Anemia at the time of diagnosis of inflammatory bowel disease: Prevalence and associated factors in adolescent and adult patients

Alfredo J. Lucendo, Ángel Arias, Óscar Ronceró, Daniel Hervías, Cristina Verdejo, Carmen Naveas-Polo, Abdelmouneim Bouhmidi, Rufo Lorente, Luis Miguel Alcázar, Irina Saluèn, Julio A. García-Quiones, María Jesús Carrillo-Ramos

A R T I C L E   I N F O
Article history:
Received 31 October 2016
Accepted 7 December 2016
Available online 14 December 2016

Keywords:
Anemia
Crohn's disease
Inflammatory bowel disease
Ulcerative colitis

A B S T R A C T
Background: The prevalence, characteristic and determinants of anemia, at the time of inflammatory bowel disease (IBD) diagnosis have yet to be fully elucidated.

Methods: Retrospective cross-sectional study. Analytical data and disease characteristics obtained upon diagnosis of 1278 IBD patients [Crohn's disease/ulcerative colitis (CD/UC): 718/560] were collected.

Results: Anemia was present in 41.2% of patients at diagnosis (47% and 33.8% of CD and UC patients, respectively; p < 0.001), being severe in 5.5%. Iron deficiency anemia represented 69.6% of cases, with no differences between CD and UC. Female sex was the strongest risk factor for anemia in both CD and UC (OR 7.11; 95%CI 4.18–12.10 and 6.55; 95%CI 3.39–12.63, respectively), followed by elevated (≥2 mg/dL) C-reactive protein (OR 4.08; 95%CI 2.39–6.97 and 4.58; 95%CI 2.26–9.27, respectively). Current smoking was a risk factor for anemia in CD (OR 2.23; 95%CI 1.24–4.02), but a protective one in UC (OR 0.36; 95%CI 0.14–0.92). A penetrating CD behavior increased the risk of anemia (OR 3.34; 95%CI 1.36–8.21); in UC, anemia increased with disease extension (E2 + E3) (OR 1.80; 95%CI 1.13–2.86).

Conclusions: Female sex and disease activity are major determinants of anemia at IBD diagnosis. Anemia is associated with disease behavior in CD and with disease extension in UC.

© 2016 Published by Elsevier Ltd on behalf of Editrice Gastroenterologica Italiana S.r.l.

1. Introduction

Anemia is the most common systemic complication and extraintestinal manifestation in inflammatory bowel disease (IBD) [1,2], significantly affecting the health-related quality of life (HRQoL) of patients [3,4] and their ability to work [5]. Anemia determines long-term disease outcomes, including the amount of treatment needed, hospital admissions [6], and the need for surgery in IBD population [7], all of which lead to substantial increases in health-care costs [8].

The reported prevalence of anemia in patients with IBD varies markedly from 6% to 74%, depending on the definition of anemia used, the moment of assessment, and the population studied [9]. Anemia presents more frequently in patients with Crohn's disease (CD) than in ulcerative colitis (UC) [10], and in hospitalized compared to outpatients [11]. Several factors underlie inter-study variations in the prevalence of anemia, including the lack of standardized definitions of anemia, the specific study populations considered, patients’ sex [12], moment of assessment during the course of the disease [13], and the disease activity [14]. Together, these factors indicate that the prevalence of anemia changes throughout the natural history of IBD.

Several factors contribute to anemia in IBD, the most common types being iron deficiency anemia and anemia of chronic disease (ACD), which often overlap [15,16]. Vitamin B12 and folic acid
deficiencies, along with the effects of pro-inflammatory cytokines, hemolysis, drug therapies, and myelosuppression, are also identified in a number of patients [1].

The heterogeneity of the populations and disease stages analyzed in most of the available literature and the varying criteria used to define anemia have limited our understanding of the prevalence and determining factors of this complex manifestation of IBD. Studying a more homogeneous population at a defined moment in the course of the disease should improve frequency estimates and provide valuable data for a better understanding of the determining factors. We thus undertook an evaluation of the overall prevalence of anemia in adult patients at the moment of IBD diagnosis, analyzing the influence of various patient and disease characteristics on the appearance of anemia.

