Original Research

Evaluation of In-patients with Iron Deficiency Anemia in terms of Etiology

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Abstract

Objectives: In this study, we aimed to evaluate in-patients with iron deficiency anemia concerning etiology.

Methods: In our study, we retrospectively evaluated 150 in-patients (60 male and 90 female) with iron deficiency anemia in Sisli Etfal Hospital, Department of Internal Diseases between 2005 and 2010. Anemia was defined as Hb <12 g/dl for women and <13 g/dl for men and transferrin saturation ≤15%.

Results: In our study, 60 male and 90 female patients were included. Analyzing the etiology of iron deficiency anemia in 150 patients, we identified erosive gastritis in 35 (23.3%) patients, gastric cancer in 15 (10%) patients, colon polyps in 14 (9.3%) patients, erosive gastritis in 14 (9.3%) patients, myoma in 14 (9.3%) patients, diverticulosis in 13 (8.6%) patients, colon cancer in seven (4.6%) patients, menometrorrhagia in seven (4.6%) patients, malabsorption in six (4%) patients, hemorrhoids in six (4%) patients, celiac disease in four (2.6%) patients, bladder cancer in three (2%) patients, hematologic malignancy in three (2%) and other diseases (unexplained etiology) in 23 (15.3%) patients.

Conclusion: When iron deficiency anemia is detected, it may be a warning of an underlying severe illness. Reasons for many cases arise from upper and lower gastrointestinal tract diseases. Endoscopic examinations are important for diagnosis. We suggest performing gastroscopy and colonoscopy together in patients with iron deficiency anemia.

Keywords: Etiology; iron deficiency anemia.

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According to the definition of the World Health Organization (WHO), anemia is defined as a hemoglobin value below 13 g/dl for men and 12 g/dl for women in adults. Iron deficiency anemia is the most common type of anemia and is more common in women than men.[1]

Like most anemias, iron deficiency anemia is not a disease itself and its etiology should be investigated and revealed in each patient. The cause of iron deficiency anemia can sometimes be multiple. Sometimes even if there is a specific cause, adult patients should be investigated for a severe cause. The frequency of etiological causes of iron deficiency anemia varies according to age groups. While the most important cause of iron deficiency anemia is menstrual bleeding in premenopausal women, it is chronic blood loss from the gastrointestinal system in postmenopausal women and adult men.[2]

In this study, we evaluated the patients admitted to our clinic due to iron deficiency anemia in terms of etiology.

Methods

A total of 150 patients who were hospitalized in the Internal Medicine Clinic of Sisli Etfal Hospital for iron deficiency anemia between 2005 and 2010 were included in this retrospective study. Ethics committee approval was obtained for our study. Age, gender, anamnesis data, laboratory tests and imaging results of the patients were obtained by searching their records. Patients over 18 years of age, without active infection and sepsis, without chronic renal and hepatic insufficiency, without a previously detected malignancy, previous gastric and bowel resection, known inflammatory bowel disease, malabsorption, intestinal polyp and diverticulosis, and patients who did not use any immunosuppressive drugs that could affect the bone marrow were included in the study. Patients with hemoglobin values <12 g/dl for women, <13 g/dl for men for anemia and transferrin saturation of ≤15% for iron deficiency were included in this study. Gastroscopy and colonoscopy were performed on all 150 patients in this study.

Statistical Analysis

SPSS 13.0 for Windows program was used for statistical analysis. Besides descriptive statistical methods (mean, standard deviation), Mann-Whitney U test and Student t-test were used for inter-group comparison while evaluating the study data. Significance was evaluated at the p<0.05 level.

Results

In this study, 150 patients, 60 men and 90 women, were included. The mean age of female patients was 48.7±19.1, and the mean age of male patients was 60.9±19.5 (Table 1).

Given that the etiological causes detected in 150 patients, 35 (23.3%) of 150 patients had erosive gastritis, 15 (10%) had gastric cancer, 14 (9.3%) had colon polyps, 14 (9.3%) had myoma, 13 (8.6%) had diverticulosis, seven (4.6%) had colon cancer, seven (4.6%) had menometrorrhagia, six (4%) had malabsorption, six (4%) had hemorrhoids, fourfour (2.6%) had celiac disease, three (2%) had bladder cancer, three (2%) had hematological malignancy and 23 (15.3%) had other diseases (unexplained etiology) (Table 2).

