

Iron Deficiency Anemia: The Contribution of Upper Digestive Endoscopy in Etiological Investigation

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Abstract

Iron-deficiency anemia is very common among patients in gastroenterology. The digestive system plays a key role in the pathophysiology of iron-deficiency. Indeed, digestive causes are one the most frequent etiology. This is why endoscopic evaluation is part of the etiological assessment of iron-deficiency anemia. The aim of this study is to investigate the usefulness of esophagogastroduodenoscopy (EGD) and histopathology in the etiological diagnosis of iron-deficiency anemias. **Materials and Methods:** This is a monocentric study conducted from January 2019 to December 2023. All patients with iron-deficiency anemia who underwent EGD were included. Various data were recorded, including patients' epidemiological information, laboratory findings, and results from endoscopic examinations. **Results:** Out of 2960 EGD, 576 (19,5%) were included in the study. The mean age of the patients was 49.81 years, ranging from 18 to 83 years. The male-to-female sex ratio was 0.67. It is notable that 47.5% of the patients had various medical histories: inflammatory bowel disease (IBD) in 19.13% of cases, history of non-steroidal anti-inflammatory drug (NSAID) use in 12.17%, coeliac disease in 6.13%, cirrhosis with portal hypertension in 8.70%. All patients underwent EGD. An abnormality was found in 63.4% of cases, including: Esophageal lesions: gastroesophageal varices in 13.3% of cases, erosive esophagitis in 7.5%, esophageal tumor in 0.6% of cases. Gastric lesions: erosive gastritis in 35% of cases, ulcerative gastritis in 22%, erythematous gastritis in 17%, gastric tumor in 15% of cases, supra-centimetric hyperplastic polyps in 5% of cases. Bulboduodenal lesions: erosive bulboduodenitis in 25% of cases, ulcerative bulboduodenitis in 18%, duodenal fold rarefaction in 16%, angiodysplasia in 3.5%. Gastric and duodenal biopsies were systematically performed. Duodenal biopsies showed a celiac disease aspect in 7.6% of cases, and nonspecific duodenitis in 4.6% of cases. Gastric biopsies revealed gastritis with *Helicobacter pylori* (*Hp*) in 57.6% of cases. Thus, the diagnostic yield of EGD was 47.33%. **Conclusion:** Iron deficiency anemia are common medical conditions in daily clinical practice. The multiple etiologies of iron deficiency anemia and the nonspecificity of symptoms make diagnosis difficult. Gastrointestinal lesions are frequently observed in patients with iron deficiency anemia. Digestive endoscopy has a great value in the etiological investigation of this pathology. Gastroscopy allows for the etiological diagnosis for many patients that's why it is systematically recommended do it.

Keywords: Iron-deficiency anemia, gastroenterology, endoscopic evaluation.

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BACKGROUND

Anemia affects more than 2 billion people worldwide and is very common among patients in gastroenterology. The digestive system plays a key role in the pathophysiology of iron-deficiency anemia; however, when intake is lower than necessary or, more frequently, when losses increase and cannot be compensated, iron deficiency becomes severe enough to reduce erythropoiesis, leading to the development of iron-deficiency anemia. This type of anemia is the most common and affects approximately 15 to 30% of the

global population. Iron deficiency anemia has multiple etiologies, and the nonspecificity of its symptoms can make diagnosis challenging.

Among these causes are gynecological factors that are predominant in women of childbearing age, as well as digestive causes. This is why endoscopic evaluation is part of the etiological assessment of iron-deficiency anemia.

The aim of this study is to investigate the usefulness of esophagogastroduodenoscopy (EGD) and

histopathology in the etiological diagnosis of iron-deficiency anemias.

MATERIALS AND METHODS

This is a monocentric study conducted from January 2019 to December 2023. All patients with iron-deficiency anemia who underwent EGD were included, regardless of the presence of occult fecal bleeding.

Iron-deficiency anemia was defined as hemoglobin levels < 13 g/dl in men and < 12 g/dl in women, with serum ferritin levels < 15 ng/ml in men and < 9 ng/ml in women.

Various data were recorded, including patients' epidemiological information, laboratory findings, and results from endoscopic examinations.

