DOI: https://doi.org/10.22516/25007440.696

Prevalence and treatment of anemia in inflammatory bowel disease in a Colombian reference center

Fabián Juliao-Baños,[1*] Mateo Arrubla,[2] Laura Osorio,[2] Joselyn Camargo,[3] Juliana Londoño,[3] Camilo Cáceres,[3] Jhon Carvajal,[1] Gabriel Mosquera-Klinger,[1] Álvaro Gómez,[1] Jorge Donado.[1,2]

OPEN ACCESS

Citation:
Juliao-Baños F, Arrubla M, Osorio L, Camargo J, Londoño J, Cáceres C, Carvajal J, Mosquera-Klinger G, Gómez A, Donado J. Prevalence and treatment of anemia in inflammatory bowel disease in a Colombian reference center. Rev Colomb Gastroenterol. 2021;36(4):446-454. https://doi.org/10.22516/25007440.696

[1] Hospital Pablo Tobón Uribe. Medellín, Colombia.
[2] Universidad Pontificia Bolivariana. Medellín, Colombia.
[3] Universidad de Antioquia. Medellín, Colombia.

***Correspondence:** Fabián Juliao-Baños.
fabianjuliao@hotmail.com

Received: 22/11/20
Accepted: 12/02/21

Abstract

Introduction: Anemia is the most frequent complication of inflammatory bowel disease (IBD). This study aims to determine the prevalence, connection, and treatment of anemia in IBD in a local context. **Materials and Methods:** This retrospective study was conducted at The Pablo Tobon Uribe Hospital, in Medellín (Colombia) with adult patients who (were admitted) came for consultation from 2001, until February 2019. Absolut and relative frequencies were calculated. The Chi square test of independence was applied for comparing two proportions and the odds ratio (OR) was estimated. **Results:** A total of 759 IBD patients were enrolled, 544 (71.6%) with ulcerative colitis (UC); 200 (26.3%) Crohn's disease (CD), and 15 (1.9%) with non-classifiable IBD. In total, 185 (24,4 %) IBD patients had a diagnosis of anemia, that is less frequent in UC patients that in CD patients (22,2 % versus 32,5 %, respectively; OR: 0,684; CI: 0,456-0,96; p = 0,03). Extensive UC patients (54,1 %) had a more recurrent level of anemia than non-extensive UC (46,3 %) (OR: 4,4; CI: 2,6-7,4; p = 0,001); the same result was observed when severe UC (66,1 %) was compared with UC non-severe (32,3 %) (OR: 4,95; CI: 2,87-8,51; p = 0,000). In the analysis of CD, patients with a non-inflammatory response (B2, B3: 73,9 %) had a more recurrent level of anemia than patients with an inflammatory response (B1: 26,2 %) (OR: 0,35; CI: 0,18-0,67; p = 0,000). 44,3 % of the total number of patients received treatment, 19,5 % received oral iron, 20,0 % received intravenous iron, and 16,2 % received a blood transfusion. **Conclusions:** In our context, Anemia is a common complication in IBD cases (24,4 %). Despite the existence of international guidelines, the treatment in our context is not optimal.

Keywords

Anemia; Inflammatory Bowel Disease; Prevalence; Parenteral Iron.

INTRODUCTION

Anemia is the most common complication of inflammatory bowel disease (IBD) [(1)]. It is associated with a more disabling disease[(2)] with a significant impact on the quality of life[(3,4)] and has historically received little attention from gastroenterologists[(5)]. Anemia is defined by the World Health Organization (WHO) as hemoglobin (Hb) levels < 12 g/dL in non-pregnant women and < 13 g/dL in men[(6)]. The European Crohn's and Colitis Organisation (ECCO) adopted the previous definition of anemia in a recent consensus, which recommends ruling out this complication in all individuals with IBD[(1)].

The etiology of anemia in IBD is multifactorial. The most common causes are iron deficiency anemia (IDA) and anemia of chronic disease (ACD), which can coexist (mixed); other causes of anemia such as those associated with vitamin B_{12} or folic acid deficiency, or induced by drugs are less frequent[(7,8)]. In a systematic review of 17 articles with CD, the prevalence ranges between 4% and 67%[(9)]. Gisbert *et al* reported a 17% average prevalence of anemia in IBD, and figures of 16% were found in outpatients and 68% in hospitalized indi-

viduals[10]. IBD prevalence in Latin America is increasing[11], and there is little data on the relationship between anemia and IBD. Two studies in Brazil found a prevalence of anemia of 21% and 24.6% in patients with IBD[12,13]. This study aims to determine the prevalence, associations, and treatment of anemia in a cohort of IBD patients in our center.

