ISSN 0973-2063 (online) 0973-8894 (print)

Bioinformation 22(10): 6924 -6930 (2026)

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BIOINFORMATION
Discovery at the interface of physical and biological sciences

BIOMEDICAL INFORMATICS

www.bioinformation.net

Volume 22(10)

Research Article

Received October 1, 2026; Revised October 31, 2026; Accepted October 31, 2026, Published October 31, 2026

DOI: 10.6026/973206300226924

SJIF 2026 (Scientific Journal Impact Factor for 2026) = 8.478
2022 Impact Factor (2023 Clarivate Inc. release) is 1.9

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Edited by P Kangueane

Citation: Ghanashree *et al.* Bioinformation 22(10): 6924-6930 (2026)

Adverse effects of proton pump inhibitors among Indians - A retrospective study

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ISSN 0973-2063 (online) 0973-8894 (print)
Bioinformation 22(10): 6924 -6930 (2026)
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Abstract:
The long-term use of Proton pump inhibitor (PPI) is common. However there is little evidence on its association with haematological and biochemical abnormalities among South Indian people. This retrospective observational study included 100 adults (60 PPI users and 40 matched non-users). We evaluated thrombocytopenia, anaemia and serum iron and ferritin and magnesium levels. Thrombocytopenia was significantly more prevalent among PPI users than non-users (53.3% vs. serum ferritin was significantly lower (41.75 vs. 144.25 ng/mL, p=0.001), while serum iron was higher (72.30 vs. 53.78 mcg/dL, p=0.005) in PPI users. PPI duration was negatively correlated with Haemoglobin (r=-0.49), serum iron (r=-0.27) and ferritin (r=-0.41) and no associations were found between anaemia and hypomagnesaemia. Thus, chronic use of a PPI is associated with thrombocytopenia and low iron stores, so it should be monitored regularly while taking this medication for a long period.

Keywords: Proton pump inhibitors (PPIs), thrombocytopenia, iron deficiency, hypomagnesaemia, adverse effects, long-term therapy

Background:
Proton Pump Inhibitors (PPIs) have revolutionized the management of acid-related disorders since their introduction in 1989, establishing themselves as the cornerstone of contemporary gastroenterology **[1]**. These agents act by irreversibly inhibiting the H+ and K+ ATPase on the gastric parietal cell, thereby suppressing gastric acid secretion **[2]**. This mechanism provides reliable symptom relief and promotes mucosal healing across a range of acid-related disorders. Currently, the United States Food and Drug Administration (FDA) has approved six major PPIs Omeprazole, Esomeprazole, Lansoprazole, Dexlansoprazole, Pantoprazole and Rabeprazole for diverse indications, including Peptic ulcer disease, Erosive esophagitis, *Helicobacter pylori* eradication, Gastroesophageal reflux disease (GERD), Zollinger-Ellison syndrome and Stress ulcer prophylaxis in critically ill patients **[3, 4].** Their proven efficacy, favorable short-term tolerability (adverse effects in <5% of users) and widespread accessibility, both by prescription and over the counter, have driven exponential growth in use worldwide **[5]**. However, despite these therapeutic advantages, growing evidence indicates that prolonged, inappropriate use of PPIs has become a significant concern in clinical practice **[6, 7]**. Multiple studies have reported that 40-60% of PPI prescriptions worldwide are unnecessary or continued beyond recommended durations. For instance, Chia *et al*. **[6]** found that nearly half of PPI prescriptions were inappropriate at a Singapore tertiary hospital, while Machado-Alba *et al*. **[7]** documented a substantial increase in healthcare costs due to unnecessary long-term therapy in Colombia. This widespread overutilization has renewed scrutiny of PPIs' long-term safety, as prolonged therapy has been linked to serious adverse effects, including community acquired pneumonia, osteoporosis, vitamin B12 deficiency, dementia, acute interstitial nephritis and *Clostridium difficile* infection; consistently reported across meta-analyses and pharmacoepidemiologic studies **[8-10]**. Beyond these well-established risks, recent clinical investigations highlighted Haematologica and biochemical abnormalities specifically hypomagnesemia, iron deficiency anaemia and thrombocytopenia as emerging long-term effects of PPIs **[11-13]**. While these adverse effects are well characterized in Western populations, epidemiological data characterizing the prevalence, incidence and mechanistic features within South Asian demographics remain limited. The Indian healthcare environment is particularly relevant for investigation due to widespread empirical PPI use, over-the-counter availability, genetic variations influencing PPI metabolism and dietary patterns that may predispose individuals to marginal magnesium and iron stores **[14]**. Therefore, it is of interest to report the adverse effects of Proton pump inhibitors (PPIs), with a focus on Haematologica and biochemical abnormalities such as thrombocytopenia, iron deficiency and hypomagnesaemia, among Indians.