2. Methods

2.1. Study design and data source

Between March 2015 and March 2016 we undertook a cross-sectional, multicenter study within the Ciudad Real province IBD working group, representing all adult IBD units in this region of Spain [17]. Patients over 13 years of age identified in the IBD unit databases of the participating hospitals with a diagnosis of IBD established according to standard clinical, endoscopic, histological, and radiological criteria [18,19] were retrospectively identified. Epidemiological and clinical data obtained at the time of diagnosis included patient age, sex, hospital of diagnosis, type and location of the disease according to the Montreal classification system, smoking habits at diagnosis, and the presence of extraintestinal manifestations at disease onset. The need for surgery during the disease course was also recorded. Patients with indeterminate colitis were excluded.

Only naïve patients with information available on hematological parameters recorded either at the moment of diagnosis or during the previous 3 months were included. Analytical parameters included hemoglobin; hematocrit; mean corpuscular volume (MCV); mean corpuscular hemoglobin (MCH); mean corpuscular hematocrit concentration (MCHC); serum ferritin, serum transferrin, iron levels; and transferrin saturation (TfS), whenever possible. Disease activity was measured in terms of C-reactive protein (CRP) serum concentration.

Anemia was considered as a binary outcome variable (yes/no) and defined according to sex- and age-specific hemoglobin and hematocrit cutoffs established by the WHO for Caucasian populations [20]. Thus, the minimum normal hemoglobin and hematocrit levels for non-pregnant adult women were 12 g/dL and 36%, respectively, while those for adult men were 13 g/dL and 39%, respectively. Anemia prevalence was calculated as the ratio of the number of anemic patients over the total number of patients included in the study.

The type of anemia at diagnosis was classified into one of the following 3 categories, defined according to the European Consensus on diagnosis of anemia in IBD [16] and expert definitions [21,22]: iron deficiency anemia, ACD, and anemia of mixed origin. Briefly, iron deficiency anemia was defined as a serum ferritin level <30 μg/L, TfS <20%, MCH <27 pg, or MCHC <31 g/dL. In cases of active inflammation (defined as CRP >2 mg/dL), serum ferritin levels <100 μg/L were considered an appropriate cut-off point [21,23]. Anemia of chronic disease was diagnosed as the presence of subnormal hemoglobin levels, increased concentration of CRP (≥2 mg/dL), and characteristic alterations of iron homeostasis with serum ferritin levels >100 μg/L and TfS levels <20% [24]. Anemia of mixed origin was defined as serum ferritin levels between 30 and 100 μg/L.

Severe anemia was arbitrarily defined as a hemoglobin value <10 g/dL [10,13,25]. Accordingly, adult patients with hemoglobin concentrations lower than their sex cutoff for the definition of anemia but above 10 g/dL were classified as mildly anemic.

2.2. Statistical analyses

Results for continuous variables are expressed as the mean and SD or as the median and interquartile range (IQR); qualitative variables are presented as absolute and relative frequencies. The χ²-test (Fisher’s exact test, where appropriate) or Student’s t-test were used to compare qualitative and quantitative variables, respectively. Odds ratios (OR) with 95%CIs were calculated for significant variables. A significance level of 0.05 was used throughout. Logistic regression was performed separately for CD and UC. Analyses and summaries were carried out with the PASW statistical program (version 18.0; SPSS Inc., Chicago, Illinois).

2.3. Ethical considerations

This study was conducted in accordance with the Declaration of Helsinki principles. The registries supporting this study were approved by the local ethics or research committees at the participating centers.

3. Results

3.1. Subject characteristics

1278 patients diagnosed with IBD between 1960 and 2016 had analytical information available; 718 (56.2%) patients presented with CD and 560 (43.8%) with UC. The median age at IBD diagnosis was 38.8 years (IQR 16.9; range 13–90); CD patients were younger [36 (16.4; 13–56)] than UC [42.5 (16.9; 13–90)] (p < 0.001). Age groups at the moment of diagnosis were as follows: A1 (<16), 6.4% of patients; A2 (between 17 and 40), 53.4% of patients; and A3 (disease onset >40), 40.2%. Table 1 shows patients characteristics at the moment of diagnosis.

Regarding CD, an ileal disease (L1) was present in 255 patients (37.2%); in 161 patients (23.5%), CD presented with a colonic involvement (L2). An ileocolonic disease was diagnosed in 265 patients (38.7%) while isolated upper digestive tract CD (L4) was present in only four patients (0.6%) (Table 1). In terms of disease behavior, 444 patients (64.8%) presented with an inflammatory (B1) pattern, 164 patients (23.9%) had a strictureing disease (B2), and the remaining 77 patients (11.2%) a penetrating disease (B3).

