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Endoscopic and Colonoscopic Findings in Patients with Iron Deficiency Anemia: The Risk of Cancer

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Abstract

Background: Anemia is a key indicator of malignancy risk and iron deficiency anemia (IDA) is the most considerable contributor, accounting for 50% of all causes of anemia. The present study aimed at evaluating the endoscopic and colonoscopic findings in patients with IDA without gastrointestinal (GI) symptoms.
Methods: One-hundred and eighteen patients with IDA were selected for this cross sectional study. IDA was defined according to the world health organization criteria. All patients were assessed by endoscopy and colonoscopy.
Results: Out of 118 patients with IDA without GI symptoms, 84 patients (71.2%) were older than 50 years and 40 patients (33.9%) were male. According to colonoscopy reports, colon cancer was prominent finding in 10.2% of patients and based on Endoscopic findings, gastritis (16.9%). Of 20 gastritis patients, 19 patients were tested for *Helicobacter pylori (H. pylori)* that was positive in 13 patients (68.4%). Out of 12 patients with colon cancer, 8 patients (66.7%) were males and 4 (33.3%) of them were females (P = 0.030) that the most common cancers were right-side colons and well differentiated adenocarcinoma.
Conclusions: Colon cancer in male patients with IDA has significant risk and asymptomatic patients with IDA have an increased risk of gastric and colorectal neoplasia and should undergo examination of the upper and lower GI tract. Also, gastritis with *H. pylori* can positively associate with colon and gastric cancers in patients with IDA. Further studies are necessary to assess the association between IDA and risk of malignancy.

Keywords: Endoscopy, Colonoscopy, Iron Deficiency Anemia, Cancer

1. Background

Anemia is the most common micronutrient deficiency that affects 24.8% of the general population, with an estimation of 1.62 billion people (1). It is a key index of cancer risk (2) and iron deficiency anemia (IDA) is the most significant contributor that accounts for 50% of all causes of anemia (3) and is a common reason of anemia either due to poor intake or chronic blood loss (4). Gastrointestinal (GI) cancer is a significant cause of chronic IDA (5), especially with right-sided tumors, and failure to check the anemia in older patients may lead to a delay in diagnosis (6). *Helicobacter pylori (H. pylori)* is the most common chronic bacterial infection in the world and is causally connected to the pathogenesis of gastric adenocarcinoma (6, 7), peptic ulcer disease, and mucosa-associated lymphoid tissue lymphoma (6). Bleeding lesions in the GI tract are identified in around 50% of patients with IDA (8). Factors such as older age, male gender, higher serum lactate dehydrogenase, and lower ferritin are evaluated markers for GI cancer in patients with IDA (9). Standard endoscopic diagnostic assessments with esophagogastroduodenoscopy (EGD) and colonoscopy show that up to 30% of patients with IDA do not have a certain diagnosis (10). The present study aimed at evaluating the endoscopic and colonoscopic findings in patients with IDA without GI symptoms, who were referred to hematologic clinic, Rasool-e-Akram hospital, Tehran, Iran.

2. Methods

2.1. Patients

This cross sectional study was authorized by the ethics committee of Iran University of Medical Sciences (Project

code: 26269) and performed on 144 consecutive patients with definitive diagnosis of idiopathic IDA, who were referred to the Colonoscopy Department at Rasoul-e-Akram hospital, Tehran, Iran, between January 2014 and December 2015. Written informed consent was obtained from the patients before their participation in the experiment. IDA was defined according to the world health organization (WHO) criteria as serum hemoglobin level < 14 g/dL in males and < 12 g/dL in females, mean corpuscular volume (MCV) less than 80 fL and serum ferritin level, less than 38 ng/mL in males and less than 9 ng/mL in females. Out of 144 patients with IDA, 22 patients had GI symptoms (dyspepsia, epigastric pain, melena, nausea, and vomiting), 2 patients took Warfarin, and 2 patients lost the follow-up. In total, 118 patients were selected for the study. All patients were assessed by endoscopy and colonoscopy. These patients also did not have a history of menorrhagia or menometrorrhagia and at the first time, they did colonoscopy that if the result was normal, then, they would have done endoscopy. Because iron deficiency anemia results from iron loss or defective absorption, we sought to determine the prevalence of potential gastrointestinal sources for IDA in patients without gastrointestinal symptoms.

2.2. Statistical Analysis

The data were analyzed with the statistical software SPSS version 21.0 for Windows (Armonk, NY: IBM Corp.). The Chi-square test was used for categorical variables (gender and age group). P value ≤ 0.05 was considered statistically significant.

