observational, deserves particular attention. An odds ratio of 85.39 is considerably larger than figures reported in most epidemiological studies of single risk factors, and likely reflects both the high prevalence of long-term PPI use in this sample and the co-linearity between B12 depletion and duration of PPI exposure. Chronic PPI therapy impairs gastric acid secretion, which in turn reduces pepsin-mediated release of protein-bound cobalamin, and may reduce intrinsic factor production, leading to impaired ileal absorption of vitamin B12. The resulting hyperhomocysteinaemia is a recognised, independent determinant of endothelial dysfunction, oxidative stress, and arterial stiffening — all contributors to hypertension.

The finding that PPI type did not significantly predict hypertension is clinically informative: it suggests that the cardiovascular risk — to the extent it exists — is likely a class effect mediated by the shared mechanism of acid suppression and its downstream metabolic consequences, rather than the product of pharmacokinetic differences between individual agents. This is consistent with current literature, which has not consistently identified any single PPI as disproportionately associated with cardiovascular harm.

The high prevalence of self-medication (86.1%) in this sample is a public health concern of independent importance. Self-administered, unsupervised PPI therapy precludes the clinical assessments (vitamin B12 monitoring, cardiovascular risk stratification, deprescribing review) that are essential for minimising long-term adverse outcomes. This reinforces the pharmacist's pivotal role in community-level medication review, counselling, and referral — a role that is currently under-utilised in the Indian healthcare system.

Several limitations constrain the interpretation of these findings. The cross-sectional design cannot establish causality; reverse causation is plausible, in that hypertensive patients on multiple medications may be more likely to receive PPI gastroprotection. The convenience sampling strategy and online recruitment method introduce selection bias and limit the generalisability of findings to the broader Indian population. The sample size, while exceeding the a priori power calculation, remains modest for multivariate analysis. Blood pressure was self-reported as a numerical value, and measurement standardisation could not be fully verified. Vitamin B12 status was self-reported rather than confirmed by serum assay, introducing potential misclassification. Occupational data were not collected, precluding stratification by professional category. Despite these limitations, the consistent directionality of findings across multiple analytical approaches — chi-square, Spearman correlation, ANOVA, and Mann-Whitney U — lends credibility to the core observations.

## V. CONCLUSION

This study demonstrates a significant, duration- and frequency-dependent association between chronic PPI use and hypertension in an Indian patient sample, with vitamin B12 deficiency emerging as a strongly associated intermediary variable. These findings contribute to an evolving body of evidence suggesting that the long-term cardiovascular safety of PPIs warrants greater clinical attention than is currently accorded to them in routine practice. They highlight the urgent need for rational prescribing, periodic deprescribing review, routine monitoring of vitamin B12 and magnesium levels in long-term PPI users, and expanded education of both patients and healthcare professionals regarding the risks of unsupervised long-term PPI therapy. Prospective cohort studies with biomarker confirmation and randomised controlled trials comparing PPI strategies with measured cardiovascular endpoints are required to establish causality and to determine whether

targeted deprescribing can mitigate the observed cardiovascular risk in this population.

## DECLARATIONS

**Ethics Approval:** Institutional ethics approval was obtained. All participants provided informed consent. No personally identifiable data were collected or retained.

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**Conflicts of Interest:** The authors declare no conflicts of interest.

**Data Availability:** Anonymised data are available from the corresponding author on reasonable request.

**Author Contributions:** Study conceptualisation, data collection, and primary analysis were conducted by the students under faculty supervision at Sunrise College of Pharmacy under the affiliation of RUHS, Jaipur.

## REFERENCES

- [1]. Tayal R, Yasmin S, Chauhan S, et al. Are Proton Pump Inhibitors Contributing in Emerging New Hypertensive Population? *Pharmaceuticals*. 2023;16(10):1387. doi:10.3390/ph16101387
- [2]. Strand DS, Kim D, Peura DA. 25 Years of Proton Pump Inhibitors: A Comprehensive Review. *Gut Liver*. 2017;11(1):27–37. doi:10.5009/gnl15502
- [3]. Scarpignato C, Gatta L, Zullo A, Blandizzi C; SIF-AIGO-FIMMG Group. Effective and safe proton pump inhibitor therapy in acid-related diseases. *BMC Med*. 2016;14:179. doi:10.1186/s12916-016-0718-z
- [4]. Bhatnagar MS, Choudhari S, Pawar D, Sharma A. Long-Term Use of Proton-Pump Inhibitors: Unravelling the Safety Puzzle. *Cureus*. 2024;16(1):e52773. doi:10.7759/cureus.52773
- [5]. Bahta M, Russom N, Ghebrenegus AS, et al. Omeprazole and Risk of Hypertension: Analysis of Existing Literature and the WHO Global Pharmacovigilance Database. *Drugs Real World Outcomes*. 2024;11(4):735–744. doi:10.1007/s40801-024-00441-2
- [6]. Prabhakaran D, Jeemon P, Roy A. Cardiovascular Diseases in India: Current Epidemiology and Future Directions. *Circulation*. 2016;133(16):1605–1620.