RESULTS

Out of 2960 EGD, 576 (19,5%) were included in the study. The mean age of the patients was 49.81 years, ranging from 18 to 83 years. The predominant age group was 36-65, representing 50.83% of the patients. The male-to-female sex ratio was 0.67, with 40.17% males and 59.83% females, of which 55.22% were in the reproductive age group and 44.77% were postmenopausal.

It is notable that 47.5% of the patients had various medical histories: inflammatory bowel disease (IBD) in 19.13% of cases, history of non-steroidal anti-inflammatory drug (NSAID) use in 12.17%, celiac disease in 6.13%, cirrhosis with portal hypertension in 8.70%, chronic kidney disease in 3.8%, and heart disease in 2.1%.

Among the patients, the initial hemoglobin levels before any transfusion or iron treatment ranged between 3.2 and 11g/dl, with an average of 9.32 g/dl. Anemia was hypochromic microcytic in 90% of cases.

All patients underwent EGD. An abnormality was found in 63.4% of cases, including: Esophageal lesions: gastroesophageal varices in 13.3% of cases, erosive esophagitis in 7.5%, esophageal tumor in 0.6% of cases.

Gastric lesions: erosive gastritis in 35% of cases, ulcerative gastritis in 22%, erythematous gastritis in 17%, gastric neoplasia in 15% of cases, supra-centimetric hyperplastic polyps in 5% of cases.

Bulboduodenal lesions: erosive bulboduodenitis in 25% of cases, ulcerative bulboduodenitis in 18%, duodenal fold rarefaction in 16%, angiodysplasia in 3.5%.

EGD was normal in 36.6% of cases. Gastric and duodenal biopsies were systematically performed. Duodenal biopsies showed a normal histological aspect

in 87.8% of cases, villous atrophy with intraepithelial lymphocytosis suggesting celiac disease in 7.6% of cases, and nonspecific duodenitis in 4.6% of cases. Gastric biopsies (excluding tumor lesions) revealed chronic gastritis with *Helicobacter pylori* (*Hp*) in 57.6% of cases: active in 82.8%, atrophic in 13.3%, with intestinal metaplasia in 6.2% of cases.

Thus, the diagnostic yield of EGD was 47.33%. It was 62.4% in patients aged 65 and older and only 27% in patients under 30 years old.

DISCUSSION

Anemia is a significant public health issue, with the most common type worldwide being iron-deficiency anemia; it is estimated that 30 to 50% of anemias are iron-deficiency, with rates as high as 56% in developing countries [1-3].

In gastroenterology, iron-deficiency anemia is considered a frequent reason for consultation (4%-13% of all referred patients), and up to two-thirds of patients with iron-deficiency anemia present severe gastrointestinal lesions detected by esophagogastroduodenoscopy (EGD) and colonoscopy [4, 5].

According to various studies conducted in Morocco, the average age was respectively 43.61 years and 42.7 years, which is consistent with our findings [6, 7]. The average age of patients increases over the years. Indeed, digestive causes of iron-deficiency anemia are more common in the elderly, and the frequency of digestive lesions increases with age [8, 9]. That's reflects our results to.

Our study, consistent with literature data, showed that iron-deficiency anemia affects women of childbearing age more. However, the trend seems to reverse beyond the age of 50, with men becoming more affected than postmenopausal women [10].

Etiological assessment is fundamental and constitutes a step that must be systematically undertaken [10]. The digestive origin of iron-deficiency anemia is frequent and dominated by repeated blood losses (94.4%) [11].

Thus, digestive endoscopy should be considered in all patients with confirmed iron-deficiency anemia unless there are significant manifest non-gastrointestinal blood losses. In the absence of suggestive symptoms, the order of examinations is determined by the physician and local availability [12].

Positive results of esophagogastroduodenoscopy with systematic biopsy, which may explain iron-deficiency anemia, include *Helicobacter pylori* gastritis, ulcers, angiodysplasia, tumor lesions, and celiac disease [10, 13, 14]. These

results align with our study, which found the main lesions explaining anemia during endoscopy to be erythematous and erosive gastritis, ulcerative and tumoral lesions, angiodysplasia, and celiac disease.