MATERIALS AND METHODS

The diagnoses of ulcerative colitis (UC) and Crohn's disease (CD) were searched in the clinical records of the Hospital Pablo Tobón Uribe in Medellín, Colombia, until February 2019, considering the following codes: K500 CD of the small intestine, K501 CD of the large intestine, K508 other types of CD, K509 CD unspecified, K519 UC unspecified, and K518 other UCs. Data from adult patients with UC and CD, who attended the emergency department, were hospitalized, or were served by the outpatient clinic, were retrospectively analyzed to determine the presence of anemia.

Definitions of anemia

Anemia was diagnosed in patients with Hb levels < 12 g/dL for non-pregnant women and < 13 g/dL for men, according to the WHO recommendation[6]. IDA was considered at ferritin levels < 30 mg/L and normal C-reactive protein (CRP) levels, or in the case of ferritin < 100 mg/L and high CRP, but with a transferrin saturation percentage < 16%. ACD was defined as normal or elevated ferritin levels, normal average transferrin saturation percentage, and elevated CRP[8]. Anemia due to deficiencies of vitamin B_{12} (< 211 ng/mL) and folic acid (< 7 ng/mL) were defined when the levels were below the average level. Other measurements such as mean corpuscular volume (MCV), red blood cell distribution width (RDW), and percentage of reticulocytes were also incorporated to classify anemia[14,15]. Patients in whom anemia could not be defined due to insufficient data were excluded from the study.

Mild anemia refers to Hb levels of 11.0–11.9 g/dL in women and 11.0–12.9 in men, moderate 8.0–10.9 g/dL, and severe with levels < 8 g/dL, according to WHO recommendations[1,6]. UC activity was defined by the Truelove and Witts classification[16], considering the activity at the time of the most severe episode of anemia for the analysis. According to the Montreal Classification[17], the extent of UC was defined. The location and behavior of the CD were determined by the Montreal Classification[17].

Data collection

A database with Excel format was built, collecting the following data from each patient for analysis:

- Type of IBD (UC, CD, and IBD not classifiable)
- Sex of the patient
- Anatomical extension of the UC
- UC activity
- Location of CD
- CD behavior
- Cumulative medical treatment (5-aminosalicylic acid [5-ASA], steroids, immunosuppressants, biological therapy)
- Surgical treatment
- Hospitalization rate
- Presence of anemia
- Type of anemia
- Severity of anemia
- Treatment of anemia

The following measurements were considered to classify anemia: Hb, hematocrit, MCV, serum ferritin, percentage of transferrin saturation, and CRP. In patients with elevated MCV, we verified vitamin B_{12} and folic acid levels.

Statistical analysis

Absolute and relative frequencies were used for qualitative variables, and mean, standard deviation (*SD*), or median and interquartile range (*IQR*; P25–P75) were used for quantitative variables after verifying the assumption of normality with the Kolmogorov-Smirnov tests. The chi-square test (χ^2) of independence was employed to compare two proportions, estimating the odds ratio (*OR*) with its appropriate 95% confidence interval (*CI*).

Ethical considerations

In this risk-free research, the patients' medical records were reviewed, ensuring the confidentiality and privacy of the information collected. The project researchers adhered to the international principles of the 2013 Declaration of Helsinki in Fortaleza, Brazil, and Articles 10 and 11 of Resolution 008430/1993 issued by the Ministry of National Health of Colombia.

RESULTS

In this retrospective, descriptive, analytical study, 759 patients who met diagnostic criteria for IBD were systematically included, of which 544 (71.6%) had a diagnosis of UC, 200 (26.3%) of CD, and 15 (1.9%) of unclassifiable IBD.

Anemia was documented in 185 of the 759 patients (24.4%) with IBD. In UC, 121 of 544 (22.2%) had anemia, compared with 65 of 200 patients (32.5%) with CD (*OR*: 0.684; *CI*: 0.456–0.96; $p = 0.03$). Regarding severe anemia,

it occurred in 87 of 185 patients (47.0%) with IBD, 61 of 121 (50.4%) with UC, and 26 of 65 (40.0%) with CD. Of the total patients with anemia, 102 had IDA (55.1%), 74 (41.1%) had mixed anemia, and seven (3.7%) had vitamin B_{12} deficiency (**Figure 1**).

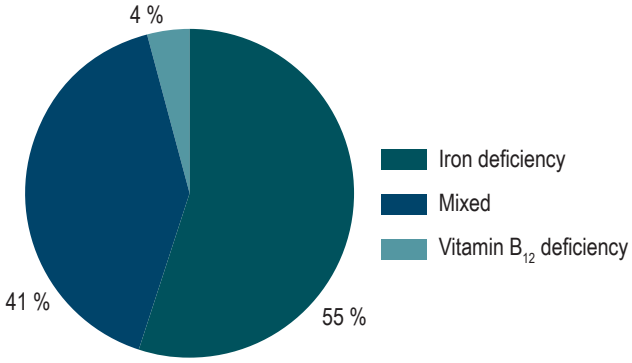

Figure 1. Type of anemia in IBD.