At diagnosis, proctitis (E1) was present in 21.6% of UC patients. A left-sided UC (E2) was found in 48.2% of patients and an extensive UC (E3) in 30.2% (Table 1).

Extraintestinal manifestations at IBD diagnosis were present in 170 patients (24.7%) with CD and 62 patients (12.1%) with UC (p < 0.001), with pelvic/perirectal abscesses, skin disorders, and osteoarticular manifestations appearing significantly more often in CD patients (Table S1). Extraintestinal manifestations were independent of anemia in both CD and UC patients (Table 2). Patients who presented with anemia tended to require surgery during the course of the disease more often than non-anemic patients (7.2% vs. 4.6%, respectively), in both CD (10.3% vs. 8.2%) and UC (1.6% vs. 0.8%) (not statistically significant). In contrast, extraintestinal manifestations at disease onset were associated with increased risk of undergoing surgery during the course of the disease: 16% of IBD patients with extraintestinal manifestations at diagnosis underwent surgery compared to 5% of those with no extraintestinal manifestations. This association was observed for CD (18.8% vs. 8.9%) and for UC (8.2% vs. 0.4%) (p < 0.001 for all comparisons). Pelvic/perirectal abscesses at diagnosis were the best predictor of
### Table 1
Demographics and clinical characteristics of IBD patients.

<table>
<thead>
<tr>
<th>n (%)</th>
<th>IBD overall</th>
<th>Crohn's disease</th>
<th>Ulcerative colitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>1278</td>
<td>718</td>
<td>560</td>
</tr>
<tr>
<td>Age [Mean (SD) (range)]</td>
<td>38.8 (16.9; 13–90)</td>
<td>36 (16.4; 13–56)</td>
<td>42.5 (16.9; 13–90)</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>685 (53.6)/593 (46.4)</td>
<td>370 (51.5)/348 (48.5)</td>
<td>315 (56.3)/245 (43.7)</td>
</tr>
<tr>
<td>Smoking habit</td>
<td>No</td>
<td>Yes</td>
<td>Former smoker</td>
</tr>
<tr>
<td></td>
<td>719 (68.2)</td>
<td>213 (20.2)</td>
<td>123 (11.7)</td>
</tr>
<tr>
<td></td>
<td>388 (62.3)</td>
<td>164 (26.3)</td>
<td>71 (11.4)</td>
</tr>
<tr>
<td>Age at diagnosis (A)</td>
<td>A1</td>
<td>A2</td>
<td>A3</td>
</tr>
<tr>
<td></td>
<td>81 (6.4)</td>
<td>671 (53.4)</td>
<td>505 (40.2)</td>
</tr>
<tr>
<td></td>
<td>59 (8.3)</td>
<td>413 (58.4)</td>
<td>235 (33.2)</td>
</tr>
<tr>
<td></td>
<td>22 (4)</td>
<td>258 (46.9)</td>
<td>270 (49.1)</td>
</tr>
<tr>
<td>Disease location (L)</td>
<td>L1</td>
<td>L2</td>
<td>L3</td>
</tr>
<tr>
<td></td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>255 (37.2)</td>
<td>161 (23.5)</td>
<td>265 (38.7)</td>
</tr>
<tr>
<td></td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>444 (64.8)</td>
<td>164 (23.9)</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>–</td>
<td>–</td>
<td>77 (11.2)</td>
</tr>
<tr>
<td>Disease behavior (B)</td>
<td>B1</td>
<td>B2</td>
<td>B3</td>
</tr>
<tr>
<td></td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>–</td>
<td>–</td>
<td>110 (21.6)</td>
</tr>
<tr>
<td>Disease extension (E)</td>
<td>E1</td>
<td>E2</td>
<td>E3</td>
</tr>
<tr>
<td></td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>–</td>
<td>–</td>
<td>154 (30.2)</td>
</tr>
</tbody>
</table>

**Notes:**
- p values are provided for comparisons between groups.
surgery, both in IBD overall (27.6% vs. 6.1%) and specifically in CD (29.6% vs. 9.8%) (p < 0.001). Elevated serum CRP values were also higher among patients with extraintestinal manifestations at IBD diagnosis (44.4 vs. 24.5%; p = 0.012).

Smoking (both current and former) was more frequent in patients with CD (37.7%) than in those with UC (23.4%) (p < 0.001) (Table 2). Smoking was associated with UC at the time of diagnosis in the subgroup of patients with severe anemia (p = 0.046).