Materials and Methods:
Study design:
Retrospective observational study

Study place:
Tertiary Care Teaching Hospital, Vishakhapatnam, Andhra Pradesh

Study duration:
Data was collected from the patient's medical records covering the period from August 2025 to October 2025. The total duration for data collection and analysis was two months.

Sample size:
The sample size of 100 patients was determined based on the availability of complete and relevant laboratory and clinical data within the defined study period. Given the retrospective design of the study and the limited eligible patient records due to the stringent inclusion and exclusion criteria. Therefore, calculation of a formal sample size was not feasible; however, this sample size is consistent with similar published retrospective analyses evaluating Haematologica/ biochemical abnormalities in PPI users and is sufficient to detect statistically significant associations with a power of approximately 80% at a 5% significance level, given the expected effect sizes from existing literature.

Sampling method:
Electronic medical records and laboratory databases were screened using purposive sampling to identify eligible patients. A total of 180 patient records were initially reviewed, from which patients with complete laboratory data on platelet count, haemoglobin percentage, serum iron, serum ferritin, total iron-binding capacity (TIBC) and serum magnesium were identified.

Inclusion criteria:

Adult patients aged ≥18 years, of either sex. Patients identified as having at least one of the following laboratory abnormalities: hypomagnesaemia, iron deficiency, or thrombocytopenia.
-Availability of complete and documented medical records.

Exclusion criteria:
Patients under 18 years and pregnant women, incomplete or missing records, those on iron/magnesium supplements or with nutritional disorders, history of recent blood loss, transfusion, major surgeries, diagnosed with infections, autoimmunity, exposure to toxins, or on oral medication.

Study subjects:
After rigorous application of these criteria, 100 patients were selected for analysis and stratified into two groups: 60 patients with documented PPI use for at least six months and 40 patients without any history of PPI exposure (non-users), matched by age and gender where possible.

Ethics approval:
The study protocol was approved by the Institutional Ethics Committee (IEC/IAEC Approval Number: (IEC-386/2024)). Since the study involved retrospective data, informed consent was waived, ensuring anonymity and confidentiality of patient information.

Methodology:
Haematologica and biochemical values are collected retrospectively from the laboratory database by reviewing records. The estimation of Hb is performed by photometry and platelet count is determined by optical light scatter. The analyzer used for Hb and platelets is SYSMEX XNL 550. Serum Iron is estimated by using the reagent Roche IRON2 REF 03183696 by the Ferrozine method with no additional deproteinization step. The Xylidyl blue methodology, using a dedicated reagent, is employed to estimate serum magnesium. The data are collected for individuals diagnosed with hypomagnesaemia, iron deficiency and thrombocytopenia who are below the normal range according to the standard biochemical reference values.

Statistical analysis:
The collected data were organised in an Excel spreadsheet and included patient demographics, relevant laboratory parameters, PPI usage details (including specific drugs and durations) and clinical diagnoses. Statistical analysis was performed using SPSS software version 30.0. Quantitative variables were described as mean ± standard deviation (SD) along **w**ith their respective ranges (minimum and maximum values), while qualitative variables were summarized as frequencies and percentages. Depending on the data distribution, appropriate statistical tests were employed: Student's t-test for normally distributed continuous variables, Mann-Whitney U test for non-normally distributed continuous variables and Fisher's exact test for categorical variables.