Of the patients with UC and anemia, 18.2% had proctitis, 28.1% left colitis, and 54.1% extensive colitis. A significant difference was found in comparing anemia in extensive versus non-extensive colitis (proctitis plus left colitis) (*OR*: 4.4; *CI*: 2.6–7.4; $p = 0.001$). Regarding UC activity, 5.0% were asymptomatic (S0), 14.0% had mild activity (S1), 15.7% moderate activity (S2), and 66.1% severe activity (S3). When comparing the presence of anemia in severe versus non-severe activity, we found a significant difference (*OR*: 4.95; *CI*: 2.87–8.51; $p = 0.000$).

Considering the location, the distribution of anemia in patients with CD was as follows: ileal (40%), ileocolonic (35.4%), colonic (20%), and upper gastrointestinal involvement (4.6%). No significant difference was found between colonic versus non-colonic location (*OR*: 1.2; *CI*: 0.66–2.19; $p = 0.54$). For CD behavior and the presence of anemia, it is inflammatory in 26.2% (B1), stenosing in 27.7% (B2), penetrating in 27.7% (B3), and perianal in 18.5%. The inflammatory behavior presented with anemia less frequently than the non-inflammatory behavior (B2 plus B3) (*OR*: 0.35; *CI*: 0.18–0.67; $p = 0.000$).

Patients with UC and anemia required more biological therapy than those without anemia (33.1% versus 14.4%); this difference was significant (*OR*: 2.29, *CI*: 1.46–3.58, $p = 0.009$). In CD, patients with anemia also required more biological therapy (61.5% vs 39.3%); however, this difference was not significant (*OR*: 1.56, *CI*: 0.94–2.6, $p = 0.08$). There was no significant difference in terms of the need for surgery in patients with anemia versus non-anemia in UC (11.5% vs 11.1%; *OR*: 1.04; *CI*: 0.55–1.95; $p = 0.87$), nor in CD (46.2% vs 34.8%; *OR*: 1.32; *CI*: 0.76–2.28; $p = 0.32$). Regarding hospitalization, patients with UC and anemia required more hospitalization compared to those without anemia (59.5% vs 47.0%; *OR*: 1.95; *CI*: 1.37–2.77; $p = 0.000$); this was not demonstrated in individuals with CD (72.3% vs 63.0%, *OR*: 1.14; *CI*: 0.72–1.82; $p = 0.63$) (**Table 1**).

For the treatment of anemia and IBD, 82 of 185 (44.3%) patients with anemia did not receive treatment, 19.5% received oral iron, 20.0% intravenous (IV) iron, and 16.2% a transfusion (**Figure 2**). In the subgroup of patients with severe anemia, 24 of 87 (27.6%) were untreated, 12.6% received oral iron, 29.9% received IV iron, and 29.9% had a transfusion. No patient received erythropoietin.

DISCUSSION

The prevalence of anemia in 759 adult patients with IBD, both outpatient and hospitalized, in our center is high (24.4%), and it is more frequent in CD (32.5%) than in UC (22.2%), as reported in the universal literature. A European meta-analysis with 2,192 patients found a prevalence of anemia in 24% of cases with IBD, 27% of cases with CD, and 21% of cases with UC[18]. The Norwegian IBSEN group also identified a higher proportion of anemia at diagnosis in CD (48.8%), compared to UC (20.2%)[19]. A Swedish study found 30% anemia in IBD patients at diagnosis, 42% in CD patients, and 24% in UC patients[20]. A more recent publication from the University of Pittsburgh detected a prevalence of anemia in patients with IBD of 33.2%, 34.3% in patients with CD, and 31.5% in patients with UC[2]. The ECCO-EPICOM cohort study noticed a higher prevalence of anemia in patients with CD of 49% and 39% in patients with UC during the first year after diagnosis[21].

The high number of patients with severe anemia in our IBD patients (40.0%), compared with other series, was striking. In a multicenter study in nine European countries with 1,404 patients with IBD, 56% of individuals with at least moderate anemia (Hb <10 g/dL) were observed, but only 15% had severe anemia[22]. The severity of anemia was mild in 76.2%, moderate in 15%, and severe in 8.8% in a report of 193 cases associated with IBD in 55 centers in Germany[23]. It can be explained by the severity of patients with IBD who are cared for in our tertiary referral center. These two series are surveys of the participants, with no analysis of IBD severity in their patients.

On the one hand, our study demonstrated a predominance of IDA (55%) and mixed (41%) over other etiologies of anemia. In a Scandinavian study[24], the etiology of anemia in IBD was IDA (20%), ACD (12%), mixed (68%), and a deficiency of vitamin B_{12} and folic acid (< 5%), as found in our study, but with a higher proportion of mixed anemia.