Table 1. Gender and mean age of the patients

	Male	Female
Number of the Patients	60	90
Age	60.9±19.5 (18-89)	48.7±19.1 (17-83)

Table 2. Etiological causes, number of patients and percentages

GI tract-related reasons	Number of the patients, n (%)
Erosive Gastritis	35 (23.3)
Gastric Carcinoma	15 (10)
Colon polyp	14 (9.3)
Diverticulosis	13 (8.6)
Colon Carcinoma	7 (4.6)
Colon polyp	12 (8)
Malabsorption	6 (4)
Hemorrhoids	6 (4)
Non-GI tract reasons	
Myomas	14 (9.3)
Menometrorrhagia	7 (4.6)
Bladder Carcinoma	3 (2)
Hematological Malignancy	3 (2)
Other Causes (unknown etiology)	23 (15.3)

When the patients were divided according to their gender, erosive gastritis was detected in 15 (25%), colon polyp in 11 (18.3%), gastric cancer in eight (13.3%), diverticulosis in eight (13.3%), colon cancer in five (8.3%), malabsorption in three (5%), bladder cancer in three (5%), celiac disease in two (3.3%) and other causes (unexplained etiology) were detected in five (8.3%), in men (Table 3).

In women, erosive gastritis was detected in 20 (22.2%), myoma in 14 (15.5%), gastric cancer in seven (7.7%), menometrorrhagia in seven (7.7%), hemorrhoids in six (6.6%), diverticulosis in five (5.5%), malabsorption in three (3.3%), hematological malignancy in three (3.3%), colon polyp in three (3.3%), colon cancer in two (2.2%), celiac disease in two (2.2%) and other causes (unexplained etiology) were detected in 18 (20%) (Table 4).

Endoscopically detected pathologies when the patients were divided into two groups as under 50 and over 50 years of age are presented in Table 5. All seven patients with colon cancer were 50 years and older. Thirteen of 15 patients with gastric cancer were 50 years and older (Table 5).

Table 3. Etiological causes in male patients

Male Patients	Number of Patients, n (%)	Age
Erosive gastritis	15 (25)	52.3±23.9
Colon polyp	11 (18.3)	67.5±10.9
Gastric carcinoma	8 (13.3)	60.3±13.8
Diverticulosis	8 (13.3)	74.3±10.6
Colon carcinoma	5 (8.3)	68.6±11.7
Malabsorption	3 (5)	29.7±9.5
Bladder carcinoma	3 (5)	78.3±6.5
Celiac disease	2 (3.3)	23±7.1
Other causes (unknown etiology)	5 (8.3)	64.8±17.9

Tablo 4. Etiological causes in female patients

Female Patients	Number of Patients, n (%)	Age
Erosive gastritis	20 (22.2)	42.8±15.2
Myomas	14 (15.5)	55±14.4
Menometrorrhagia	7 (7.7)	32.3±9.9
Gastric carcinoma	7 (7.7)	65.6±12.9
Hemorrhoids	6 (6.6)	42.8±15.2
Diverticulosis	5 (5.5)	65.4±9.2
Colon polyp	3 (3.3)	67.4±9.9
Malabsorption	3 (3.3)	38±10.8
Hematological malignancy	3 (3.3)	46±5.3
Colon carcinoma	2 (2.2)	68±12.7
Celiac disease	2 (2.2)	26.7±8.3
Other causes (unknown etiology)	18 (20)	52.3±18.8

Table 5. Distribution of lesions detected in endoscopic examination by age

Endoscopic Diagnosis	Age <50 (n=44), %	Age ≥50 (n=79), %
Erosive gastritis	15 (34)	20 (25.3)
Colon polyp	0 (0)	14 (17.7)
Gastric carcinoma	2 (4.5)	13 (16.4)
Diverticulosis	0 (0)	13 (16.4)
Colon Carcinoma	0 (0)	7 (8.8)
Hemorrhoids	2 (4.5)	4 (5)
Malabsorption	6 (13.6)	0 (0)
Celiac disease	4 (9)	0 (0)
Other reasons	15 (34)	8 (10.1)

Discussion

Iron deficiency anemia is the most common type of anemia and is detected in 1-2% of adults according to the data of the National Health and Nutrition Examination Survey (NHANES III; 1988 to 1994). The rates of iron deficiency without anemia are up to 11%.[3]

The frequency and causes of iron deficiency anemia vary according to age and gender. Nutrition in children and menstrual loss in women of reproductive age are in the foreground. In postmenopausal women and adult men, the cause is usually occult, chronic blood loss from the gastrointestinal tract and examination of the gastrointestinal tract is necessary to find the source of bleeding.

There are few publications in the literature investigating the etiology of iron deficiency anemia in hospitalized patients. There are different approaches among clinicians to evaluate patients with iron deficiency. The findings of 150 patients who were hospitalized to help the evaluation of the etiology of iron deficiency anemia between 2005 and 2010 in the Internal Medicine Clinic of Sisli Etfal Hospital were shared in our study.