Results:

A total of 100 patients were included in the study, of which 60 (60%) were Proton Pump Inhibitor (PPI) users and 40 (40%) were non-users. **Table 1** summarizes the demographic and laboratory characteristics of the study participants. The average age of all patients was 49.64 ± 15.41 years, with ages ranging from 18 to 87 years **(Table 2)**. Notably, PPI users were slightly older (mean age: 52.20 ± 16.23 years) compared to non-users (mean age: 45.80 ± 13.37 years) and this difference was statistically significant (Student's t-test: $t = 2.07$, $p = 0.041$). Among the PPI users, 37 were male (61.7%) and 23 were female (38.3%), with no significant difference in gender distribution between the two groups (Fisher's exact test: $p = 0.735$). The mean duration of PPI use was 22.78 ± 26.18 months, ranging from 2 to 120 months. Pantoprazole was the most prescribed PPI (n=22, 36.7%), followed by Rabeprazole (n=17, 28.3%), Omeprazole (n=13, 21.7%) and Esomeprazole (n=8, 13.3%) **(Table 2)**. The average duration of use varied slightly across PPI types: Pantoprazole users (25.36 ± 29.01 months), Rabeprazole users (23.29 ± 28.88 months), Esomeprazole users (21.88 ± 27.11 months) and Omeprazole users (18.31 ± 17.96 months). Mean platelet count was significantly higher in PPI users (1.62 ± 0.74 L/cumm) compared to non-users (1.25 ± 0.15 L/cumm) as assessed by Student's t-test ($t = 3.15$, $p = 0.002$). However, thrombocytopenia was significantly more frequent in PPI users (53.3%, n=32) than in non- users (0%, n=0), indicating a strong association between PPI use and thrombocytopenia prevalence (Fisher's exact test: Chi-square = 25.93, $p < 0.001$) **(Table 3)**. Among PPI types, Omeprazole users demonstrated the highest mean platelet count (1.74 ± 0.67 L/cumm), followed by Rabeprazole (1.65 ± 0.77 L/cumm), Pantoprazole (1.61 ± 0.78 L/cumm) and Esomeprazole users had the lowest (1.35 ± 0.70 L/cumm) **(Table 3).** Mean haemoglobin levels were comparable between PPI users (10.47 ± 2.32 g/dL) and non- users (10.38 ± 2.90 g/dL), with no significant difference detected by Student's t-test ($t = 0.18$, $p = 0.854$). Anaemia prevalence was high in both groups—PPI users (85%, n=51) and non- users (77.5%, n=31)—but showed no significant association with PPI use (Fisher's exact test: $p = 0.339$) **(Table 4).** Among PPI types, Omeprazole users exhibited the highest mean haemoglobin levels (10.98 ± 1.66 g/dL), while Rabeprazole users demonstrated the lowest (10.22 ± 3.04 g/dL) **(Table 4)**. Mean serum iron was significantly higher in PPI users (72.30 ± 27.45 mcg/dL) compared to non-users (53.78 ± 37.37 mcg/dL) as determined by Student's t-test ($t = 2.86$, $p = 0.005$). Low serum iron prevalence was comparable between groups—PPI users (95%, n=57) and non-users (92.5%, n=37)—with no statistically significant difference (Fisher's exact test: $p=0.612$) **(Table 5)**. Among PPI types, Esomeprazole users demonstrated the highest mean serum iron (88.13 ± 23.76 mcg/dL), while Pantoprazole users exhibited the lowest (66.82 ± 24.50 mcg/dL) **(Table 5).** Serum Ferritin Levels: Conversely, PPI users had significantly lower ferritin levels (41.75 ± 22.92 ng/mL) compared to non-users as assessed by Student's t-test ($t = -3.31$, $p = 0.001$), indicating possible depletion of iron stores in PPI users. Low serum ferritin was observed in 21.7% (n=13) of PPI users versus 27.5% (n=11) of non-users, a difference that was not statistically significant using Fisher's exact test ($p = 0.393$) **(Table**