3.2. Basic hematological profile and prevalence of anemia at IBD diagnosis

The mean ± SD hemoglobin concentration at IBD diagnosis was 13.4 ± 2.0 g/dL, being lower in CD (13.1 ± 2.0 g/dL) than in UC (13.7 ± 2.0 g/dL) (p < 0.001). Overall, 371 IBD patients (41.2%) presented with anemia at diagnosis; a higher prevalence was found in CD (47%) than in UC patients (33.8%) (p < 0.001).

After analyzing case series divided into five year periods, prevalence of anemia significantly increased in CD over time (p = 0.045) but remained unchanged in UC (Fig. 1). The age–sex stratified prevalence of anemia at the time of IBD diagnosis was estimated for the age strata 16 to >65 years. Overall, patients with CD aged between 26 and 65 had a lower risk for anemia than patients between 16 to 25 years, and those >65 (p < 0.01) (Fig. 2A). These differences were more marked for male patients (p = 0.039). In UC patients, we found no significant association between age and anemia (Fig. 2B).

Proportionally, more women than men presented with anemia at the moment of IBD diagnosis (65.5% vs. 34.5%). This was also observed independently for CD and UC (p < 0.001 for all comparisons) (Table 2). Severe anemia (Hb <10 g/dL) was present in 6% and 5% of patients with CD and UC, respectively (p = ns).

Iron deficiency anemia was the predominant type in IBD (69.6%). ACD represented the second cause, present in 20.1% of IBD patients, while anemia of mixed origin presented in 10.4% of patients at diagnosis. No differences in the distribution of types of anemia were noted between CD and UC (Table 3).

Hemoglobin, hematocrit, MCV, MCH, MCHC, and iron levels were all significantly lower in CD compared to UC; however, CRP concentrations were higher in CD (p < 0.001). No differences in serum ferritin, serum transferrin, or TfS levels were observed between the two diseases (Table 3).

3.3. Associations and determinants of anemia at IBD diagnosis

Bivariate analyses demonstrated a significantly higher proportion of anemia in IBD women compared to men, irrespective of disease type or age. Disease activity, defined as serum CRP concentrations ≥2 mg/dL, was higher in CD than in UC (p < 0.001) as well as in anemic compared to non-anemic patients, in IBD overall, CD and UC (p < 0.001 for all comparisons) (Table 4).

No differences in the prevalence of anemia were observed when small intestine location (L1 + L3) was compared to exclusive colonic location (L2) in CD. In contrast, anemia was more common in CD patients with a penetrating (B3) compared to a non-penetrating (B1 + B2) disease behavior (13% vs. 7%, respectively) (p = 0.028). Patients with a penetrating disease also exhibited higher serum CRP values than those with non-penetrating disease (5.59 ± 6.49
Prevalence of anemia and hematological profile at the time of diagnosis in patients with inflammatory bowel disease.