In our study, the gastrointestinal system-related findings were the cause of iron deficiency in 87% of male patients and 53% of female patients. Erosive gastritis was the most common cause, with a rate of 22.2% in women. The second most common cause of iron deficiency anemia was the causes with unknown etiology, including patients with no significant endoscopic pathology. Among the findings related to the lower gastrointestinal system were diverticulosis with a rate of 5.5% and colon cancer with a rate of 2.2%. Myoma uteri were an etiological cause with a rate of 15.5%. While erosive gastritis was the most common cause, with a rate of 25% in male patients, colon polyp was found with a rate of 18.3%, gastric cancer as 13.3% and colon cancer as 8.3%, malabsorption and bladder cancer as 5%, and celiac disease as 3.3%.

When the literature on the etiology of iron deficiency anemia and approach to iron deficiency anemia is reviewed, there are few studies and there is no standard approach to iron deficiency among clinicians.

In a prospectively designed study in which 37 patients (23 women, 14 men) with iron deficiency anemia were hospitalized and evaluated with lower and upper gastrointestinal endoscopy,[4] gastrointestinal lesions were detected in 29 of the patients (78%). Eight cases (27%) had lesions in both the upper and lower gastrointestinal systems. Gastritis was the most common lesion detected in the upper gastrointestinal system (60.8% of all patients), and gastric cancer was detected in two cases. Hemorrhoids were the most common lesions in the lower gastrointestinal system (71.4%). Rectal cancer was detected in one case and polyps in one case. Malabsorption was detected in one, and celiac was detected in one of three cases without lesions and in whom the small intestine was examined. The findings obtained in this study showed that there was no relation between gastrointestinal-specific symptoms and lesion location and it was concluded that endoscopic examination of both regions is required due to the coexistence of upper and lower gastrointestinal lesions in 27% of the patients.

Gordon et al. investigated the role of endoscopy in the evaluation of iron deficiency anemia in their study on 170 patients over the age of 50, and as a result, although there was more upper gastrointestinal pathology, no correlation was found between the history of the cases and the lesion area.[5] It is recommended to evaluate the upper and lower gastrointestinal systems together in this age group.

Cook et al.[6] performed esophagogastroduodenoscopy, small bowel biopsy, colonoscopy and flexible sigmoidoscopy and barium swallow in 100 patients with iron defi-

ciency. They concluded that colonic examination should be performed in all elderly patients with benign lesions on gastrointestinal endoscopy.

Hooper et al.[7] found pathological findings in 12 (12.2%) of 98 iron deficiency patients with celiac disease, three of which were colon cancer, and they recommended performing combined upper and lower gastrointestinal tract endoscopy in patients with iron deficiency.

In a prospective study involving 100 patients with iron deficiency anemia, Rockey and Cello performed an endoscopy on the lower and upper gastrointestinal tract together and found at least one potentially bleeding lesion in 62 patients. Those with no lesion at endoscopy were performed enteroclysis and small bowel radiographic studies showed no benefit. In this study, unlike Gordon et al.'s study, they concluded that research into regions with symptoms was required and found synchronous upper and lower gastrointestinal lesions as rare.[8]

Zuckerman and Benitez prospectively investigated 100 cases of occult gastrointestinal bleeding with lower and upper gastrointestinal system endoscopy and found that esophagogastroduodenoscopy was more significant than colonoscopy. They recommended that upper gastrointestinal endoscopy is sufficient and colonoscopy is unnecessary for young people, and colonoscopy should be performed in the elderly because colorectal cancer is common. In cases where colonoscopy did not contribute to the diagnosis, they found a bleeding focus in 36% of the cases with upper gastrointestinal endoscopy.[9]

Unlike Hooper et al.,[10] The British Society of Gastroenterology does not recommend colonoscopy in patients with an ulcer or celiac disease detected with the upper gastrointestinal system endoscopy.