3. Results

Out of 118 patients with IDA without GI symptoms, 84 patients (71.2%) were older than 50 years and 40 patients (33.9%) were male (Table 1). Gastritis was the most common endoscopic finding, followed by duodenal ulcer, gastric ulcer, gastric cancer, duodenitis, and esophagitis, respectively. Also, according to colonoscopy reports, colon cancer was the most common finding, followed by polyp, hemorrhoid, diverticular, and colitis, respectively. All patients were checked for *H. pylori* that 9 patients had unknown result, but in the rest of the patients, 19/109 (17.4%) had positive results and 90/109 (82.6%) had negative results for *H. pylori*. Of 20 gastritis patients, 19 patients were tested for *H. pylori* that it was positive in 13 patients (68.4%).

Out of 12 patients with colon cancer, 8 patients (66.7%) were males and 4 (33.3%) of them were females (P = 0.030) that the most common cancers were right-side colons and well differentiated adenocarcinoma (Table 2). Therefore, the prevalence of colon cancer in patients with IDA was more in men. Out of 3 patients with gastric cancer, 2 patients (66.7%) were females and 1 patient (33.3%) was male. Therefore, the prevalence of gastric cancer in patients with IDA was more in women.

Table 3 shows that out of 12 patients with colon cancer, 9 patients (75%) were older than 50 years (P = 0.45). All patients with gastric cancer had age > 50 years. Therefore, the prevalence of colon or gastric cancer in patients with IDA was age > 50 years. Overall, the risk of colon cancer for IDA men with age > 50 was higher and the risk of gastric

Table 1. The Baseline Variables of Patients with Iron Deficiency Anemia (N = 118)

Variables	No. (%)
Age, y	
> 50	84 (71.2)
≤ 50	34 (28.8)
Gender	
Male	40 (33.9)
Female	78 (66.1)
Endoscopic findings	
NAF[a]	80 (67.8)
Gastritis	20 (16.9)
Duodenal ulcer	5 (4.3)
Gastric ulcer	5 (4.3)
Gastric cancer	3 (2.5)
Duodenitis	3 (2.5)
Esophagitis	2 (1.7)
Colonoscopic findings	
NAF[a]	90 (76.3)
Colon Cancer	12 (10.2)
Polyp	7 (5.9)
Hemorrhoid	4 (3.4)
Diverticular	3 (2.5)
Colitis	2 (1.7)
H. pylori	
Positive	19 (17.4)
Negative	90 (82.6)
Unknown	9
***H. pylori* in Gastritis**	
Positive	13 (68.4)
Negative	6 (31.6)
Unknown	1

[a]There was no abnormal finding.

Table 2. Endoscopic and Colonoscopic Findings Based on Gender in the Patients with Iron Deficiency Anemia

Variables	Male, N = 40	Female, N = 78
Endoscopic findings		
NAF[a]	28 (70)	52 (66.7)
Gastritis	7 (17.5)	13 (16.7)
Duodenal ulcer	2 (5)	3 (3.7)
Gastric ulcer	1 (2.5)	4 (5.1)
Gastric cancer	1 (2.5)	2 (2.6)
Duodenitis	1 (2.5)	2 (2.6)
Esophagitis	0	2 (2.6)
Colonoscopic findings		
NAF[a]	24 (60)	66 (84.6)
Colon Cancer	8 (20)	4 (5.2)
Polyp	4 (10)	3 (3.7)
Hemorrhoid	3 (7.5)	1 (1.3)
Diverticular	1 (2.5)	2 (2.6)
Colitis	0	2 (2.6)

[a]There was no abnormal finding.

cancer for IDA women with age > 50 years was higher.

Table 3. Endoscopic and Colonoscopic Findings Based on Age Group in the Patients with Iron Deficiency Anemia

Variables	≤ 50 Years, N = 34	> 50 Years, N = 84
Endoscopic findings		
NAF[a]	22 (64.7)	58 (69)
Gastritis	7 (20.7)	13 (15.5)
Duodenal ulcer	0	5 (5.9)
Gastric ulcer	3 (8.8)	2 (2.4)
Gastric cancer	0	3 (3.6)
Duodenitis	1 (2.9)	2 (2.4)
Esophagitis	1 (2.9)	1 (1.2)
Colonoscopic findings		
NAF[a]	26 (76.6)	64 (76.2)
Colon cancer	3 (8.8)	9 (10.7)
Polyp	1 (2.9)	6 (7.1)
Hemorrhoid	1 (2.9)	3 (3.6)
Diverticular	3 (8.8)	0
Colitis	0	2 (2.4)

[a]There was no abnormal finding.