6). Among PPI types, mean ferritin levels were relatively consistent: Omeprazole (44.69 ± 23.06 ng/mL), Pantoprazole (42.14 ± 24.83 ng/mL), Rabeprazole (40.18 ± 23.65 ng/mL) and Esomeprazole (39.25 ± 18.90 ng/mL) (**Table 6**). Total Iron Binding Capacity (TIBC): No significant difference was observed in TIBC between PPI users (384.78 ± 118.85 mcg/dL) and non-users (364.73 ± 90.49 mcg/dL) when evaluated using Student's t-test (t = 0.91, p = 0.367). High TIBC was equally prevalent in PPI users (56.7%, n=34) and non-users (40%, n=16), with no significant association (Fisher's exact test: p = 0.089) **(Table 7).** Among PPI types, Esomeprazole users had the highest mean TIBC (430.00 ± 53.65 mcg/dL), while Rabeprazole users demonstrated the lowest (359.71 ± 107.90 mcg/dL) **(Table 7).** Mean serum magnesium levels were marginally lower in PPI users (1.68 ± 0.48 mg/dL) compared to non-users (1.77 ± 0.31 mg/dL), but this difference was not statistically significant as determined by Student's t-test (t = -0.99, p = 0.323). Hypomagnesaemia was prevalent in both PPI users (68.3%, n=41) and non-users (52.5%, n=21), with no significant association with PPI use (Fisher's exact test: Chi-square = 1.98, p = 0.159) **(Table 8).** Among PPI types, Pantoprazole users had the lowest mean magnesium levels (1.49 ± 0.42 mg/dL), while Esomeprazole users demonstrated the highest (1.86 ± 0.46 mg/dL) **(Table 8). (Table 9)** presents a comparison of Haematological and Biochemical abnormalities between proton pump inhibitor (PPI) users and non-users. Duration of PPI use exhibited clinically relevant negative correlations with several haematological and biochemical parameters, as determined by Pearson correlation analysis. Haemoglobin levels: Strong negative correlation (r = -0.49, p < 0.001, 95% CI: -0.66 to -0.27), indicating that prolonged PPI exposure is associated with declining haemoglobin levels. **(Figure 1)** moderate negative correlation (r = -0.27, p = 0.039, 95% CI: -0.49 to - 0.01), suggesting diminishing serum iron with extended PPI duration **(Figure 2).** Serum Ferritin: Moderate negative correlation (r = -0.41, p = 0.001, 95% CI: -0.60 to -0.17), indicating progressive iron store depletion with longer PPI use **(Figure 3)**. Conversely, no significant correlations were found between PPI duration and platelet count (r = 0.02, p = 0.866), TIBC (r = 0.10, p = 0.445), or serum magnesium (r = 0.17, p = 0.207) when assessed using Pearson correlation analysis **(Table 10)**.

Table 1: Baseline characteristics of the study population (n=100)

Parameter	Mean ± SD	Minimum	Maximum
Age (years)	49.64 ± 15.41	18	87
Platelet Count (L/cumm)	1.47 ± 0.60	0.3	3.58
Hemoglobin (g/dL)	10.43 ± 2.55	4.2	16.8
Serum Iron (µg/dL)	64.89 ± 32.9	8	180
Serum Ferritin (ng/mL)	82.75 ± 159.27	3	900
TIBC (µg/dL)	376.76 ± 108.36	38	920
Serum Magnesium (mg/dL)	1.72 ± 0.42	0.7	3
Duration of PPI Use (months)	22.78 ± 26.18	2	120

Table 2: Comparison of the duration of proton pump inhibitor (PPI) use among different PPI types

Type of PPI	Frequency (n)	Mean Duration (months)	Standard Deviation (months)
Pantoprazole	22	25.36	29.01
Rabeprazole	17	23.29	28.88
Esomeprazole	8	21.88	27.11
Omeprazole	13	18.31	17.96
No PPI Use	**40**		

Table 3: Frequency of proton pump inhibitor (PPI) use and corresponding Mean Platelet Counts (L/cumm) with Standard deviation

Type of PPI	Frequency (n)	Mean Platelet Count (L/cumm)	Standard Deviation
Pantoprazole	22	1.61	0.78
Rabeprazole	17	1.65	0.77
Esomeprazole	8	1.35	0.7
Omeprazole	13	1.74	0.67
No PPI Use	40	1.25	0.15
Total	**100**	**1.47**	0.6

Table 4: Frequency of proton pump inhibitor (PPI) use and corresponding Mean Haemoglobin% (g/dL) with Standard deviation

