Prevalence of Iron Deficiency and Iron Deficiency Anemia in Pediatric Patients with Inflammatory Bowel Disease: A Systematic Review

AALBORG UNIVERSITET

Author: Rami Dika
Student number: 20204040
Project number: 82e25au5
5th Semester candidate, Medicine, Aalborg University
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Main supervisor: Tine Jess
Project supervisors: Serife Ayten & Maiara Brusco De Freitas

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Abstract:

Background & aims: Iron deficiency anemia (IDA) and iron deficiency (ID) are among the most common extraintestinal manifestations of inflammatory bowel disease (IBD) in children and adolescents. However, reported prevalence estimates vary widely, and the relationship between anemia, disease activity, and patient-centered outcomes is still not fully defined. We aimed to systematically review the literature and provide a comprehensive overview of the prevalence of IDA and ID and its association with disease activity, quality of life, and growth and development.

Methods: Literature was searched systematically on the 15th of October 2025 in PubMed, Embase, Scopus, Cochrane Library, and Web of Science to identify studies reporting prevalence data or association outcomes. Screening was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Two authors independently performed study selection and data extraction and assessed the risk of bias using the Newcastle-Ottawa scale.

Results: Fourty-two of the 1,067 identified records met the inclusion criteria. Anemia prevalences ranged from 20-80% depending on diagnostic thresholds, population variations, and sample sizes. ID was especially prevalent in anemic patients, often exceeding 70%, and IDA accounted for a substantial proportion of cases. IDA and ID were generally more prominent in patients with Crohn's disease (CD) than Ulcerative colitis (UC) and were consistently associated with increased disease activity, while remission was associated with lower prevalence. Limited evidence also suggested a negative impact on quality of life and growth impairment in pediatric patients.

Conclusion: IDA and ID are highly prevalent among pediatric patients, and studies report significant associations with inflammation and disease activity. Evidence also suggests a negative impact on quality of life and growth and development; however, this remains insufficiently studied. Standardized diagnostic criteria and prospective studies assessing clinical outcomes are needed to clarify the long-term consequences of anemia.

Keywords: Pediatric inflammatory bowel disease, Iron deficiency anemia, Prevalence, Disease activity

Indholdsfortegnelse

Introduction

Inflammatory bowel disease (IBD) is a chronic inflammatory disease encompassing Crohn's disease (CD), ulcerative colitis (UC), and indeterminate colitis [1]. These diseases are characterized by periods of active inflammation interspersed with remission that can lead to nutritional deficiencies [2,3].

Recent epidemiological data suggest a rising trend in the prevalence of these diseases, predominantly in developing countries. Studies indicate global prevalence rates of 230, 84 and 120 per 100.000 for IBD, CD and UC respectively, and an incidence of 9.7 per 100,000 person-years, ultimately contributing to a persistently high burden of the disease [4] .

While IBD can develop at any age, up to 25% of patients with IBD are diagnosed in childhood or adolescence, with the incidence steadily increasing over the past decades [5,6]. The primary clinical features of IBD include, weight loss, fatigue, nutritional deficiencies, the presence of mucopurulent blood in stools and diarrhea, and abdominal pain [7]. This is especially prevalent in children, where IBD often presents with a more extensive and aggressive nature compared to adults [8].

Since children are still undergoing crucial stages of physical and mental development, the nutritional deficiencies that follow IBD can lead to complications such as growth failure, delayed puberty, reduced bone mass, impaired school functioning, and reduced quality of life [9]. These extraintestinal manifestations and systemic effects are therefore especially important in pediatric patients.

Up to 20–40% of pediatric patients experience extraintestinal manifestations at some stage of their disease. These include dermatologic conditions, liver diseases, musculoskeletal involvement, ocular inflammation, and blood abnormalities [10]. The most prevalent manifestation is anemia. In children with IBD, anemia can take a toll on energy levels, cognitive function, stamina, and overall quality of life [11]. Anemia can arise from multiple overlapping mechanisms, most commonly iron deficiency (ID), iron deficiency anemia (IDA), and anemia of chronic disease (ACD). IDA results from depleted iron stores, while ACD is caused by impairment of iron mobilization, often hepcidin-mediated [12]. This is likely due to a combination of factors, including chronic inflammation, inadequate dietary intake, iron malabsorption, gastrointestinal blood loss, and reduced iron utilization [13].

Prevalence estimates of ID and anemia in pediatric IBD vary widely across studies, ranging from 20% to over 70% [14]. This variation is likely due to differences in study populations, disease activity, diagnostic criteria, and laboratory thresholds. Many children are already anemic at the time of diagnosis, reflecting a long period of untreated inflammation and blood loss prior to the diagnosis [15].