<table>
<thead>
<tr>
<th>Type of anemia</th>
<th>IBD overall</th>
<th>Crohn’s disease</th>
<th>Ulcerative colitis</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>371 (41.2)</td>
<td>236 (47)</td>
<td>230 (46)</td>
<td>p &gt; 0.001</td>
</tr>
<tr>
<td>Severe anemia (Hb &lt;10 g/dL)</td>
<td>50 (5.5)</td>
<td>30 (6)</td>
<td>20 (5)</td>
<td>0.549</td>
</tr>
<tr>
<td>Type of anemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iron deficiency anemia</td>
<td>215 (69.6)</td>
<td>144 (71.3)</td>
<td>71 (66.4)</td>
<td>p &gt; 0.487</td>
</tr>
<tr>
<td>Anemia of chronic disease</td>
<td>62 (20.1)</td>
<td>40 (19.8)</td>
<td>22 (20.6)</td>
<td></td>
</tr>
<tr>
<td>Anemia of mixed origin</td>
<td>32 (10.4)</td>
<td>18 (8.9)</td>
<td>14 (13.1)</td>
<td></td>
</tr>
<tr>
<td>Hemoglobin (g/dL) [mean (SD; range)]</td>
<td>13.4 (2.6; 6.1–19.6)</td>
<td>13.1 (2; 6.1–18)</td>
<td>13.7 (2; 6.1–19.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hematocrit [%] [mean (SD; range)]</td>
<td>40 (5.6; 18.5–58)</td>
<td>39.5 (5.7; 18.5–54)</td>
<td>40.8 (5.6; 20.5–58)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RBC × 10^6 [mean (SD; range)]</td>
<td>4.6 (0.6; 2.6–3.6)</td>
<td>4.6 (0.6; 2.6–3.6)</td>
<td>4.6 (0.6; 2.6–3.6)</td>
<td>0.358</td>
</tr>
<tr>
<td>MCV (fl) [mean (SD; range)]</td>
<td>86.5 (69; 48.6–110)</td>
<td>85.3 (72; 48.6–103)</td>
<td>88.6 (62; 52.3–110)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MCH (pg) [mean (SD; range)]</td>
<td>29.1 (3.8; 12.4–90.3)</td>
<td>28.6 (3.6; 12.4–75)</td>
<td>29.8 (4; 15.3–90.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MCHC (%Hb) [mean (SD; range)]</td>
<td>33.4 (1.5; 14.1–47.7)</td>
<td>33.3 (1.5; 14.1–37)</td>
<td>33.5 (1; 15.5–47.7)</td>
<td>0.024</td>
</tr>
<tr>
<td>Serum iron (μg/dL) [mean (SD; range)]</td>
<td>61 (37.6; 1–294)</td>
<td>56.1 (36.8; 1–294)</td>
<td>61.5 (38.3; 1–294)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum ferritin (μg/L) [mean (SD; range)]</td>
<td>119.7 (165.4; 1–1551)</td>
<td>119.3 (153.1; 1–1551)</td>
<td>120.3 (181; 1–1451)</td>
<td>0.935</td>
</tr>
<tr>
<td>Serum transferrin (mg/dL) [mean (SD; range)]</td>
<td>247.6 (63.8; 72–417)</td>
<td>243 (65.8; 72–399)</td>
<td>254.8 (60; 89.3–417)</td>
<td>0.097</td>
</tr>
<tr>
<td>Transferrin saturation [%] [mean (SD; range)]</td>
<td>19.8 (12.1; 0.4–61)</td>
<td>18.6 (11.6; 1.9–56.2)</td>
<td>21.9 (12.8; 0.4–61)</td>
<td>0.110</td>
</tr>
<tr>
<td>C-reactive protein (mg/dL) [mean (SD; range)]</td>
<td>3.2 (3.1; 0–32)</td>
<td>3.8 (5.5; 0–32)</td>
<td>2.4 (4.5; 0–32)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

vs. 3.67 ± 5.43; p = 0.033). The proportion of CD patients with serum CRP ≥2 mg/dL was also higher for penetrating than for non-penetrating disease behavior (59.5% vs. 40.6%; p = 0.019).

For UC, the prevalence of anemia significantly increased with disease extension at diagnosis, being higher for left-sided and extensive disease than for proctitis (p = 0.002).

A logistic regression was performed separately for CD and UC to determine the exact contribution of various factors in anemia. For CD, anemia was significantly associated with female sex (OR 7.11; 95%CI 4.18–12.10; p < 0.001); current smoking (OR 2.23; 95%CI 1.24–4.02; p = 0.007); elevated serum CRP (OR 4.08; 95%CI 2.39–6.97; p < 0.001); current smoking (OR 2.23; 95%CI 1.24–4.02; p = 0.007); and penetrating disease behavior (OR 3.34; 95%CI 1.36–8.21; p = 0.009). For UC patients, anemia at disease diagnosis was associated with female sex (OR 6.55; 95%CI 3.39–12.63; p < 0.001), elevated CRP serum levels (OR 4.58; 95%CI 2.26–9.27; p < 0.001), and disease extension (E2/E3 compared to E1) (OR 1.80; 95%CI 1.13–2.86; p = 0.013). Current smoking was clearly identified as a protective factor (OR 0.36; 95%CI 0.14–0.92; p = 0.032); former smoking seemed to have a significantly lower risk for anemia than younger or older patients, while for women, the prevalence was virtually equal at every stage of life. This coincidence in the higher risk of anemia in younger and older male patients both at the time of CD diagnosis and over time requires further research on additional age- and sex-related factors that come into play from IBD diagnosis throughout the course of the disease. Anemia was significantly higher in CD than in UC, which is in strong agreement with most of the previous research [10,14,28,29,38].

