Effect of *Helicobacter pylori* Treatment on Unexplained Iron Deficiency Anemia

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ABSTRACT

Background: A large number of patients with iron deficiency anemia have no known cause of their anemia despite a full evaluation. Optimal management and follow-up for this issue is unclear. Results of previous studies have implicated *Helicobacter pylori* infection as a potential cause of iron deficiency anemia.

Objectives: To investigate whether *H pylori* infection could be a cause of unexplained iron deficiency anemia.

Methods: All adult patients with both unexplained iron deficiency anemia and *H pylori* infection diagnosed between January 1, 2008 and April 30, 2015 were identified from Kaiser Permanente Northern California's electronic medical records database and were followed-up for up to 2 years. We employed bivariate statistics to analyze demographic and clinical characteristics between *H pylori* treatment groups (treated and untreated). Multivariable logistic regression was used to assess the odds of continued presence of anemia at follow-up.

Results: Of 508 subjects who fit our inclusion criteria, 408 subjects were treated for *H pylori*. The median initial level of hemoglobin was 10.5 g/dL and ferritin was 7.0 ng/mL. No difference existed in the continued presence of iron deficiency anemia at follow-up between those treated for *H pylori* and those not treated (24.3% vs 26.5%, p = 0.71). Both groups had improved levels of hemoglobin (25.4% mean increase in treated vs 27.5% mean increase in untreated) at follow-up.

Conclusion: In contrast to the findings of previous studies, we found no evidence that *H pylori* is involved in causing iron deficiency anemia. Iron deficiency anemia resolved in most subjects regardless of *H pylori* treatment status.

INTRODUCTION

Iron deficiency is the most common nutritional disorder in the world, and it is estimated that at least 500 million people have iron deficiency anemia (IDA) worldwide.[1] IDA can develop from poor iron intake, chronic blood loss, or impaired iron absorption. Additionally, in women of reproductive age, IDA is commonly attributed to increased blood loss from menstruation. Standard care for adults with IDA includes a complete evaluation of the gastrointestinal tract to exclude an abnormality. However, even after a full investigation, approximately 30% of IDA cases remain without a clear cause.[2] Many of these patients undergo repeated rounds of invasive and expensive gastrointestinal procedures and testing.

Helicobacter pylori is a common infection worldwide. It is estimated that 30% to 40% of the US population are infected with *H pylori*.[3] Most of those infected with *H pylori* are clinically asymptomatic; however, *H pylori* infection is associated with several important upper gastrointestinal tract conditions, including chronic gastritis, peptic ulcer disease (PUD), and gastric malignancy. Established indications for *H pylori* testing and treatment include PUD, gastric mucosa-associated lymphoid tissue lymphoma, gastric cancer, and uninvestigated dyspepsia.[4] Current treatment regimens for *H pylori* infection involve an antisecretory agent combined with antimicrobials. Cure rates of 80% to 90% have been attained with these regimens.[3]

Multiple studies have implicated an association between *H pylori* infection and IDA.[5-7] Lesions from PUD or gastric cancer can bleed and eventually lead to IDA. More commonly, however, *H pylori* infection causes chronic gastritis without overt symptoms. Several theories have been put forward as to how *H pylori* infection can lead to IDA, including impairing iron absorption, competing with the host for uptake of iron, or elevating the pH and reducing vitamin C concentration.[8,9] The American College of Gastroenterology has called for further studies to assess whether *H pylori* eradication offers benefit to patients with unexplained IDA, and several guidelines now recommend *H pylori* eradication in these patients.[4,10,11]

We therefore conducted a retrospective cohort study of patients with a diagnosis of unexplained IDA and the presence of *H pylori* to determine whether treatment of *H pylori* infection leads to significant improvement of IDA.