Various studies in the literature have shown that inflammatory lesions are a more frequent cause of iron-deficiency anemia than vascular lesions in the upper digestive tract [15, 16].

Helicobacter pylori infections lead to iron deficiency through several mechanisms. Firstly, infection is a risk factor for ulcers, especially gastric ulcers. Secondly, infection leads to achlorhydria, resulting in changes in solubility and alteration of iron absorption [17].

In our study, we found *H. pylori* gastritis in 57.6% of cases, which is high. This, may be explained by the higher prevalence of *H. pylori* in developing countries.

International guidelines recommend *H. pylori* eradication for the treatment of iron-deficiency anemias of unknown origin [11, 18]. Particularly, bismuth-based eradication therapy is more effective in terms of increasing hemoglobin and iron reserves [19].

NSAIDs are commonly used in various inflammatory conditions and can cause gastritis, gastroduodenal ulcers, and even small bowel enteropathies; thus iron deficiency anemia is the most common manifestation [20, 21]. Although the toxicity of NSAIDs on the upper gastrointestinal tract is well documented, the fact that NSAID-induced damage extends beyond the duodenum is less well recognized. Endoscopic lesions related to NSAIDs include erythema, edema, mucosal bleeding, erosions, or ulcers. Some studies report that such lesions are very common and can be observed in up to 40% of rheumatic patients taking NSAIDs and that these lesions effectively explain anemia due to iron deficiency [21, 22].

In our study, 19% of patients had a history of IBD, which could lead to iron deficiency anemia due to malabsorption, following resection, or secondary to inflammation [23, 24]. In a variety of populations with IBD, the prevalence of iron deficiency anemia ranged from 36% to 76% [25, 26].

In celiac disease, impaired iron absorption through the duodenal lumen is a major cause of chronic anemia. This disease can be revealed by subtle, atypical, or extraintestinal symptoms. Among these symptoms, refractory iron deficiency anemia is notable. Therefore, it is recommended that all patients with iron deficiency anemia undergo screening for celiac disease. [12] Angiodysplasias are fragile vascular malformations with thin walls, prone to rupture and cause serious gastrointestinal bleeding. They account for up to 5% of

cases of gastrointestinal bleeding and up to 40% of cases of obscure GI bleeding [28]. Angiodysplasia was present in 61% of patients over 60 years of age, often in the presence of coexisting conditions [29, 30].

Gastropathy of portal hypertension (HTP) and antral vascular ectasia can cause chronic gastrointestinal bleeding in patients with liver cirrhosis and can also occur in non-cirrhotic patients [31]. Chronic bleeding due to HTP gastropathy often leads to iron deficiency anemia in 3 to 26% of patients, similar to the results of our study in which 15.3% of cases showed features of HTP gastropathy [32]. In practice, even in the presence of overt signs of portal hypertension, any iron deficiency in a cirrhotic patient warrants an endoscopic evaluation, analyzing the benefit-risk ratio in cases of severe cirrhosis [33].

Thus, in our study, upper gastrointestinal endoscopy did explain the anemia in 47.33% of cases.

In a prospective Spanish study of 100 consecutive patients with iron deficiency anemia, gastrointestinal endoscopies revealed at least one potentially responsible lesion in 62 patients, with 36% identified by gastroscopy [34]. Although the diagnostic yield is good, upper endoscopy should always be accompanied by lower endoscopy either simultaneously or subsequently. This allows for a comprehensive etiological assessment and maximizes diagnostic yield.

In "obscure" situations, it is important to consider repeating bidirectional endoscopies if they were not performed under optimal conditions [35].

CONCLUSION

Iron deficiency and iron deficiency anemia are global health issues and common medical conditions in daily clinical practice. The multiple etiologies of iron deficiency anemia and the nonspecificity of symptoms can, however, make diagnosis difficult. Gastrointestinal lesions, both in the upper gastrointestinal tract and in the colon, are frequently observed in patients with iron deficiency anemia. Digestive endoscopy is thus of great value in the etiological investigation of iron deficiency anemia. Gastroscopy allows for the etiological diagnosis in many patients. In addition to ulcerative gastritis, celiac disease, IBD, or tumors, *H. pylori* gastritis is a frequent and now well-documented cause of iron deficiency.

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