On the other hand, in our study, patients with UC and anemia presented with more strenuous activity (S3), more significant anatomical extension, and more disabling

Table 1. Clinical features of IBD and anemia

	CD		UC		*p*
Patients (n)	200		544		
	Anemia	**No anemia**	**Anemia**	**No anemia**	
	65 (32.5 %)	135 (67.5 %)	121 (22.2 %)	423 (77.8 %)	0.03
UC extension					
- E1: proctitis + E2: left			56 (45.9 %)		0.001
- E3: extensive colitis			65 (54.1 %)		
CD location					
- L1: terminal ileum	26 (40.0 %)				0.54
- L3: terminal ileum + colon	23 (35.4 %)				
- L4: upper GI	3 (4.6 %)				
- L2: colon	13 (20.0 %)				
Severity of UC symptoms					
- Non-severe activity (S1 + S2)			40 (33.9 %)		0.000
- Severe activity (S3)			81 (66.1 %)		
Behavior of CD					
- B1: inflammatory	17 (26.2 %)				0.000
- B2 + B3 + P	48 (73.9 %)				
Biological/surgery/hospitalization for UC			**Anemia**	**No anemia**	
- Biological			40 (33.1 %)	61 (14.4 %)	0.009
- Surgery			14 (11.5 %)	47 (11.1 %)	0.87
- Hospitalization			72 (59.5 %)	199 (47 %)	0.000
Biological/surgery/hospitalization for CD	**Anemia**	**No anemia**			
- Biological	40 (61.5 %)	53 (39.3 %)			0.08
- Surgery	30 (46.2 %)	47 (34.8 %)			0.32
- Hospitalization	47 (72.3 %)	85 (63 %)			0.63

disease due to a higher hospitalization rate and greater use of biological therapy. In individuals with CD, anemia was associated with non-inflammatory behavior (stenosing or penetrating), so these patients are more complicated and have a worse prognosis than patients with inflammatory behavior. In the ECCO-EPICOM study already mentioned, patients with extensive UC and penetrating CD had a higher risk of anemia, just like in this study[21]. In the Swedish study, anemia was also associated with extensive UC[20]. Data from the University of Pittsburgh study above also show a significant correlation of anemia with higher rates of disease activity and hospitalization[2].

The ECCO guidelines[1] recommend using oral iron in IBD patients with mild IDA defined by the WHO with Hb levels of 11–11–9 g/dL, whose IBD is clinically inactive and with good tolerance to the drug. IV iron should be considered as the first line of treatment in patients with intolerance to oral iron, active IBD, Hb levels < 10 g/dL, and in patients requiring erythropoietin[1]. A recent review article, considering the 2019 coronavirus disease pande-

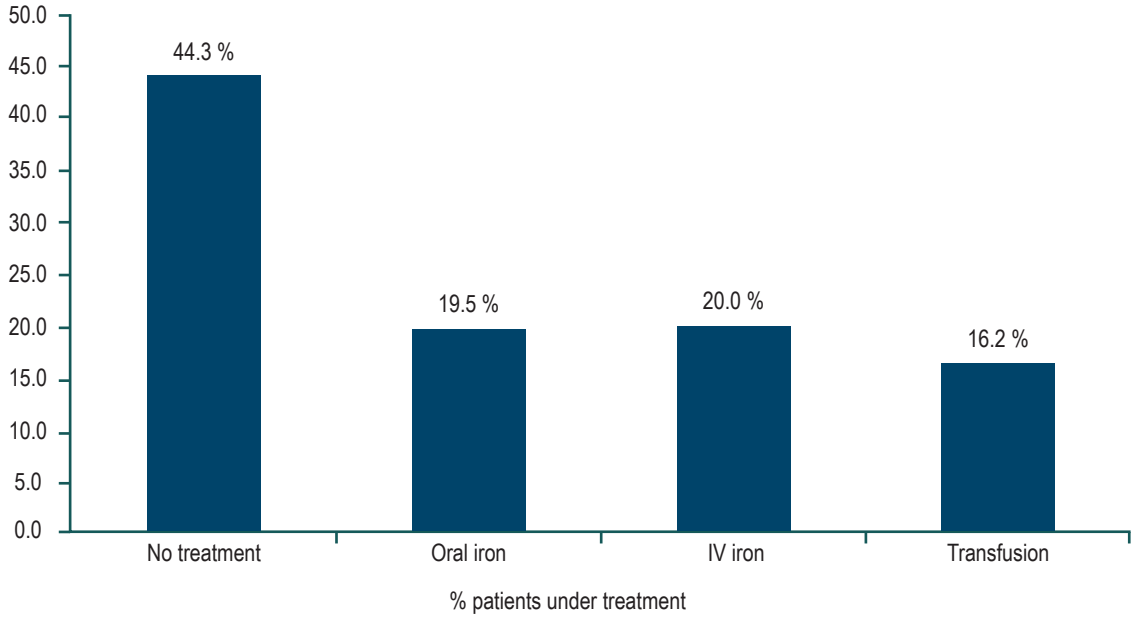

Figure 2. Treatment of anemia and IBD.

mic (COVID-19), suggests using oral iron during these times in patients with IBD and mild and moderate anemia to prevent them from attending hospitals to receive parenteral iron and reserve the latter only for subjects with IBD and severe anemia (Hb < 8 g/dL)[25].