METHODS

Setting

This study was conducted in Kaiser Permanente Northern California (KPNC), an integrated health care delivery organization serving approximately 3.85 million patients as of 2016, across 18 medical centers covering urban, suburban, and semirural areas.[12] The KPNC member population approximates the socially and racially/ethnically diverse general population of Northern California.[12]

Study Design

Data such as diagnosis codes and procedure codes; laboratory tests and results; vital signs; and physician notes from outpatient, inpatient, and Emergency Department visits are recorded and maintained in KPNC electronic medical records. In this retrospective cohort study, International Classification of Diseases,

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Ninth Revision codes (280.9, 281.8, 281.9, 285.9, 280.0, 280.1, and 280.8) were used to identify patients between age 18 and 89 years who had a diagnosis of anemia coded from January 1, 2008, to April 30, 2015. IDA was defined as having iron deficiency and a low hemoglobin value. We used normal hemoglobin parameters adjusted for sex and age using data derived from the second National Health and Nutrition Examination Survey (NHANES II).[13] Serum ferritin is the most sensitive and specific test used for the identification of iron deficiency.[14] Other commonly used laboratory tests provide little diagnostic value over ferritin.[15] For this study, we relied on expert recommendations to determine a serum ferritin level less than 30 ng/mL as iron deficient, providing a sensitivity of 92% and specificity of 98%.[16-18] Subjects with low serum ferritin and hemoglobin values within 2 months of a coded diagnosis of anemia were considered to have IDA.

Data on endoscopic procedures were obtained and manually reviewed. Only those patients with a documented "negative" workup—results that did not yield a cause of their anemia—were included in the cohort. A *negative workup* was defined as a normal esophagogastroduodenoscopy (EGD) and colonoscopy within 6 months after an IDA diagnosis. We considered the date of the first endoscopic procedure as the index date for the purposes of the study. If a capsule endoscopy was performed, the results were examined, and only those patients whose capsule endoscopy results did not reveal the cause of anemia were included in the study. Clinically significant gastrointestinal findings included masses, ulcerations, villous blunting of the small bowel mucosa suggestive of celiac disease, colitis, vascular ectasia or arteriovenous malformation, inflammatory polyps, or large bleeding hemorrhoids. Nonspecific descriptive findings such as inflammation or mucosal erythema of the gastric mucosa were not excluded.

We identified *H pylori* infection by a biopsy with histopathologic evidence of *H pylori*, a stool antigen positive for *H pylori*, a urea breath test positive for *H pylori,* or positive serum anti-*H pylori* antibody obtained within 6 months of the endoscopic procedures. Those patients who did not have a positive or abnormal *H pylori* result were excluded.

