# Iron Deficiency Anemia in Men and Older Women

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**Since there are no accepted guidelines for diagnosis and management, some patients with this condition may receive less than optimal treatment.**

In the United States, iron deficiency anemia (IDA) is encountered commonly in clinical practice, occurring in 3.5% of all adult men, 5.3% of postmenopausal women, and 7% of all geriatric patients.[1] In these populations, prompt and accurate diagnosis is particularly critical, as the condition is usually a sign of gastrointestinal (GI) or genitourinary blood loss—and may be the only indication of such serious underlying diseases as cancer of the GI tract, peptic ulcer disease, or vascular malformations.

In 10% to 41% of patients, there is no clear cause of IDA.[2,3] Comprehensive reviews of IDA diagnosis and treatment are scarce in medical literature, and lapses in the management of this disorder have been reported. A 1996 British audit of 200 adult patients with probable IDA found that, of 109 incident cases possibly attributable to GI disease, only 19% had prompted investigation of both the upper and lower GI tract, 21% of the upper GI tract alone, and 7% of the lower GI tract only.[4] More than 50% of these patients had either no GI investigation performed or only fecal occult blood testing.[4]

In order to evaluate diagnostic accuracy, management, and follow-up of IDA at the Dayton VA Medical Center (VAMC) in Dayton, OH, we conducted a five-year, retrospective review of all patients diagnosed with IDA at the Dayton VAMC and at a large, teaching community medical center (CMC) in Montgomery County, OH. In this article, we'll describe how we conducted this review, detail our results, and discuss the immediate need for IDA management guidelines to ensure optimal care for all patients—especially those for whom IDA most likely points to a serious underlying medical condition.

## A RETROSPECTIVE REVIEW

From January 1 to December 31, 1993, 199 patients with a diagnosis of IDA (and, in some cases, other medical problems) presented at the two study hospitals. We reviewed the inpatient and outpatient medical records of these patients at the time of their admission in 1993 and during any subsequent admissions or follow-up through November 1998. All patient records were analyzed carefully for the following:

- accuracy of initial IDA diagnosis,
- investigations performed to reveal the etiology,
- treatment with iron supplements for at least three months and any additional therapy, and
- resolution of anemia.

Three or more of the following findings were considered diagnostic of IDA: serum iron level less than 20 mg/dL, serum ferritin level less than 40 µg/mL, serum iron saturation less than 16%, mean corpuscular volume (MCV) less than 80 fL,[5] red blood cell distribution width greater than 17%, and evidence of microcytic hypochromic

Continued on page 17

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Continued from page 14

**Table 1. Characteristics of study patients**

| Characteristics | CMC* (n = 52) | VAMC† (n = 32) | *P* value |
|---|---|---|---|
| Male/female ratio | 12/40 | 29/3 | .001 |
| Mean age | 60.9 | 66.4 | .18 |
| Mean Hb‡ level (g/dL) | 8.4 | 9.1 | .13 |
| No. (%) with Hb level below 10 g/dL | 40 (77%) | 18 (56%) | .047 |
| No. (%) over 60 years of age | 29 (56%) | 22 (69%) | .24 |

*CMC = community medical center. †VAMC = VA medical center. ‡Hb = hemoglobin.

**Table 2. Etiologic investigations into iron deficiency anemia**

| Etiologic workup | CMC* (n = 52) | VAMC† (n = 32) | *P* value |
|---|---|---|---|
| No. (%) with EGD‡ | 6 (12%) | 7 (22%) | .20 |
| No. (%) with colonoscopy | 7 (14%) | 10 (31%) | .049 |
| No. (%) with EGD and colonoscopy | 14 (27%) | 11 (34%) | .47 |
| No. (%) with no GI§ workup | 25 (48%) | 4 (13%) | .001 |
| No. (%) with upper GI exam | 6 (12%) | 2 (6%) | .70 |
| No. (%) with barium enema | 7 (13%) | 7 (22%) | .32 |
| No. (%) with small bowel follow through | 7 (13%) | 2 (6%) | .47 |

*CMC = community medical center. †VAMC = VA medical center. ‡EGD = esophagogastroduodenoscopy. §GI = gastrointestinal.

anemia on peripheral smear or decreased or absent iron stores in bone marrow.