- doi:10.1161/CIRCULATIONAHA.114.008729
- [7]. Prabhakaran D, Jeemon P, Sharma M, et al. The changing patterns of cardiovascular diseases and their risk factors in the states of India: GBD Study 1990–2016. *Lancet Glob Health*. 2018;6(12):e1339–e1351.
- [8]. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA Guideline for Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults. *J Am Coll Cardiol*. 2018;71(19):e127–e248.
- [9]. Freedberg DE, Kim LS, Yang YX. The Risks and Benefits of Long-term Use of Proton Pump Inhibitors. *Gastroenterology*. 2017;152(4):706–715. doi:10.1053/j.gastro.2017.01.031
- [10]. Lam JR, Schneider JL, Zhao W, Corley DA. Proton pump inhibitor and histamine 2 receptor antagonist use and vitamin B12 deficiency. *JAMA*. 2013;310(22):2435–2442.
- [11]. Garje Y, Saikia R, Gupta S, et al. Assessment of Burden of Partial Response to Standard Doses of PPIs in Patients with GERD: A Real-World Evidence Study in India. *Drugs Real World Outcomes*. 2025;12(3):411–424.
- [12]. Soliman AI, Wactawski-Wende J, Millen AE, et al. Proton Pump Inhibitor Use and Incident Hypertension in Menopausal Women. *J Am Heart Assoc*. 2025;14(13):e040009.
- [13]. Dalal J, Dutta AL, Hiremath J, et al. Cardiovascular Compatibility of Proton Pump Inhibitors: Practice Recommendations. *Cardiol Ther*. 2023;12(4):557–570.
- [14]. Yibirin M, De Oliveira D, Valera R, et al. Adverse Effects Associated with Proton Pump Inhibitor Use. *Cureus*. 2021;13(1):e12759.
- [15]. Sachs G, Shin JM, Howden CW. Review article: the clinical pharmacology of proton pump inhibitors. *Aliment Pharmacol Ther*. 2006;23 Suppl 2:2–8.
- [16]. Andrawes M, Andrawes W, Das A, Siau K. Proton Pump Inhibitors: An Evidence-Based Review of Indications, Efficacy, Harms, and Deprescribing. *Medicina*. 2025;61(9):1569.
- [17]. Mir AA, Wani ZA, Bhat AR, et al. Widening spectrum of adverse effects caused by long-term use of proton pump inhibitors. *LabMedDiscov*. 2024;1(2):100027.
- [18]. Amrutha A, Karumarakkal J. Association of Long-Term Proton Pump Inhibitors Use with Hypomagnesemia. *J Adv Med Pharm*. 2023;5(6). doi:10.47009/jamp.2023.5.6.227
- [19]. Wald DS, Law M, Morris JK. Homocysteine and cardiovascular disease: evidence on causality from a meta-analysis. *BMJ*. 2002;325(7374):1202.
- [20]. Marcuard SP, Albernaz L, Khazanie PG. Omeprazole therapy causes malabsorption of cyanocobalamin (vitamin B12). *Ann Intern Med*. 1994;120(3):211–215.
- [21]. Roth GA, Mensah GA, Johnson CO, et al. Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019: Update From the GBD 2019 Study. *J Am Coll Cardiol*. 2020;76(25):2982–3021.
- [22]. Engevik AC, Kaji I, Goldenring JR. The Physiology of the Gastric Parietal Cell. *Physiol Rev*. 2020;100(2):573–602.
- [23]. Duarte GJ, Lopez J, Sosa F, et al. Proton pump inhibitors and cardiovascular risk: a critical review. *Future Cardiol*. 2024;20(14):779–794.
- [24]. Padhi BK, Khatib MN, Zahiruddin QS, et al. Adverse cardiovascular outcomes associated with PPI use after percutaneous coronary intervention: a systematic review and meta-analysis. *BMC Cardiovasc Disord*. 2024;24(1):372.
- [25]. Sarnaik MK, Modi S, Pisipati Y, et al. Proton Pump Inhibitors: Exploring Cardiovascular Complications and Prescription Protocol. *Cureus*. 2021. doi:10.7759/cureus.16744