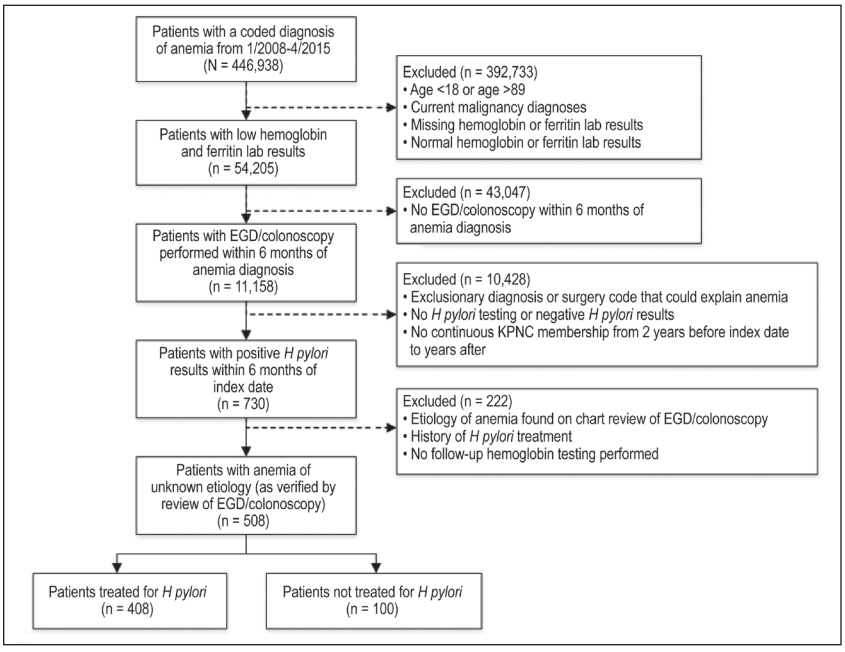

Figure 1. Cohort assembly: Idiopathic iron deficiency anemia with *Helicobacter pylori* assembly.
EGD = esophagogastroduodenoscopy; *H pylori* = *Helicobacter pylori,* KPNC = Kaiser Permanente Northern California; lab = laboratory test.

We further excluded those with a previous history of *H pylori* infection, malignancy, anemia of other cause, inflammatory bowel disease, gastrointestinal hemorrhage, chronic kidney disease, PUD, celiac disease, presence of arteriovenous malformation, pregnancy within 9 months of the endoscopic procedures (before or after), or history of gastrointestinal surgery.

Treatment of *H pylori* was extracted from pharmacy records. The cohort was divided into those who were treated and those who were not treated for *H pylori* infection. At follow-up closest to 24 months, the groups were evaluated for continued presence of IDA, the presence of anemia without iron deficiency, and the change in ferritin level.

We gathered information on demographic factors, including age, sex, and race/ethnicity. Socioeconomic status was obtained measuring census block-level median family income and median education levels. Comorbid conditions were measured with the Charlson Comorbidity Index.[19] Pharmacy data were collected with respect to the medical regimens used to eliminate *H pylori*. For 2 years from the index date (date of the first endoscopic procedure), information on treatment with medications that could affect bleeding tendencies or treat gastrointestinal tract conditions (eg, histamine 2 [H_2] blockers, proton-pump inhibitors [PPIs], nonsteroidal anti-inflammatory drugs [NSAIDs], antiplatelet agents, and anticoagulants) was extracted electronically, as well as by manual chart review because these medications are also available in over-the-counter forms. Because PPI use is included in the treatment regimen for *H pylori*, we were unable to separate PPI use for other indications. As iron supplements can improve ferritin and hemoglobin levels, manual and electronic chart review was once more employed to search for use of oral or intravenous iron.

This study was approved with a waiver of consent by the Kaiser Foundation Institute's institutional review board.

Statistical Analysis

We employed bivariate statistics to analyze demographic and clinical characteristics between *H pylori* treatment groups. The association between *H pylori*

treatment and continued presence of IDA was examined. Bivariate comparisons on categorical variables, such as study group and the patient's sex, race/ethnicity, median education level (census-block level), Charlson comorbidity score, test used for diagnosis of *H pylori*, and medication use were made using the χ^2 test and Fisher exact test. The Student *t*-test was used for comparison of means for age, which was a normally distributed continuous variable. Other continuous variables, including baseline hemoglobin level, baseline ferritin level, and family income (census-block level), were found to be nonnormally distributed; they were reported using medians and interquartile ranges and were compared using the Wilcoxon rank sum (Mann-Whitney) nonparametric test.

We performed multivariable logistic regression to assess the odds of continued presence of anemia at follow-up in subjects in the treated group compared

Table 1. Baseline characteristics of patients with unexplained iron deficiency anemia and history of *Helicobacter pylori* infection at Kaiser Permanente Northern California