We retrieved the results of any outpatient procedures and follow-up laboratory tests after hospitalization. If we found no follow-up, we recorded the resolution as unknown. Etiology of IDA included colorectal cancer, bleeding ulcers, bleeding vascular malformations, erosive esophagitis, gastritis and duodenitis, diverticulosis, polyps, and hemorrhoids. Non-GI causes included genitourinary and other causes of blood loss or unknown etiology. We analyzed continuous variables using a *t* test and categorical measures with the chi-square test or Fisher's exact test. Inference was made at the .05 level of significance.

## WHAT WE FOUND

Out of the 199 patients (120 at the CMC and 79 at the VAMC) who were diagnosed with IDA in 1993, only 84 (42%) met our criteria for IDA, suggesting that IDA frequently is diagnosed inaccurately. Between the two study sites, these patients differed significantly only in terms of gender ratio and hemoglobin level (Table 1).

Within the confirmed IDA group, 25 patients (30%) had both esophagogastrodudenoscopy (EGD) and colonoscopy performed, 17 (20%) had a colonoscopy only, and 13 (15%) had EGD only (Table 2). An assessment of the etiologic investigations into IDA at each medical center revealed that 25 (48%) of the CMC patients had no GI workup, compared with four (13%) of those at the VAMC—a statistically significant difference. We also found that significantly more patients at the VAMC had a colonoscopy than at the CMC.

Of the 55 patients from both medical centers who had an endoscopic evaluation, 41 (75%) had potential GI causes of IDA and eight (15%) had non-GI causes of bleeding. Non-GI causes also were found in seven (24%) of the 29 patients who had no GI workup. There were no differences between the study sites in this regard.

The review revealed discrepancies with regard to the treatment and resolution of IDA in patients at the CMC versus the VAMC (Table 3). A significantly higher proportion of patients at the VAMC received a blood transfusion, iron supplements, or both—with better resolution of IDA during a minimum follow-up of six months. Additionally, there was a significant gender-based difference in the resolution of anemia among the patients who

**Table 3. Iron deficiency anemia treatments and outcomes**

| Treatment/ outcome | CMC* patients (n = 52) | VAMC† patients (n = 32) | *P* value |
|---|---|---|---|
| Transfusion | 25 (48%) | 23 (72%) | .042 |
| Iron supplement | 33 (64%) | 29 (91%) | .006 |
| Anemia resolved | 11 (21%) | 15 (47%) | .013 |

*CMC = community medical center. †VAMC = VA medical center.

had a GI workup. Anemia resolved in 19 of the 41 men from both medical centers (46%) compared to only seven of the 43 women (16%) ($P$ = .003). There were no significant, gender-based differences in the potential causes of IDA or treatment with iron supplements.

## ETIOLOGIC INVESTIGATION

The primary goal of our study was to perform a comprehensive review of IDA focused on diagnostic accuracy, management, and outcome of treatment. Previous studies of IDA have shown diagnostic accuracy varying anywhere from 38% to 82%.[3,5] In our study, 58% of the patients who had been diagnosed with IDA failed to meet our diagnostic criteria.

The diagnostic criteria for anemia vary widely from study to study, with diagnostic hemoglobin levels ranging from below 10 g/dL to 11.5 g/dL for women and from below 12.5 g/dL to 13 g/dL for men.[6] Microcytosis is a characteristic finding in IDA but also may be present in other, less common, conditions, such as thalassemia, sideroblastic anemia, and some chronic diseases.

Serum ferritin level is one of the most useful tests for IDA,[7,8] with a concentration of less than 12 µg/dL considered diagnostic. Serum ferritin may be higher than 15 µg/dL, however, in patients whose IDA is associated with chronic inflammation, malignancy, or hepatic disease.[9] In such cases, IDA can be ruled out only if the ferritin concentration is over 100 µg/dL.[9]

Most previous studies of IDA investigated both the lower and upper GI tract when looking for bleeding sources. The battery of investigative tests have included colonoscopy, EGD, barium enema, and an upper GI series.[3–6,10] Our study showed that a reasonable GI workup (colonoscopy, EGD, or both) was more likely to be performed at the VAMC than at the CMC. We speculate that this difference might reflect varying degrees of investigative aggression and differences in health insurance coverage.