In this study, 44.3% of the patients did not receive treatment regarding IDA. A high percentage of the subgroup of individuals with severe anemia did not receive it either (27.6%). We believe that the concept of asymptomatic anemia is still used in the medical body without considering the alteration in the quality of life that this complication entails. In a previous survey of gastroenterologists throughout Colombia, when asked what the best management of a patient with IBD and IDA <10 g/dL would be, 66% would treat it with oral iron, 15% with parenteral iron, 9% transfused iron, and 10% did not treat it[26]. In the German multicenter study mentioned above, only 43.5% of patients with IDA and IBD received treatment; from this portion, 56% were treated with oral iron, 15% with parenteral iron, and 10% in transfusion[23]. In the UK, a survey was conducted on outpatients with anemia and IBD who received oral iron; only 42% completed the treatment, but the treatment was not adequate for the control of anemia in 2 out of 3 patients[27]. In the European study above, 92% of IDA patients received iron supplementation, 67% oral iron, and only 28% IV iron, even though 56% had Hb < 10 g/dL[21]. A retrospective study conducted in the United States found that only 37% of anemic patients with IBD received oral iron, and 2.8% received IV iron during follow-up[28]. A global survey of patients with anemia and IBD found that 33% reported not receiving treatment for their anemia. Of those treated, 52% received oral iron, 27% IV iron, and 19% other types of supplements. Of the patients with oral iron, 74% were not satisfied with the treatment, while 72% were satisfied with IV iron[29].

The Crohn's & Colitis Foundation of America (CCFA) recently appointed a committee of experts to make recommendations and develop an algorithm for the screening, evaluation, intervention, and follow-up of patients with anemia and IBD[30]. A later publication assessed adherence to these recommendations and found that iron therapy in anemic patients increased from 30% to 80%, and the prevalence of anemia decreased from 48% to 25%. However, the percentage of iron deficiency screening did not change; only 20% of anemic patients underwent a ferritin measurement[31]. A recent review article recommends a treat-to-target approach for patients with IDA associated with IBD, as proposed for the treatment of IBD, divided into three steps: early detection, treat-to-target (normalization of Hb and iron stores), and strict monitoring (ferritin and transferrin saturation percentage every 3–6 months) due to the high risk of recurrence[32].

Within the limitations of this study, it may contain interpretation biases, as it is a retrospective study based on data collected from the medical records. Additionally, this study was carried out in a tertiary referral hospital, a reference center for IBD patients throughout the country, with probably more severe and complicated patients than those from other centers in the country.

CONCLUSIONS

There is a high prevalence of anemia associated with IBD in our setting, which is more frequent in CD than in UC, consistent with other studies worldwide. It could be explained by insufficient diagnosis, ineffective treatment, and a lack of monitoring of these individuals with anemia. Anemia in patients with IBD is associated with greater severity of the disease. Additionally, the preferred route of administration of iron in IDA, both in this and other series cited, is oral, regardless of the severity of the anemia, the high percentage of intolerance to oral iron, and international guidelines. It is necessary to become more aware of this complication in patients with IBD and make more efforts in medical education to implement guideline recommendations and apply them to the early diagnosis, adequate management, and monitoring of these individuals. Nonetheless, the most important thing will always be the timely and adequate treatment of IBD to prevent this complication. A proposal for the management of anemia in patients with IBD is presented in **Figure 3**.

Conflicts of interest

None of the study authors reported conflicts of interest.

Funding source

No funding was received from any entity to carry out this study.

Author contribution

F. Juliao-Baños participated in the study design, recruitment of patients, and writing of the paper. M. Arrubla, L. Osorio, J. Camargo, J. Londoño, and C. Cáceres carried out the data collection. J. Carvajal, G. Mosquera, and A. Gomez participated in the recruitment of patients. J. Donado performed the statistical analysis.