Iron deficiency anemia represents the most common type of anemia in IBD at diagnosis, with no significant differences between CD and UC. These results contrast with those from prior research conducted in western Hungary [29] and focused on extraintestinal manifestations, which described a higher proportion of iron deficiency anemia in CD. However, it provided no information regarding the diagnostic criteria of anemia. Iron deficiency anemia as a consequence of intestinal bleeding, dietary restrictions, or malabsorption is recognized as the most prevalent one in IBD at all stages [9,15]. An additional feature of our study was the assessment of the severity of anemia at IBD diagnosis: only 5.5% of patients had severe anemia (representing 13.5% of all anemic patients), without differences between CD and UC.

In the absence of full-blown anemia, iron deficiency itself lowers the perceived HRQoL in IBD patients [30]. We showed that serum iron levels were significantly lower in CD patients. Other biochemical parameters related to iron deposits, such as serum transferrin and TIS, were also lower in CD compared to UC. However, no differences were observed in serum ferritin levels between the two diseases, limiting the diagnostic value of this acute phase reactant. Multivariate analyses demonstrated that female sex and disease activity were the determinant factors significantly associated with anemia at IBD diagnosis for both CD and UC patients. Previous studies assessing the prevalence and associated factors of anemia throughout the course of IBD have also found that female...
sex [14,31,32] and disease activity [28,32] were independent risk factors. CRP levels have been proposed as a predictor of oral iron supplementation unresponsiveness [30]. This marker may thus be useful in identifying IBD patients who can benefit from first-line treatment with i.v. administration of iron [34].

The finding that tobacco consumption is an independent risk factor for anemia in CD, but a protective one in UC at disease onset is novel. Although smokers develop compensatory polycythemia as a result of the carbon monoxide in cigarette smoke [35], multivariate analysis clearly identified tobacco as a risk factor for anemia at CD diagnosis. Indeed, current smoking was associated with a two-fold prevalence of this complication among CD patients. On the contrary, tobacco protected UC patients from developing anemia. Strong evidence links smoking with IBD onset risk, clinical course [36], and disease outcomes [37], with opposite effects in CD and UC [38]. To our knowledge, the association of current smoking with increased risk of anemia in CD and reduced risk in UC has not been described before, adding to the body of evidence for the differing effects of tobacco in CD and UC. However, we failed in identifying potential effects of smoking cessation on anemia presentation at IBD diagnosis.

We also examined whether IBD location or extension could impact on the prevalence of anemia. Risk of anemia was not increased in CD small intestine location (L1 + L3) compared to colonic (L2). For UC, the prevalence of anemia significantly increased with the extension of the disease, suggesting that anemia in IBD appears to be more a consequence of intestinal bleeding rather than iron malabsorption.

A penetrating disease (B3) was a significant risk factor for anemia in CD compared to inflammatory (B1) and stricturing (B2) behavior. Higher CRP levels observed in B3 compared to B1 + B2 (5.59 vs. 3.67; p = 0.033) along with the higher proportion of patients with elevated CRP levels among the B3 group (59.5% vs. 40.6%; p = 0.019) suggest disease activity as an explanation.

In order to reduce selection bias, our study exhaustively included all IBD patients attending gastroenterology/IBD units of participating public regional hospitals who had available laboratory records. This broad coverage along with the absence of private healthcare resources potentially ensured the inclusion of the majority of IBD diagnosed patients in the region. Still, the external validity of our results should be studied further as we cannot assume our region is representative of the entire IBD population.

The retrospective nature of the analytical data collection represents a limitation. However, recovering archived well identified analytical data reduced subjectivity. We assessed widespread used analytical values, thereby reducing the risk of bias in the results obtained. Disease activity was measured exclusively by CRP, since clinical activity indexes were not available or could not be accurately calculated for every patient. Finally, our study provides no data on pediatric onset IBD, but the prevalence of anemia at diagnosis in these patients has recently been published [13] and mostly agrees with our adolescent and adult data.

Anemia represents a frequent complication of IBD from the very moment of diagnosis, affecting up to half of patients with CD and one third of UC of all ages. Its main cause is iron deficiency. Female sex and disease activity are significant risk factors, while smoking exerts opposite effects in CD and UC. Penetrating disease behavior and disease extension are additional risk factors in CD and UC, respectively. Finally, advances in IBD diagnosis and management over the past few decades had no significant impact on the prevalence of anemia at IBD onset.

Conflicts of interest

None declared.

Authorship

Guarantor of the article: Alfredo J Lucendo.

Disclaimers

None.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.dld.2016.12.005.

References