Characteristic	Patient total (N = 508)	*H pylori* treatment status		p value (χ^2)
		Yes (n = 408)	No (n = 100)	
Sex, no. (%)				0.008
Women	317 (62.4)	243 (59.6)	74 (74.0)	
Men	191 (37.6)	165 (40.4)	26 (26.0)	
Mean age (SD), y	58.2 (15.1)	58.3 (13.0)	57.7 (13.4)	0.68[a]
Age group, y				0.75
18-45	86 (16.9)	68 (16.7)	18 (18.0)	
46-55	159 (31.3)	125 (30.6)	34 (34.0)	
56-65	103 (20.3)	82 (20.1)	21 (21.0)	
66-75	101 (19.9)	86 (21.1)	15 (15.0)	
> 75	59 (11.6)	47 (11.5)	12 (12.0)	
Median baseline Hb, g/dL (IQR)	10.5 (9.5-11.3)	10.5 (9.5-11.3)	10.4 (8.7-11.3)	0.09[b]
Median baseline ferritin, ng/mL (IQR)	7.0 (4.9-11.0)	7.0 (4.9-11.5)	7.0 (4.9-10.0)	0.32[b]
Race/ethnicity, no. (%)				0.19
White	137 (27.0)	108 (26.5)	29 (29.0)	
Black	48 (9.5)	42 (10.3)	6 (6.0)	
Hispanic	172 (33.9)	130 (31.9)	42 (42.0)	
Asian	111 (21.9)	94 (23.0)	17 (17.0)	
Other/missing	40 (7.9)	34 (8.3)	6 (6.0)	
Median family income, $US (IQR)[c]	83,266 (60,949-107,375)	85,213 (63,210-108,269)	73,259 (54,888-94,787)	0.02[b]
Median education level, no. (%)[c]				0.39
High school or below	87 (17.1)	67 (16.4)	20 (20.0)	
Some college or above	421 (82.9)	341 (83.6)	80 (80.0)	
Charlson Comorbidity Index score, no. (%)				0.50
0	269 (52.9)	213 (52.2)	56 (56.0)	
≥ 1	239 (47.1)	195 (47.8)	44 (44.0)	
Medication use, no. (%)				
Iron, documented	340 (66.9)	270 (66.2)	70 (70.0)	0.47
PPI	388 (76.4)	329 (80.6)	59 (59.0)	< 0.001
H_2 blocker	124 (24.4)	107 (26.2)	17 (17.0)	0.05
NSAID	335 (65.9)	268 (65.7)	67 (67.0)	0.80
Antiplatelet agent	14 (2.8)	11 (2.7)	3 (3.0)	0.74[d]
Anticoagulant	29 (5.7)	26 (6.4)	3 (3.0)	0.19
Test used for diagnosis, no. (%)				0.10[d]
Serologic analysis	111 (21.9)	80 (19.6)	31 (31.0)	
Biopsy on endoscopy	355 (69.9)	293 (71.8)	62 (62.0)	
Stool antigen	3 (0.6)	3 (0.7)	0 (0)	
Urease breath test	39 (7.7)	32 (7.8)	7 (7.0)	

[a] p value for comparison calculated by Student *t*-test.
[b] p value for comparison calculated by Wilcoxon rank sum test.
[c] Family income and education level are on the census block level.
[d] p value for comparison calculated by Fisher exact test.
Hb = hemoglobin; H_2 = Histamine 2; IQR = interquartile range; NSAID = nonsteroidal anti-inflammatory drug; PPI = proton-pump inhibitor; SD = standard deviation.

with the untreated group. Multivariable analyses were adjusted for the covariates: Age, sex, race and ethnicity, comorbid conditions, census-block level median income, census-block level median education level, medication use, and test used to detect *H pylori* infection. All data management and analyses were performed using statistical software (SAS Version 9.3, SAS Institute, Cary, NC). A p value of < 0.05 was considered significant.

Table 2. Presence of anemia at follow-up by treatment status

Continued presence of anemia at follow-up	Patient total, no. (%) (N = 508)	*Helicobacter pylori* treatment status, no. (%)		p value (χ^2)
		Yes (n = 408)	No (n = 100)	
Any anemia	138 (27.2)	114 (27.9)	24 (24.0)	0.43
Iron-deficiency anemia	83 (24.7)[a]	65 (24.3)[b]	18 (26.5)[c]	0.71

[a] A total of 172 subjects were missing serum ferritin results, and the percentage is calculated from 236.
[b] A total of 140 subjects were missing ferritin results, and the percentage is calculated from 268.
[c] A total of 32 subjects were missing ferritin results, and the percentage is calculated from 68.