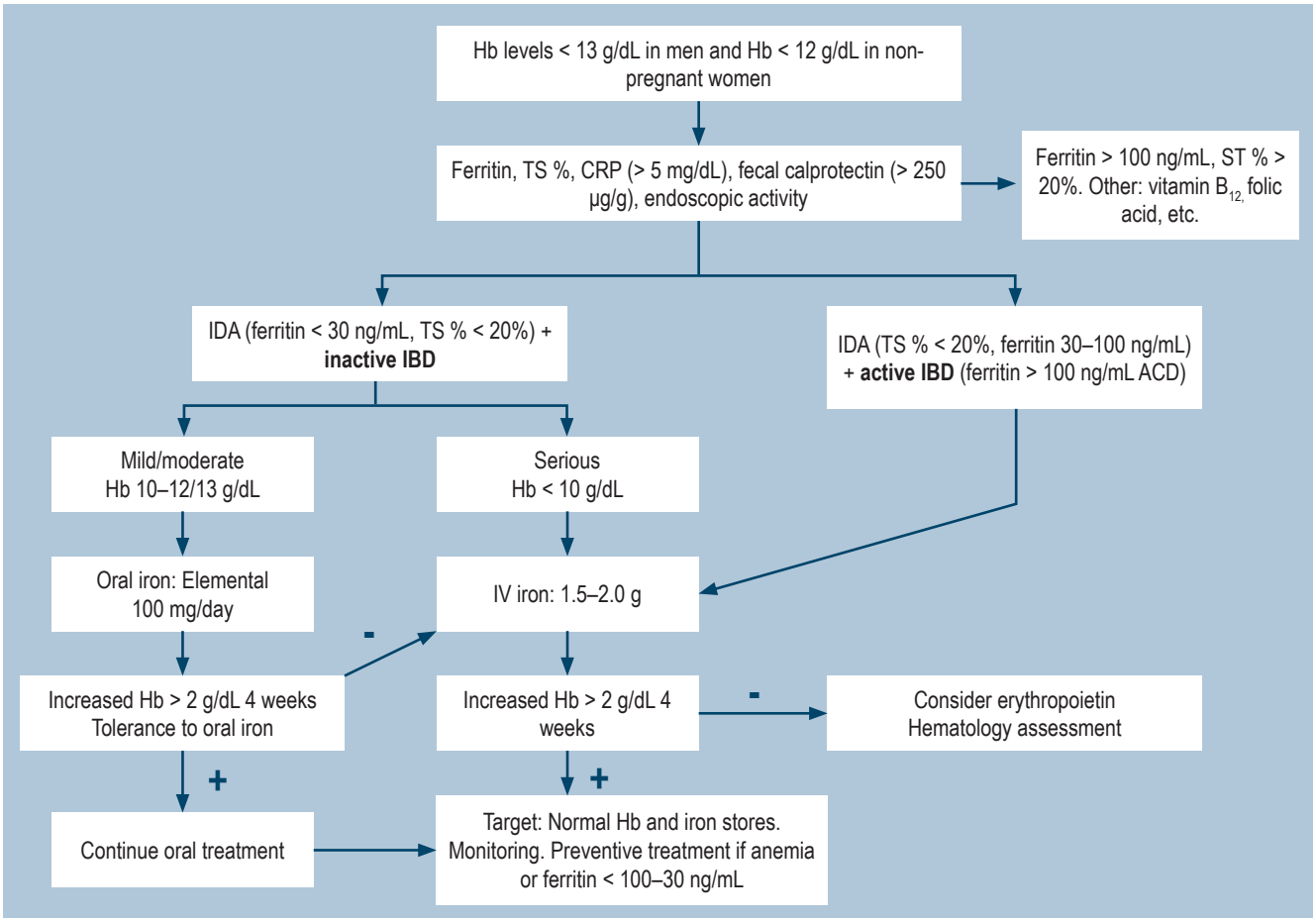

Figure 3. Anemia management algorithm in IBD. TS: Transferrin saturation.