4. Discussion

In this study, gastritis and colon cancer in patients were the most common endoscopic and colonoscopic findings, respectively. More patients with gastritis had *H. pylori* positively. Also, the risk of colon cancer for IDA males with age > 50 was higher and the risk of gastric cancer for females with IDA with age > 50 years was higher. The prevalence of IDA in patients with malignancy ranges from 32% to 60% and most patients with iron deficiency are also anemic (5). Rockey reported that GI endoscopy showed at least one lesion potentially responsible for blood loss in 62% patients. Endoscopic examination of the upper GI tract revealed a bleeding source in 36% and colonoscopy a lesion in 25% patients. The most frequently abnormality in the upper GI tract was peptic ulceration (duodenal ulcer in 11 patients, gastric ulcer in 5, and anastomotic ulcer in 3). The malignancies that were detected in 11 patients were the most frequently colonic lesions (11). Kepczyk and Kadakia showed that at endoscopy, at least one lesion potentially accounted for IDA in 71% patients and at colonoscopy, 30% patients had 22 lesions (4 colon cancers); at esophagogastroduodenoscopy (EGD), 56% patients had 43 lesions (gastric cancer: 3, gastric ulcer: 3, duodenal ulcer: 3, gastric polyp more than 1 cm: 2) (12). Out of 142 patients with IDA (28 %), 9 (6.3%) of them had colon cancer, including 1 (1.2 %) woman and 8 (14%) men (13). Out of 71 patients with IDA, colon cancer was observed in 10 patients, gastric cancer in 2 patients and colonic polyps in 2 patients (14). Of 440 patients with colorectal cancer in Acher's study (15), 166 (38%) had IDA at diagnosis. Another study on 32,390 patients with IDA (3) identified 75.98% of whom were women and 24.0% were men. A total of 2051 patients were diagnosed with malignancy within the observation period. Compared with the general population, patients with IDA had an increased overall cancer risk ($P < 0.001$). James et al. (9) evaluated a total of 695 patients with IDA (the mean age 67.35 years with 236 men (34%(34%)). Cancer was diagnosed in 13.1% and GI cancer was 11.2%. The most common diagnosed malignancies were colonic (6.3%), gastric (3.6%), and renal tract (1%). GI cancer, as a reason of IDA, was significantly higher for man gender and age > 50 years. Men referred with IDA had a considerable risk of having colon malignancy and the risk was lower in females. In this study (71.2% had age > 50 years and 40 patients 33.9% were male), 10.2% patients had colorectal cancer and 2.5% had gastric cancer. Also, the prevalence of colon or gastric cancer in patients with IDA was more in age > 50 years and the risk of colon cancer for IDA men with age > 50 was higher; likewiase, the risk of gastric cancer for women with IDA with age > 50 years was higher and our results was similar to other reports. In addition, the endoscopic findings showed one le-

sion potentially accounted for the IDA in 38 patients (32.2%) and colonoscopic findings in 28 patients (23.7%). A study (5) reported that IDA is a common clinical manifestation of patients with colorectal cancer, and occurs more prevalent in women, patients with right colon cancer, and with larger tumors. Acher et al. (15) showed that IDA was more prevalent in right-sided tumors (65%) than those arising in left side of the colon and rectum (26%). Other studies (13, 16) reported that the first presentation of IDA can be in right-sided colon cancer and in this study, similar to other studies, the most common site in patients with IDA with colon cancer was right colon. Moreover, the most common type of pathology was well differentiated adenocarcinoma. Ullman et al. (17) reported that increased colorectal and gastric malignancy risks could be related to chronic diseases, such as ulcerative colitis or gastritis. *H. pylori* infection causes chronic inflammation, significant increase of the risk of developing duodenal, gastric ulcer disease, and gastric malignancy (18, 19). Najafi et al. (20) reported that the incidence of gastric cancer may be related to the prevalence of *H. pylori* infection. Annibale et al. (14) reported that 13/71 patients with IDA had *H. pylori* gastritis. In this study, 20 patients with IDA (16.9%) had gastritis that 13/19 patients (68.4%) were positive for *H. pylori* (missing: 1 patient). Therefore, gastritis can associate with colon and gastric cancers in patients with IDA. In conclusion, asymptomatic patients with IDA have an increased risk of gastric and colorectal neoplasia and should undergo examination of the upper and lower GI tract. Colon cancer in male patients with IDA has significant risk and gastritis with *H. pylori* positively could associate with colon and gastric cancers in patients with IDA. Further studies are necessary to evaluate the association between IDA and risk of malignancy.

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Footnotes

Authors' Contribution: Study concept and design, Ali Shahriari-Ahmadi; writing the paper, analysis and interpretation of data, Masoud Sadeghi; acquisition of data, collecting the materials, statistical analysis, technical and material support, Neda Shalbaf and Mohsen Masoodi; contributing in data entry and laboratory operation, Maryam Shalbaf and Vida Bozorgi.

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