RESULTS

A total of 446,938 subjects had a coded diagnosis of anemia between January 1, 2008, and April 30, 2015. After we applied preliminary exclusions on active malignancy and age, 54,205 subjects had laboratory evidence of IDA (defined as low ferritin and low hemoglobin results within 2 months of coded anemia diagnosis). Further exclusions ultimately yielded 730 subjects with positive *H pylori* tests within 6 months of their EGD/colonoscopy procedure. After additional exclusionary criteria were applied (history of *H pylori* treatment, the cause found for anemia on EGD/colonoscopy, or no follow-up laboratory testing), the final cohort included 508 subjects. Of these, 408 were treated for *H pylori* infection (Figure 1).

Results for demographic and clinical characteristics between subjects treated for *H pylori* and those not treated are shown in Table 1. Overall, the median age of the cohort was 58 years, and most patients were women (62.4%), possibly because women of menstruating age were included. At baseline, the median hemoglobin level for the entire cohort was 10.5 and median ferritin level was 7.0 ng/mL (interquartile range = 4.9-11.0 ng/mL). There was a diverse range of ethnicities represented. Median family income for the entire cohort was $83,266 but was significantly lower in the untreated group than the treated group (p = 0.02). The Charlson comorbidity score and the test used for diagnosis were similar between the treated and untreated groups. Medication use was also similar between the 2 groups except for significantly higher use of PPIs in the treated group (p < 0.001; Table 1). Of the 508 subjects in our cohort, only 25 (4.9%) had capsule endoscopies performed. Among 408 subjects treated for *H pylori*, most (84.6%, n = 345) were treated with 10- or 14-day courses of amoxicillin, clarithromycin, and omeprazole. The remainder (15.4%, n = 63) were treated with omeprazole and metronidazole combined with clarithromycin or amoxicillin.

Table 2 displays the continued presence of anemia and IDA at the time of follow-up overall as well as by treatment group. There were 172 subjects with no follow-up ferritin results, so their iron deficiency status at follow-up could not be assessed. No significant difference existed in the continued presence of IDA at follow-up between those treated for *H pylori* and those not treated (24.3% vs 26.5%, p = 0.71). The mean (standard deviation) time for follow-up hemoglobin results for untreated patients was 21.7 (6.4) months compared with 22.7 (6.0) months for treated subjects. For ferritin, the mean (standard deviation) time for follow-up was 19.4 (9.4) months in the untreated group, whereas for those treated it was 18.6 (8.9) months.

Laboratory values, including hemoglobin and ferritin, at baseline and at

Table 3. Hemoglobin and ferritin levels at follow-up by *Helicobacter pylori* treatment status

Laboratory test	Treated for *H pylori*				Untreated for *H pylori*				p value
	At baseline	At follow-up	Absolute difference	Percentage change	At baseline	At follow-up	Absolute difference	Percentage change	
Hemoglobin, mean (SD), g/dL									
Overall	10.29 (1.58)	12.90 (1.89)	2.61 (2.31)	25.4	9.95 (1.72)	12.69 (1.62)	2.73 (2.29)	27.5	0.64[a]
Women	9.98 (1.35)	12.31 (1.67)	2.33 (2.21)	23.3	9.76 (1.57)	12.31 (1.52)	2.56 (2.17)	26.1	0.44[a]
Men	10.75 (1.77)	13.77 (1.86)	3.02 (2.40)	28.1	10.51 (2.03)	13.74 (1.46)	3.23 (2.60)	30.7	0.68[a]
Ferritin, mean (SD), ng/mL									
Overall	8.86 (5.61)	47.28 (64.61)[b]	38.43 (64.26)	433.6	8.24 (5.59)	40.76 (54.87)[c]	32.78 (53.41)	394.7	0.85[d]
Women	8.08 (5.44)	40.28 (58.97)[e]	32.22 (59.15)	398.5	8.23 (6.26)	41.83 (62.65)[f]	34.07 (60.93)	408.3	0.81[d]
Men	10.0 (5.67)	60.67 (72.69)[g]	50.31 (71.91)	506.7	8.26 (3.05)	38.00 (26.99)[h]	29.43 (26.51)	360.0	0.57[d]

