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Anemia and iron deficiency in inflammatory bowel disease patients: prevalence and risk factors

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Abstract

Background: To study prevalence and risk of anemia and iron deficiency anemia in inflammatory bowel disease patients.

Materials & Methods: A total of 100 subjects were enrolled. Complete blood investigation was done. The data was collected and results were analysed using SPSS software. The level of significance was set at $P<0.05$.

Results: A total of 100 patients were evaluated. IDA was calculated in 40% patients. The prevalence of anemia in IBD patients was 28%. Additionally, based on the severity of IBD, individuals with CD had a notably greater likelihood of being classified as having moderate to severe symptoms.

Conclusion: Anemia and iron deficiency anemia emerged as frequent manifestations of IBD.

Keywords: Anemia, Inflammatory bowel disease, Iron deficiency.

Introduction

Inflammatory Bowel Diseases (IBD)—Ulcerative Colitis (UC) and Crohn's Disease (CD) are a group of chronic inflammatory diseases of the gastrointestinal tract. They are characterized by the chronic and unpredictable course of the disease. Their multifactorial etiopathogenesis has not been clearly defined to date. They include, among others, immunological background, genetic, and environmental factors. [1,2] The highest incidence rates are observed in Europe and North America. [3] Today, more than 2 million Europeans and more than 2 million people in North America suffer from IBD, and the incidence of this disease is steadily increasing.[4]

Anemia is the most common systemic manifestation of Inflammatory Bowel Disease (IBD): Crohn's disease (CD), Ulcerative Colitis (UC), and IBD-unclassified (IBD-U). The reported prevalence varies between 6% and 74%. [5,6] Patients with IBD are susceptible to anemia due to chronic gastrointestinal blood loss, medication-induced myelosuppression, and nutritional deficiencies caused by malnutrition or micronutrient malabsorption. Despite the plethora of predisposing factors, the most common causes of anemia in IBD are absolute iron deficiency (ID) and functional ID, which is characterized by inflammation-induced myelosuppression and iron restriction within enterocytes, hepatocytes, and macrophages. The reported prevalence of ID in IBD varies between 36% and 90%. [5] Data on the prevalence of ID and anemia, including risk factors, are inconsistent due to heterogeneous study populations and ID(A) definitions. Key symptoms of anemia, such as dyspnea and tachycardia, are caused by decreased blood oxygen levels and peripheral hypoxia. Compensatory blood shifting from the mesenteric arteries may worsen perfusion of the intestinal mucosa.[7] Motility disorder, nausea, anorexia, and even malabsorption have been attributed to anemia. Reduced metabolic and energy efficiency during physical activity also contribute to weight loss in anemia.[8]

Central hypoxia may lead to symptoms such as headache, dizziness, vertigo, or tinnitus. Several studies have confirmed that treatment of anemia improves cognitive function. [9] Iron

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is a component of hemoglobin myoglobin, cytochromes, and many other enzymes. Thus, anemia negatively impacts almost every aspect of daily life in patients with IBD. Men with iron deficiency anemia (IDA) may suffer from impotence. Loss of libido contributes to impaired quality of life in both sexes. [10] Hence, this study was conducted to study prevalence and risk of anemia and iron deficiency anemia in inflammatory bowel disease patients.

Materials & Methods

A total of 100 subjects were enrolled. Clinicoepidemiological information, hemoglobin measurements, and serum ferritin levels were obtained. Complete blood investigation was done. The prevalence of anemia was assessed in individuals with ulcerative colitis (UC) and Crohn's disease (CD) phenotypes. Furthermore, the risk factors associated with anemia were also determined. The data was collected and results were analysed using SPSS software. The level of significance was set at $P<0.05$.

Results

A total of 100 patients were evaluated. IDA was calculated in 40% patients. The prevalence of anemia in IBD patients was 28%. A significantly higher prevalence of male patients was observed among those diagnosed with CD, whereas a higher prevalence of female patients was noted in the UC group (P=0.01). The average age at the time of inflammatory bowel disease (IBD) diagnosis was lower in CD patients compared to UC patients. Additionally, based on the severity of IBD, individuals with CD had a notably greater likelihood of being classified as having moderate to severe symptoms.

Table 1: Characteristics

Characteristics	CD	UC	P – value
Mean age (years)	42.2	49.4	0.01
Gender			
Male	50.5	43.7	0.01
Female	46.2	59.4	0.01
Mean age at diagnosis (years)	31.5	37.6	0.04
Moderate to severe disease (%)	84.5	72.1	0.001
Biological therapy (%)	64.8	23.4	0.001

Table 2: Factors associated with risk of anemia

Risk factor	P –value
CD	0.005
Active disease (IBD)	0.004
CD who underwent surgical resection	0.0001

IBD: inflammatory bowel disease; CD: Crohn's disease. P-value<0.05: significant

Discussion

Diagnosis of absolute and functional ID is challenging in patients with IBD. [11] Iron indices, such as ferritin or transferrin, can be difficult to interpret due to their dual role as acute-phase reactants, i.e., ferritin increases and transferrin decreases during (systemic) inflammation that could falsely indicate sufficient iron stores. [12] In addition, patients with IBD often suffer from inflammation that can restrict enteral iron absorption and lead to excess luminal iron that—according to data from animal studies—might exacerbate the disease. [13] Despite a lack of consistent research on hepcidin (the systemic iron regulator), iron absorption, and the effect of excess luminal iron in patients with IBD, the latest ECCO guidelines suggest intravenous iron as the first-line treatment in active disease and oral iron only in quiescent or mild

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disease. [14] Hence, this study was conducted to study prevalence and risk of anemia and iron deficiency anemia in inflammatory bowel disease patients.