Type of PPI	Frequency (n)	Mean Haemoglobin% (g/dL)	Standard Deviation
Pantoprazole	22	10.35	2.29
Rabeprazole	17	10.22	3.04
Esomeprazole	8	10.51	1.78
Omeprazole	13	10.98	1.66
No PPI Use	40	10.38	2.9
Total	**100**	**10.43**	2.55

Table 5: Frequency of proton pump inhibitor (PPI) use and corresponding Mean Serum Iron (mcg/dL) with Standard deviation

Type of PPI	Frequency (n)	Mean Serum Iron (mcg/dL)	Standard Deviation
Pantoprazole	22	66.82.	24.5
Rabeprazole	17	71.76	35.1
Esomeprazole	8	88.13	23.76
Omeprazole	13	72.54	21.47
No PPI Use	40	53.78	37.37
Total	**100**	**64.89**	32.9

And corresponding Mean Serum Ferritin (ng/mL) with Standard deviation

Table 6: Frequency of proton pump inhibitor (PPI) use

Type of PPI	Frequency (n)	Mean Serum Ferritin (ng/mL)	Standard Deviation
Pantoprazole	22	42.14	24.83
Rabeprazole	17	40.18	23.65
Esomeprazole	8	39.25	18.9
Omeprazole	13	44.69	23.06
No PPI Use	40	144.25	239.03
Total	**100**	**82.75**	159.27

Table 7: Frequency of proton pump inhibitor (PPI) use and corresponding Mean TIBC Level (mcg/dL) with Standard deviation

Type of PPI	Frequency (n)	Mean Serum TIBC Level (mcg/dL)	Standard Deviation
Pantoprazole	22	396.36	160.76
Rabeprazole	17	359.71	107.9
Esomeprazole	8	430	53.65
Omeprazole	13	370.15	65.51
No PPI Use	40	364.73	90.49
Total	**100**	**376.76**	108.36

Table 8: Frequency of proton pump inhibitor (PPI) use and corresponding Mean Serum Magnesium (mg/dL) with Standard deviation

Type of PPI	Frequency (n)	Mean Serum Iron (mcg/dL)	Standard Deviation
Pantoprazole	22	1.49	0.42
Rabeprazole	17	1.76	0.48
Esomeprazole	8	1.86	0.46
Omeprazole	13	1.81	0.52
No PPI Use	40	1.77	0.31
Total	**100**	**1.72**	0.42

ISSN 0973-2063 (online) 0973-8894 (print)
Bioinformation 22(10): 6924 -6930 (2026)
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Table 9: Comparison of Haematologica and Biochemical abnormalities between proton pump inhibitor (PPI) users and non-users

Parameter	PPI Users (Mean ± SD)	Non- Users (Mean ± SD)	% with Abnormality (PPI Users)
Platelet Count (L/cumm)	1.62 ± 0.74	1.25 ± 0.15	53.30%
Haemoglobin (g/dL)	10.47 ± 2.32	10.38 ± 2.90	85% Anemia
Serum Iron (mcg/dL)	72.30 ± 27.45	53.78 ± 37.37	95% Low Serum Iron
Serum Ferritin (ng/mL)	41.75 ± 22.92	144.25 ±239.03	21.6 % Low Serum Ferritin

Table 10: Correlation of duration of proton pump inhibitor (PPI) use with Haematologica and Biochemical Parameters

Parameter	Correlation Coefficient (r)	p-value	95% CI
Platelet Count	0.02	0.866	(-0.23,0.27)
Haemoglobin	-0.49	<0.001	(-0.66, -0.27)
Serum Iron	-0.27	0.039	(-0.49, -0.01)
Serum Ferritin	-0.41	0.001	(-0.60, -0.17)
TIBC	0.1	0.445	(-0.16, 0.40)
Serum Magnesium	**0.17**	**0.207**	(-0.09, 0.40)