REFERENCES

1. Dignass AU, Gasche C, Bettenworth D, Birgegård G, Danese S, Gisbert JP, Gomollon F, Iqbal T, Katsanos K, Koutroubakis I, Magro F, Savoye G, Stein J, Vavricka S; European Crohn's and Colitis Organisation [ECCO]. European consensus on the diagnosis and management of iron deficiency and anaemia in inflammatory bowel diseases. J Crohns Colitis. 2015;9(3):211-22. https://doi.org/10.1093/ecco-jcc/jju009
2. Koutroubakis IE, Ramos-Rivers C, Regueiro M, Koutroumpakis E, Click B, Schoen RE, Hashash JG, Schwartz M, Swoger J, Baidoo L, Barrie A, Dunn MA, Binion DG. Persistent or Recurrent Anemia Is Associated With Severe and Disabling Inflammatory Bowel Disease. Clin Gastroenterol Hepatol. 2015;13(10):1760-6. https://doi.org/10.1016/j.cgh.2015.03.029
3. Wells CW, Lewis S, Barton JR, Corbett S. Effects of changes in hemoglobin level on quality of life and cognitive function in inflammatory bowel disease patients. Inflamm Bowel Dis. 2006;12(2):123-30. https://doi.org/10.1097/01.MIB.0000196646.64615.db
4. González Alayón C, Pedrajas Crespo C, Marín Pedrosa S, Benítez JM, Iglesias Flores E, Salgueiro Rodríguez I, Medina Medina R, García-Sánchez V. Prevalence of iron deficiency without anaemia in inflammatory bowel disease and impact on health-related quality of life. Gastroenterol Hepatol. 2018;41(1):22-29. https://doi.org/10.1016/j.gastrohep.2017.07.011
5. Gasche C. Anemia in IBD: the overlooked villain. Inflamm Bowel Dis. 2000;6(2):142-150. https://doi.org/10.1097/00054725-200005000-00013
6. WHO U, UNU. Iron Deficiency Anemia: Assessment, Prevention and Control. Report of a Joint WHO/UNICEF/UNU Consultation. Geneva, Switzerland: World Health Organization 2001. Disponible en: https://www.who.int/nutrition/publications/en/ida_assessment_prevention_control.pdf
7. Stein J, Hartmann F, Dignass AU. Diagnosis and management of iron deficiency anemia in patients with IBD. Nat Rev Gastroenterol Hepatol. 2010;7(11):599-610. https://doi.org/10.1038/nrgastro.2010.151
8. Oustamanolakis P, Koutroubakis IE, Kouroumalis EA. Diagnosing anemia in inflammatory bowel disease: beyond the established markers. J Crohns Colitis. 2011;5(5):381-91. https://doi.org/10.1016/j.crohns.2011.03.010
9. Kulnigg S, Gasche C. Systematic review: managing anaemia in Crohn's disease. Aliment Pharmacol Ther. 2006;24(11-12):1507-23. https://doi.org/10.1111/j.1365-2036.2006.03146.x
10. Gisbert JP, Gomollón F. Common misconceptions in the diagnosis and management of anemia in inflammatory bowel disease. Am J Gastroenterol. 2008;103(5):1299-307. https://doi.org/10.1111/j.1572-0241.2008.01846.x
11. Kotze PG, Underwood FE, Damião AOMC, Ferraz JGP, Saad-Hossne R, Toro M, Iade B, Bosques-Padilla F, Teixeira FV, Juliao-Banos F, Simian D, Ghosh S, Panaccione R, Ng SC, Kaplan GG. Progression of Inflammatory Bowel Diseases Throughout Latin America and the Caribbean: A Systematic Review. Clin Gastroenterol Hepatol. 2020;18(2):304-312. https://doi.org/10.1016/j.cgh.2019.06.030
12. Antunes CV, Hallack Neto AE, Nascimento CR, Chebli LA, Moutinho IL, Pinheiro Bdo V, Reboredo MM, Malaguti C, Castro AC, Chebli JM. Anemia in inflammatory bowel disease outpatients: prevalence, risk factors, and etiology. Biomed Res Int. 2015;2015:728925. https://doi.org/10.1155/2015/728925
13. Parra RS, Feitosa MR, Ferreira SDC, Rocha JJRD, Troncon LEA, FÉres O. Anemia and iron deficiency in inflammatory bowel disease patients in a referral center in brazil: prevalence and risk factors. Arq Gastroenterol. 2020;57(3):272-277. https://doi.org/10.1590/S0004-2803.202000000-51
14. Gasche C, Berstad A, Befrits R, Beglinger C, Dignass A, Erichsen K, Gomollon F, Hjortswang H, Koutroubakis I, Kulnigg S, Oldenburg B, Rampton D, Schroeder O, Stein J, Travis S, Van Assche G. Guidelines on the diagnosis and management of iron deficiency and anemia in inflammatory bowel diseases. Inflamm Bowel Dis. 2007;13(12):1545-53. https://doi.org/10.1002/ibd.20285
15. Reinisch W, Staun M, Bhandari S, Muñoz M. State of the iron: how to diagnose and efficiently treat iron deficiency anemia in inflammatory bowel disease. J Crohns Colitis. 2013;7(6):429-40. https://doi.org/10.1016/j.crohns.2012.07.031
16. Truelove Sc, Witts LJ. Cortisone in ulcerative colitis; final report on a therapeutic trial. Br Med J. 1955;2(4947):1041-8. https://doi.org/10.1136/bmj.2.4947.1041
17. Silverberg MS, Satsangi J, Ahmad T, Arnott ID, Bernstein CN, Brant SR, Caprilli R, Colombel JF, Gasche C, Geboes K, Jewell DP, Karban A, Loftus EV Jr, Peña AS, Riddell RH, Sachar DB, Schreiber S, Steinhart AH, Targan SR, Vermeire S, Warren BF. Toward an integrated clinical, molecular and serological classification of inflammatory bowel disease: report of a Working Party of the 2005 Montreal World Congress of Gastroenterology. Can J Gastroenterol. 2005;19 Suppl A:5A-36A. https://doi.org/10.1155/2005/269076
18. Filmann N, Rey J, Schneeweiss S, Ardizzone S, Bager P, Bergamaschi G, Koutroubakis I, Lindgren S, Morena Fde L, Moum B, Vavricka SR, Schröder O, Herrmann E, Blumenstein I. Prevalence of anemia in inflammatory bowel diseases in european countries: a systematic review and individual patient data meta-analysis. Inflamm Bowel Dis. 2014;20(5):936-45. https://doi.org/10.1097/01.MIB.0000442728.74340.fd
19. Høivik ML, Reinisch W, Cvancarova M, Moum B; IBSEN study group. Anaemia in inflammatory bowel disease: a population-based 10-year follow-up. Aliment Pharmacol Ther. 2014;39(1):69-76. https://doi.org/10.1111/apt.12541