In the present study, a total of 100 patients were evaluated. IDA was calculated in 40% patients. The prevalence of anemia in IBD patients was 28%. A significantly higher prevalence of male patients was observed among those diagnosed with CD, whereas a higher prevalence of female patients was noted in the UC group (P=0.01). A study by Parra S et al, a total of 529 (91%) patients had complete blood counts available in their medical records. Only 35.5% of IBD patients were fully screened for anemia. The prevalence of anemia in IBD patients was 24.6% (29.1% in CD and 19.1% in UC, P=0.008). The anemia was moderate to severe in 16.9% (19.8% in CD and 11.4% in UC, P=0.34). The prevalence of iron deficiency was 52.3% (53.6% in CD and 51.2% in UC, P=0.95). Anemia of chronic disease was present in 14.1% of IBD patients. A total of 53.8% of patients with anemia were in clinical remission. CD was associated with an increased prevalence of anemia (P=0.008; OR=1.76; CI 95% =1.16-2.66) compared to UC. The penetrant disease phenotype in CD was associated with a lower risk of anemia (P<0.0001; OR=0.25; CI 95% =0.14-0.43). Active disease compared to the disease in clinical remission was associated with an increased risk of anemia (P=0.0003; OR=2.61; CI 95% =1.56-4.36) in CD. The presence of anemia was less frequent in patients with CD who underwent surgical bowel resection compared to those who did not undergo surgery (P<0.0001; OR=0.24; CI 95% =0.14-0.40). No differences in anemia prevalence were observed regarding CD localization, age at diagnosis, UC extension or biological therapy (P>0.05). [15]

In the present study, the average age at the time of inflammatory bowel disease (IBD) diagnosis was lower in CD patients compared to UC patients. Additionally, based on the severity of IBD, individuals with CD had a notably greater likelihood of being classified as having moderate to severe symptoms. Another study by Loveikyte R et al, in total, 2197 patients (1271 Crohn's Disease, 849 Ulcerative Colitis, and 77 IBD-unclassified) were included. Iron parameters were available in 59.3% of cases. The overall prevalence of anemia, ID, and IDA was: 18.0%, 43.4%, and 12.2%, respectively. The prevalence of all three conditions did not differ between IBD subtypes. ID(A) was observed more frequently in patients with biochemically active IBD than in quiescent IBD (ID: 70.8% versus 23.9%; $p < 0.001$). Contrary to the guidelines, most respondents prescribed standard doses of intravenous or oral iron regardless of biochemical parameters or inflammation. Lastly, 25% of respondents reported not treating non-anemic ID. One in five patients with IBD suffers from anemia that—despite inconsistently measured iron parameters—is primarily caused by ID. Most medical professionals treat IDA with oral iron or standard doses of intravenous iron regardless of biochemical inflammation; however, non-anemic ID is often overlooked. Raising awareness about the management of ID(A) is needed to optimize and personalize routine care. [16] IBD disease activity has been linked with anemia. CD with structuring disease and extensive disease in UC are risk factors of anemia in IBD patients. [17] Elevated C-reactive protein (CRP) levels is an independent factor known to increase the prevalence of anemia in patients with IBD. [18] Moreover, Woźniak et al. demonstrated that ACD was predominant in CD in contrast to UC, where IDA was prevalent.[19] Oral supplementation has been known to cause oxidative stress and mucosal damage, which aggravates inflammation and promotes carcinogenesis. [20] The chronic local inflammation characteristic of this disease inhibits its absorption. Unabsorbed in earlier sections, iron enters the colon, where it interacts with the intestinal microbiota. The release of lipocalin 2 (Lcn2) causes the sequestration of iron from bacterial siderophores. Studies conducted on healthy subjects are inconclusive. They show both positive and negative effects of iron supplementation on intestinal microflora and intestinal inflammation. [21] In comparison, no effect of oral iron supplementation on the severity of colitis has been demonstrated in patients with IBD. [22] In iron-deficient mice, it has

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been shown that oral iron administration can result in a decrease in beneficial microbiota and expansion of intestinal pathogens. [23]

Conclusion

Despite the limited implementation of comprehensive screening, anemia and iron deficiency anemia emerged as frequent manifestations of IBD. Notably, CD showed a significant association with an increased risk of anemia, particularly in cases with active disease.

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