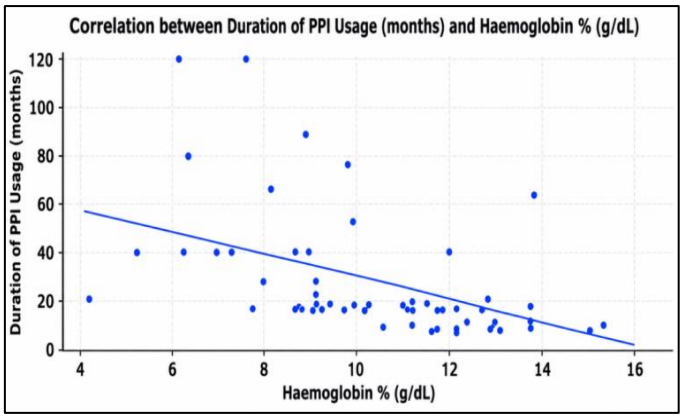


Figure 1: Scatter diagram showing a negative correlation between the duration of PPI therapy and Hemoglobin percentage, with a trend line indicating decreasing ferritin levels with prolonged PPI use

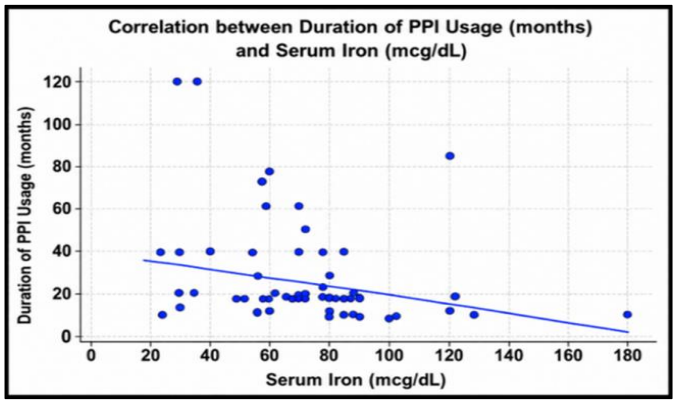


Figure 2: Scatter diagram showing a negative correlation between the duration of PPI therapy and Serum Iron concentration, with a trend line indicating decreasing ferritin levels with prolonged PPI use

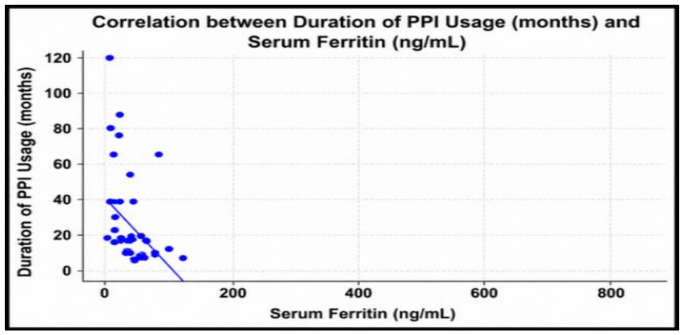


Figure 3: Scatter diagram showing a negative correlation between the duration of PPI therapy and Serum Ferritin concentration, with a trend line indicating decreasing ferritin levels with prolonged PPI use

Discussion:

The present study investigated the haematological and biochemical consequences of prolonged proton pump inhibitor (PPI) therapy in a tertiary care hospital among 100 patients, including 60 PPI users and 40 non-users. The study focused on thrombocytopenia, anaemia, iron deficiency and hypomagnesaemia and evaluated their association with PPI exposure and treatment duration. A significant association was observed between PPI use and thrombocytopenia. Thrombocytopenia was present in 53.3% of PPI users, compared with none among non-users ($p < 0.001$). This prevalence is considerably higher than that reported in the literature, in which PPI-associated thrombocytopenia is considered a rare adverse event. A systematic analysis of published case reports identified only 18 cases of PPI-associated thrombocytopenia, with pantoprazole being the most frequently implicated drug, followed by lansoprazole, omeprazole and esomeprazole **[15].** Differences in patient characteristics, prescribing patterns, population susceptibility and individual drug effects may contribute to variations in reported findings. In contrast, no significant differences in haemoglobin levels or anaemia prevalence were observed between PPI users and non-users. Mean haemoglobin was 10.47 ± 2.32 g and dL in PPI users and 10.38 ± 2.90 g and dL in non-users ($p = 0.854$), while anaemia was observed in 85% and 77.5%, respectively ($p = 0.339$). The high prevalence of anaemia in both groups suggests that factors unrelated to PPI therapy, including chronic disease, nutritional deficiencies and the high disease burden among hospitalized patients, may have substantially influenced these findings. Previous epidemiological studies, however, have reported an association between prolonged acid-suppressive therapy and iron deficiency **[16, 17].** Nevertheless, among PPI users in the present study, PPI duration showed a significant negative correlation with haemoglobin ($r = -0.49$, $p < 0.001$), suggesting that prolonged exposure may be associated with progressive reduction in haemoglobin levels. Iron parameters demonstrated an interesting dissociation. Serum ferritin was significantly lower among PPI users than non-users (41.75 ± 22.92 vs. 144.25 ± 239.03 ng or mL; $p = 0.001$), whereas serum iron was