In a prospective study in which combined gastroscopy and colonoscopy were performed on patients with iron deficiency anemia in the age group of 63.6+/-15 years, the prevalence of colon cancer was 13%. Synchronous lesions in the upper and lower gastrointestinal systems were detected in 12% of the patients. Gastroscopy was recommended at first and colonoscopy was recommended in addition, even if benign pathology was detected in the upper gastrointestinal system.[11]

In a study conducted in our country with 75 patients over 60 years of age with iron deficiency anemia and investigating the importance of screening the upper gastrointestinal system,[12] histopathological lesions, such as Helicobacter pylori gastritis, chronic gastritis, which were described as risk-free lesions were found in 31 patients, adenocarcinoma was found in three (4%) patients and a risky lesion requiring follow-up was detected in 41 (55%) patients. As

a result of this study, in which patients with lesions that would cause iron deficiency anemia found in concurrent colonoscopies were not included, it was stated that even if there were lesions in the lower gastrointestinal system that would explain the iron deficiency anemia, the upper gastrointestinal system screening should be performed due to the high frequency of malignancy, high-risk lesions and the relationship between iron deficiency and H. pylori, even if there were no symptoms.

In our study, 10% of the patients had gastric cancer and 4.6% of them had colon cancer. When the patients were divided according to gender, 8.3% of male patients had colon cancer, 13.3% had gastric cancer, while 7.7% of female patients had gastric cancer and 2.2% of them had colon cancer. Twenty of the 22 patients with gastric and colon cancer were over the age of 50 (Table 5). Since the incidence of both gastric and colon cancer is high in both genders, it is rational to perform upper and lower gastrointestinal endoscopy together, at least in this age group.

In our study, celiac disease was found in 2.6% of the patients (3.3% in males and 2.2% in females). It is reasonable to perform a duodenal biopsy, even if the mucosa appears normal during upper gastrointestinal endoscopy in patients investigated for celiac disease.

Emami et al.[13] found the incidence of celiac disease to be 10% in duodenal biopsy samples taken from 130 patients with iron deficiency, without visible explanatory endoscopic findings.

Iron deficiency anemia due to gastric petechial bleeding, ulcers and erosions are common in nonsteroidal anti-inflammatory drugs and aspirin users. In our study, erosive gastritis was detected in 35 (23.3%) patients (15 male and 20 female) as the etiological cause of an iron deficiency.

Iron deficiency may be the first sign of a malignancy in the gastrointestinal tract. Caecal carcinomas are usually silent until anemia occurs. In our study, gastric carcinoma was detected in 15 (10%) patients and colon carcinoma in seven (4.6%) patients.

Anemia does not develop until the iron stores are emptied in little bleeding of the gastrointestinal system. On the other hand, it is common for patients with massive bleeding to have anemia despite their iron stores not being emptied. In patients with ulcerative colitis, blood loss is 6-25 ml/day, and 81% of the patients have iron deficiency.[14] However, in our study, patients with known inflammatory bowel disease and recent bleeding were excluded from this study, so there were no data available for this group.

Hemorrhoidal bleeding should be questioned in patients with iron deficiency anemia.[4] In our study, hemorrhoids

were found as an etiological cause in six (4%) patients.

Celiac disease should definitely be considered in iron deficiency anemias that are unexplained or do not respond to treatment. In our study, celiac disease was found in four (2.6%) patients.

As mentioned, genitourinary losses, especially menstrual losses, are in the first place in iron deficiency anemia in adult women. The menstrual periods of the patients should be questioned very well in this regard. However, in our study, erosive gastritis, which was found in 20 (22.2%) patients, took the first place as etiological causes in female patients, and other causes (unknown etiology) took second place in 18 (20%) patients. Myoma uteri were detected in 14 (15.5%) patients and menometrorrhagia in seven (7.7%) patients.

There are studies showing that symptoms specific to a particular region in the gastrointestinal tract are helpful[8] and unhelpful in choosing the starting site for endoscopy.[5, 9] There are studies in which the diagnostic advantage of gastroscopy was higher than colonoscopy.[5, 11] Patient characteristics (age, gender) are important in the selection of gastrointestinal endoscopy method in patients presenting with iron deficiency. In our study, causes related to the upper gastrointestinal system were mainly responsible for the etiology in women. In this context, it can be suggested to start the examination with upper gastrointestinal system endoscopy in women. In our study, colon and gastric cancer had an important place in the etiology and almost all patients were over 50 years old. In this age group, it may be an appropriate approach to perform upper and lower endoscopy in both genders. The general view is that colonoscopy should be performed even if a benign upper gastrointestinal lesion is detected to explain anemia in the advanced age group.[6, 9] Patients with benign lesions on gastroscopy also have colon malignancies at a significant rate.[6, 11]

Although gastrointestinal causes are generally considered in the etiology of iron deficiency anemia in the elderly, we detected bladder cancer in three patients in our study. It is important to carefully investigate other causes of iron deficiency anemia before endoscopic procedures. In conclusion, although upper gastrointestinal system pathology is more common in iron deficiency anemia, upper and lower endoscopic examinations should be performed together in adult men and postmenopausal women with suspected gastrointestinal loss.

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