[a] p value for comparison calculated by Student *t*-test.
[b] A total of 140 subjects were missing serum ferritin results.
[c] A total of 32 subjects were missing ferritin results.
[d] p value for comparison calculated by Wilcoxon rank sum test.
[e] A total of 67 subjects were missing ferritin results.
[f] A total of 25 subjects were missing ferritin results.
[g] A total of 73 subjects were missing ferritin results.
[h] Seven subjects were missing ferritin results.
SD = standard deviation.

follow-up are described in Table 3. Overall, both groups had improved levels of hemoglobin (25.4% increase in those treated vs 27.5% increase in those untreated; p = 0.64). The improvements were similar for both men and women. Unfortunately, our results for ferritin were limited because a large number of subjects did not have follow-up ferritin tests performed. Predictably, the ferritin levels also improved, by an average of 38.43 ng/mL for treated and an average of 32.78 ng/mL for those untreated for *H pylori* infection (p = 0.85). Interestingly, men had a much greater improvement in ferritin levels in the treated group, but the results were not significant (follow-up ferritin of 60.67 ng/mL vs 38.00 ng/mL, p = 0.57; Table 3). Because of concerns that menstruating women may have different causes for IDA, subanalyses were performed excluding women younger than age 50 years, excluding women younger than age 55 years, or just involving women younger than age 50 years. There were 107 women younger than age 50 years and 171 younger than age 55 years. No significant differences were found between treated and untreated groups in any of the subgroups.

After adjusting for demographic, socioeconomic, and clinical characteristics in multivariable logistic regression, treatment of *H pylori* was not a significant predictor of continued presence of anemia (adjusted odds ratio [OR] = 1.25, 95% confidence interval [CI] = 0.72-2.17; Table 4).

Table 4. Multivariate analysis of continued presence of anemia in treated group compared with untreated group at follow-up

Characteristic	Adjusted odds ratio	95% confidence interval
Age, y		
18-45	0.92	0.50-1.71
46-55 (reference)	—	—
56-65	0.77	0.41-1.42
66-75	0.87	0.47-1.62
> 75	0.48	0.22-1.04
Sex		
Men (reference)	—	—
Women	1.29	0.83-2.03
Race		
White (reference)	—	—
Asian	0.55	0.28-1.10
Black	2.24	1.07-4.73
Hispanic	1.45	0.83-2.55
Other	1.75	0.78-3.92
Charlson Comorbidity Index score		
0 (reference)	—	—
≥ 1	1.09	0.70-1.69
Helicobacter pylori		
Untreated (reference)	—	—
Treated	1.25	0.72-2.17
Medication use		
PPI	0.87	0.54-1.41
H_2 blocker	1.40	0.87-2.26
NSAID	1.28	0.82-2.02
Iron	0.73	0.47-1.14
Test used to detect infection		
Serologic analysis	0.79	0.46-1.34
Biopsy on endoscopy (reference)	—	—
Stool antigen or urease breath test	0.80	0.38-1.72
Median income (per $10,000)	1.01	0.95-1.08
Median education level		
High school or less (reference)	—	—
Some college or above	0.91	0.51-1.66

H_2 = histamine 2; NSAID = nonsteroidal anti-inflammatory drug; PPI = proton-pump inhibitor.