significantly higher in PPI users (72.30 ± 27.45 vs. 53.78 ± 37.37 mcg or dL; p = 0.005). The reduced ferritin levels are consistent with evidence suggesting impaired iron absorption during prolonged PPI therapy **[18].** Gastric acid facilitates the absorption of non-haemoglobin iron and suppression of gastric acidity may reduce iron bioavailability **[19, 20].** In addition, experimental evidence suggests that PPIs may influence iron metabolism through hepcidin upregulation and reduced ferroportin expression **[21].** The paradoxical increase in serum iron despite reduced ferritin in the present study may reflect mobilization of stored iron, inflammatory elevation of ferritin among non-users, diurnal variation in serum iron, or unrecorded iron supplementation. Importantly, duration of PPI therapy was negatively correlated with both serum iron (r = -0.27, p = 0.039) and ferritin (r = -0.41, p = 0.001). The stronger correlation with ferritin suggests that depletion of iron stores may be a more sensitive indicator of prolonged PPI-associated alterations than circulating serum iron. Previous studies have similarly demonstrated an increased risk of iron deficiency with long-term PPI exposure, particularly with longer duration and greater acid suppression **[16, 17].** TIBC did not differ significantly between groups and showed no significant correlation with treatment duration, indicating that iron transport capacity may remain relatively preserved despite changes in iron storage and absorption. Serum magnesium levels and hypomagnesaemia also did not differ significantly between groups. Hypomagnesaemia occurred in 68.3% of PPI users and 52.5% of non-users (p = 0.159). Although this finding does not demonstrate a significant association with PPI use, the high prevalence in both groups suggests that dietary deficiency, gastrointestinal disorders, diuretic therapy and underlying comorbidities may have contributed substantially. Long-term PPI use has nevertheless been associated with hypomagnesaemia in observational studies and case reports, with impaired intestinal magnesium absorption proposed as an important mechanism **[22-28].** Overall, duration analysis demonstrated significant negative correlations with haemoglobin, serum iron and serum ferritin, but not with platelet count, TIBC, or magnesium. These findings suggest that prolonged PPI exposure may have cumulative effects, particularly on haemoglobin and iron parameters, whereas thrombocytopenia and hypomagnesaemia may involve more complex, acute, or idiosyncratic mechanisms. The absence of a duration-dependent relationship for platelet count is also consistent with reports suggesting that PPI-associated thrombocytopenia may represent an uncommon, potentially immune-mediated adverse reaction rather than a simple cumulative-dose effect **[15-17, 29-30]**. Thus, the study hypothesis was strongly supported for thrombocytopenia but was not supported for anaemia or hypomagnesaemia when comparing PPI users with non-users. The high prevalence of anaemia and hypomagnesaemia among non-users indicates that multiple underlying clinical and nutritional factors may contribute to these abnormalities in hospitalized populations. The study has several limitations. Its retrospective, single-centre design, moderate sample size and reliance on medical records limit generalizability and causal interpretation. Potential confounders, including nutritional status, socioeconomic factors, lifestyle, comorbidities, concurrent medications and iron supplementation, were not adequately assessed. Ferritin may have been influenced by inflammation, as it is an acute-phase reactant, whereas serum iron is subject to biological and diurnal variation. Differences in PPI type, dose and treatment duration, together with possible inaccuracies in recorded duration, further limit interpretation. Future studies should use prospective, multicentre designs with larger sample sizes and standardized laboratory sampling. Detailed assessment of nutritional status, comorbidities, concomitant medications, PPI type and dose and supplementation is recommended. Longitudinal studies and controlled deprescribing interventions could further determine whether haematological abnormalities are reversible and clarify the causal relationship between prolonged PPI exposure and these abnormalities.