20. Sjöberg D, Holmström T, Larsson M, Nielsen AL, Holmquist L, Rönnblom A. Anemia in a population-based IBD cohort (ICURE): still high prevalence after 1 year, especially among pediatric patients. Inflamm Bowel Dis. 2014;20(12):2266-70. https://doi.org/10.1097/MIB.0000000000000191
21. Burisch J, Vegh Z, Katsanos KH, Christodoulou DK, Lazar D, Goldis A, et al; EpiCom study group. Occurrence of Anaemia in the First Year of Inflammatory Bowel Disease in a European Population-based Inception Cohort-An ECCO-EpiCom Study. J Crohns Colitis. 2017;11(10):1213-1222. https://doi.org/10.1093/ecco-jcc/jjx077
22. Stein J, Bager P, Befrits R, Gasche C, Gudehus M, Lerebours E, Magro F, Mearin F, Mitchell D, Oldenburg B, Danese S. Anaemia management in patients with inflammatory bowel disease: routine practice across nine European countries. Eur J Gastroenterol Hepatol. 2013;25(12):1456-63. https://doi.org/10.1097/MEG.0b013e328365ca7f
23. Blumenstein I, Dignass A, Vollmer S, Klemm W, Weber-Mangal S, Stein J. Current practice in the diagnosis and management of IBD-associated anaemia and iron deficiency in Germany: the German AnaemIBD Study. J Crohns Colitis. 2014;8(10):1308-14. https://doi.org/10.1016/j.crohns.2014.03.010
24. Bager P, Befrits R, Wikman O, Lindgren S, Moum B, Hjortswang H, Dahlerup JF. The prevalence of anemia and iron deficiency in IBD outpatients in Scandinavia. Scand J Gastroenterol. 2011;46(3):304-9. https://doi.org/10.3109/00365521.2010.533382
25. D'Amico F, Peyrin-Biroulet L, Danese S. Oral Iron for IBD Patients: Lessons Learned at Time of COVID-19 Pandemic. J Clin Med. 2020;9(5):1536. https://doi.org/10.3390/jcm9051536
26. Juliao F, Agudelo Y, Yepes C. Variación en el cuidado de pacientes con Enfermedad Inflamatoria Intestinal (EII): resultado de una encuesta. Rev Col Gastroenterol. 2014;29(1):11-18.
27. Lugg S, Beal F, Nightingale P, Bhala N, Iqbal T. Iron treatment and inflammatory bowel disease: what happens in real practice? J Crohns Colitis. 2014;8(8):876-80. https://doi.org/10.1016/j.crohns.2014.01.011
28. Patel D, Yang YX, Trivedi C, Kavani H, Xie D, Medvedeva E, Lewis J, Khan N. Incidence, Duration, and Management of Anemia: A Nationwide Comparison Between IBD and Non-IBD Populations. Inflamm Bowel Dis. 2020;26(6):934-940. https://doi.org/10.1093/ibd/izz206
29. Danese S, Hoffman C, Vel S, Greco M, Szabo H, Wilson B, Avedano L. Anaemia from a patient perspective in inflammatory bowel disease: results from the European Federation of Crohn's and Ulcerative Colitis Association's online survey. Eur J Gastroenterol Hepatol. 2014;26(12):1385-91. https://doi.org/10.1097/MEG.0000000000000200
30. Hou JK, Gasche C, Drazin NZ, Weaver SA, Ehrlich OG, Oberai R, Zapala S, Siegel CA, Melmed G. Assessment of Gaps in Care and the Development of a Care Pathway for Anemia in Patients with Inflammatory Bowel Diseases. Inflamm Bowel Dis. 2017;23(1):35-43. https://doi.org/10.1097/MIB.0000000000000953
31. Qureshi T, Peter Nguyen T, Wang R, Willis D, Shah R, Hou JK. Improving Anemia in Inflammatory Bowel Disease: Impact of the Anemia Care Pathway. Dig Dis Sci. 2019;64(8):2124-2131. https://doi.org/10.1007/s10620-019-05559-w
32. Peyrin-Biroulet L, Lopez A, Cummings JRF, Dignass A, Detlie TE, Danese S. Review article: treating-to-target for inflammatory bowel disease-associated anaemia. Aliment Pharmacol Ther. 2018;48(6):610-617. https://doi.org/10.1111/apt.14922