DISCUSSION

The presence of IDA with normal upper endoscopy and colonoscopy findings continues to present a diagnostic dilemma for primary care physicians and gastroenterologists. Experts have recommended screening for celiac disease, autoimmune gastritis, *H pylori,* and hereditary forms of IDA.[20] If the IDA is still unexplained, options for management of these cases include examination of the small intestine through capsule endoscopy, imaging studies, repeated endoscopic studies, double balloon enteroscopy, or simply supportive monitoring of anemia status with iron supplementation over time.[21] An investigation into capsule endoscopy showed a low diagnostic yield of 25.7%, with capsule endoscopy results not altering management in most patients and the conclusion that the utility of this technique is limited.[22]

Previous studies have implicated *H pylori* infection as a cause of IDA. Most are epidemiologic surveys in developing countries or involve children.[5,6] Cardenas et al[7] found that among more than 8000 adults and children in an Alaska population, *H pylori* infection was associated with an increased risk of IDA (OR = 2.6, 95% CI = 1.5-4.6), with the chance of infection more common in immigrants, poor individuals, and nonbreastfed children. A meta-analysis on the role of *H pylori* infection in IDA found a relationship between *H pylori* and IDA (OR = 2.22, 95% CI = 1.52-3.324, p < 0.0001).[23] Other studies have examined whether treatment of *H pylori* infection can resolve anemia. For example, Monzon et al[24] prospectively evaluated 89 patients with refractory IDA and with *H pylori* infection, who had normal EGD and colonoscopy results. Resolution of IDA after treatment of *H pylori* was found in 80% of men (8 of 10), 71%

of postmenopausal women (10 of 14), but only 23% of premenopausal women (14 of 60).[24] Similarly, a case series of 30 patients with IDA, *H pylori*–associated gastritis, and negative workup were followed after treatment of *H pylori* infection and discontinuation of iron therapy for 12 months.[25] At 6 months, 74% of patients had recovered from anemia, and 91.7% had recovered at 12 months.[25]

In contrast, our study does not show any difference in improvement of IDA after treatment of *H pylori* when followed-up for up to 2 years compared with those who were not treated. More specifically, even though studies have found that IDA resolves with treatment of *H pylori*, our findings show that anemia resolves in most patients regardless of whether the infection was treated or not. It was reassuring that even though the cause of IDA was unknown in these cases, the anemia resolved in all but 27.2% of our population. This finding suggests that the initial cause of the anemia may have been self-limited and did not require specific treatment; however, that leaves almost 30% of our patients with persistent, unexplained anemia.

It was interesting to see the marked improvement, although not statistically significant, in ferritin levels in the treatment group among men. Additional studies with a larger cohort may be helpful in determining if there are significant differences in iron levels by sex over time.

Because of the retrospective design, limitations of our study include selection bias and being confined to the data available in existing databases. The latter limitation is evident in the use of nonprescription medications such as NSAIDs and iron because of the reliance on patient self-report for medical documentation. However, any major NSAID-related cause of gastrointestinal hemorrhage and IDA would likely be diagnosed through endoscopic evaluation. There was also a substantial loss to follow-up and lack of follow-up laboratory studies performed. This was most noticeable in the deficiency of follow-up ferritin levels that were available. Furthermore, we were unable to measure or ensure compliance with treatment or document eradication of *H pylori* infection in all patients. Tracking nonprescription medications was limited by the accuracy of written electronic documentation. Because of differences in physician practice patterns, the outcome measures in this study were not standardized, with variability of laboratory testing at different time points.

To the best of our knowledge, our study is the first to assess the impact of *H pylori* treatment on IDA in a large population-based setting. The study shows the importance of having an appropriate comparison group when examining causation. Our use of an untreated *H pylori* group, in contrast to previous studies on this subject, could explain the reason for our disparate results. Although most prior studies were conducted in developing countries where poverty and malnutrition are common, our study population represents a racially, ethnically, and socioeconomically diverse population in the US. Thus, it is possible that the underlying causes of IDA in our population are different than those seen in the study populations of previous studies.

CONCLUSION

We found no evidence that the treatment of *H pylori* has an effect on resolving unexplained IDA in our population of insured adults in an industrialized country. Our findings call into question the recommended and common practice of testing for *H pylori* in patients with IDA. Although the cause of IDA is unknown, the condition appears to resolve in most patients in our cohort. It would be reasonable on the basis of our findings to support careful monitoring of anemia with iron supplementation in this population. ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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