Conclusion:

Data shows clear associations between thrombocytopenia and altered iron stores. This study highlights the importance of evidence-based prescribing and judicious use of PPIs, considering their long-term adverse effects. However, further prospective multicentre study is needed to validate the associations and ensure the safe use of long-term PPIs in clinical practice.

Conflict of interest: Nil

References:

[1] Strand DS *et al. Gut Liver.* 2017 **11**:27. [PMID: 27840364]
[2] https://www.ncbi.nlm.nih.gov/books/NBK557385/
[3] El Rouby N *et al. Expert Opin Drug Metab Toxicol.* 2018 **14**:447. [PMID: 29620484]
[4] Savarino V *et al. Eur J Intern Med.* 2017 **37**:19. [PMID: 27784575]
[5] Thurber KM *et al. Am J Health Syst Pharm.* 2023 **80**:487. [PMID: 36629265]
[6] Chia CTW *et al. Singapore Med J.* 2014 55:363. [PMID: 25091884]
[7] Machado-Alba J *et al. Colomb Med (Cali).* 2013 **44**:13. [PMID: 24892316]
[8] Ito T & Jensen RT. *Curr Gastroenterol Rep.* 2010 **12**:448. [PMID: 20882439]
[9] Maideen NMP. *Chonnam Med J.* 2023 **59**:115. [PMID: 37303818]
[10] Bhatnagar MS *et al. Cureus.* 2024 **16**: e52773. [PMID: 38389608]
[11] Arj A *et al. Caspian J Intern Med.* 2022 **13**:107. [PMID: 35178215]
[12] Tran-Duy A *et al. J Intern Med.* 2019 **285**:205. [PMID: 30141278]
[13] Mukherjee S *et al. Case Rep Gastrointest Med.* 2018 **2018**:4294805. [PMID: 29854491]
[14] Shikha D *et al. Int J Basic Clin Pharmacol.* 2025 **17**: 57. [DOI: 10.31838/ijpr/2025.17.03.007]

[15] Yue X & Tian H. *Open Med (Wars)*. 2025 **20**:20251297. [PMID: 41216201]
[16] Lam JR *et al*. *Gastroenterology*. 2017 **152**:821.e1. [PMID: 27890768]
[17] Ali MD. *Curr Rev Clin Exp Pharmacol*. 2023 **18:**158. [PMID: 35255801]
[18] Boxer M *et al*. *EJHaem*. 2020 **1**:548. [PMID: 35845020]
[19] Tempel M. *Turk J Haematol*. 2013 **30**:307. [PMID: 24385811]
[20] Hamano H *et al*. *Toxicol Lett*. 2020 **318**:86. [PMID: 31669099]
[21] Hess MW *et al*. *Aliment Pharmacol Ther*. 2012 **36**:1109. [PMID: 22762246]
[22] William JH & Danziger J. *World J Nephrol*. 2016 **5**:152. [PMID: 26981439]
[23] Gommers LMM *et al*. *Acta Physiol (Oxf)*. 2022 **235**:e13846. [PMID: 35652564]
[24] Kallam A *et al*. *Platelets*. 2015 **26**:598. [PMID: 25207666]
[25] Chen Y *et al*. *Cardiovasc Toxicol*. 2026 **26**:103. [PMID: 42701947]
[26] Hadi KN *et al*. *Pak J Med Sci*. 2025 **41**:1388. [PMID: 40469125]
[27] Yibirin M *et al*. *Cureus*. 2021 **13**:e12759. [PMID: 33614352]
[28] Jenkins D & Modolell I. *BMJ*. 2023 **383**:e070752. [PMID: 37957000]
[29] Lakshmisai SS *et al*. *Cureus*. 2025 **17**:e90606. [PMID: 40843060]
[30] Andrawes M *et al*. *Medicina (Kaunas)*. 2025 **61**:1569. [PMID: 41010960]

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