In our study, we were able to identify potential GI or non-GI causes of bleeding in 56 of the 84 patients with IDA (67%). We were unable to identify a potential cause of IDA in the remaining 28 (33%). In previous studies, an underlying etiology was revealed in 40% to 60% of all cases.[2,3,6] An audit of IDA management in 334 British patients revealed that the cause of IDA was found in only about 38% of cases.[5] In this study, the low yield of identified causes was said to be due to low rates of colonoscopy following negative upper GI endoscopy.[5] After studying 170 patients with anemia, documented iron deficiency, and a mean age of 60, Gordon and Smith concluded that EGD with small bowel biopsy should be included in the evaluation of IDA in older patients—especially in the absence of a colonic cause of IDA.[2] In their study, IDA was more often attributed to upper GI than to lower GI causes (41% versus 18%).[2]

Rockey and Cello performed an enteroclysis exam on 26 patients with IDA and negative endoscopies, but found no additional causes for anemia.[3] In our study, we identified potential GI causes of IDA in 75% of those who had endoscopic evaluation and non-GI causes of IDA in 15%. Within the group of patients whose IDA was determined to be of non-GI origin, cancer was found in 80%. The IDA etiology remained unknown in the other 10% of the patients despite GI workup. This yield is similar to that of previous studies.[1,2,5] We conclude, therefore, that GI investigation of all patients with IDA should include, at the very least, colonoscopy and EGD.[1] Capsule endoscopy is a promising diagnostic tool for small bowel evaluation, with a yield of 55% versus 30% for the push enteroscopy.[11] In patients with severe IDA, EGD, colonoscopy, and capsule endoscopy may turn out to be the ideal investigation in the future.

## TREATING IDA

The aim of IDA treatment should be to restore hemoglobin and MCV to normal levels and to replenish body stores of iron. In our study, significantly more patients at the VAMC had supplemental iron treatment for three months and subsequent resolution of anemia than did

Continued on page 21

Continued from page 18

patients at the CMC (91% and 47% versus 64% and 21%, respectively). In published studies of IDA, the proportion of cases that ultimately resolve varies from less than 50% to nearly 90%.[3,5,10] The difference in resolution we observed between the two medical centers in our study might be due in part to the fact that follow-up data is more easily available at the VAMC. We also found a significant difference in the resolution of anemia between men and women (46% versus 16%, respectively), despite no difference in their therapy. This might be due to a lower rate of investigation in women compared to men, despite the fact that the average age of the women in the study was similar to that of the group as a whole.

*Patients at the VAMC appeared to have received more thorough investigation, more therapy, and better follow-up than did those at the CMC.*

Once the hemoglobin level is normalized, many clinicians suggest that it should be monitored at three-month intervals for one year, and then once more at year two.[9,10] Patients with IDA whose EGD and colonoscopy findings are negative should have a duodenal biopsy to rule out celiac disease, which is the cause of IDA in 5% to 10% of such cases.[1,5]

Our findings may be particularly useful to VA clinicians because 61% of our study patients were older than 60 years, 69% had hemoglobin less than 10 g/dL, and we included non-GI causes for IDA. Limitations of our study were as follows: 48% of the women had no workup, follow-up of six months or more was available for only 36% of the patients, some cases of celiac disease might have been missed (since duodenal biopsies weren't performed routinely in patients with negative EGD and colonoscopy), and we couldn't determine how many patients had subsequent investigations performed at other facilities.

## A CALL FOR IDA GUIDELINES

National guidelines for managing IDA are available in the United Kingdom.[9] There's a need for developing such guidelines in the United States. Although we found the management and follow-up of IDA to be unsatisfactory at both medical centers reviewed, patients at the VAMC appeared to have received more thorough investigation, more therapy, and better follow-up than did those at the CMC. While there are national recommendations to prevent and control iron deficiency, these focus mainly on nutritional deficiencies, especially in children and women of childbearing age.[12] In their prospective evaluation, Iannou and colleagues found that the proportion of patients evaluated for IDA increased after their institution adopted the locally accepted clinical guidelines for the diagnosis and management of IDA. Accordingly, they also saw an increase in the number of serious GI lesions detected, including treatable cancers. Such findings serve to reinforce the need for developing national guidelines addressing minimum criteria for diagnostic accuracy, optimal investigation, proper treatment, and sufficient follow-up of IDA—and a need to explore the differences in the way the condition is investigated and treated in men and women in both the VA and non-VA settings. ●

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