Several studies suggest that ID may be associated with increased disease activity, though the exact nature of this remains unclear [16]. Chronic inflammation leads to ID, but insufficient iron may also worsen immune function, potentially affecting disease progression. Effective correction of ID has been associated with improved patient-reported outcomes [17].

A significant challenge in diagnosing ID in IBD is the effect of inflammation on laboratory values. Ferritin, an acute-phase protein, can increase during inflammation, thereby masking a potential underlying iron deficiency [18]. Transferrin saturation decreases in both ID and inflammation, making interpretation more complex [18]. As a result, a combination of markers is usually required, including ferritin, transferrin saturation, hemoglobin, C-reactive protein (CRP) and when available, soluble transferrin receptor [19].

Unlike adult IBD guidelines, there is no universal agreement on diagnostic thresholds for ID in children, especially in the presence of active inflammation. Pediatric reference values vary by age and sex, and studies differ widely in the definitions they apply [20]. This lack of consistency may lead to the large variation in reported prevalence rates.

The existing literature on ID and anemia in pediatric IBD is substantial but fragmented. Studies vary in diagnostic criteria, population characteristics, timing of measurements, and outcomes assessed. Additionally, there's a limited understanding of how ID and IDA relate to disease activity and remission, as well as consequences for growth, development, and quality of life.

A systematic review is therefore warranted to help summarize the available evidence, identify patterns and limitations, and highlight areas where further research is needed. The aim of this systematic review was to assess the prevalence of ID and IDA in children and adolescents with IBD, and how these conditions are associated with disease course, remission, growth, development, and quality of life.

Method

Study Design

This study is a systematic review of published literature on iron deficiency and anemia in pediatric patients with IBD. The review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and was registered with PROSPERO (https://www.crd.york.ac.uk/prospero/) with the registration number CRD420251154524. The aim of the review was to investigate the prevalence and incidence of ID, IDA, and ACD, as well as their

associations with disease course, remission, disease activity, quality of life, growth, and development in pediatric IBD patient.

Search strategy

Literature was searched systematically to identify studies that investigated the prevalence of ID, IDA, and ACD in pediatric patients with IBD, as well as their association with disease progression and remission. The search was performed on the 15th of October 2025 across the following databases: PubMed, Embase, Scopus, Cochrane Library, and Web of Science. Titles, abstracts, and keywords were searched using the search strings listed in Figure 1.

Database	Search string
PubMed	("Inflammatory Bowel Diseases"[Mesh] OR "Crohn Disease"[Mesh] OR "Colitis, Ulcerative"[Mesh] OR "inflammatory bowel disease*" OR Crohn* OR "ulcerative colitis" OR IBD) AND ("Anemia"[Mesh] OR "Iron Deficiency Anemia"[Mesh] OR "Anemia, Chronic Disease"[Mesh] OR "iron deficiency" OR "iron deficiency anemia" OR "iron-deficiency anaemia" OR "anemia of inflammation" OR "anemia of chronic disease" OR "iron status" OR anemia OR anaemia) AND ("Child"[Mesh] OR "Adolescent"[Mesh] OR "Infant"[Mesh] OR "Pediatrics"[Mesh] OR child* OR adolescent* OR pediatric* OR paediatric* OR teen* OR youth OR "young patient*" OR juvenile)
Embase	(('inflammatory bowel disease'/exp OR 'crohn disease'/exp OR 'ulcerative colitis'/exp OR crohn*:ti,ab OR "ulcerative colitis":ti,ab OR "inflammatory bowel disease":ti,ab OR ibd:ti,ab) AND ('iron deficiency anemia'/exp OR 'iron deficiency'/exp OR 'anemia of chronic disease'/exp OR "iron deficiency":ti,ab OR "iron deficiency anemia":ti,ab OR "iron-deficiency anaemia":ti,ab OR "anemia of inflammation":ti,ab OR "anemia of chronic disease":ti,ab OR anemia:ti,ab OR anaemia:ti,ab OR "iron status":ti,ab) AND ('child'/exp OR 'adolescent'/exp OR 'pediatric patient'/exp OR pediatric*:ti,ab OR paediatric*:ti,ab OR child*:ti,ab OR adolescent*:ti,ab OR teen*:ti,ab OR youth:ti,ab OR juvenile*:ti,ab)) AND (("inflammatory bowel disease" NEAR/5 anemia):ti,ab OR (crohn* NEAR/5 anemia):ti,ab OR ("ulcerative colitis" NEAR/5 anemia):ti,ab OR ("inflammatory bowel disease" NEAR/5 "iron deficiency":ti,ab))
Scopus	TITLE-ABS-KEY(("inflammatory bowel disease*" OR Crohn* OR "ulcerative colitis" OR IBD)) AND TITLE-ABS-KEY(("iron deficiency" OR "iron deficiency anemia" OR "iron-deficiency anaemia" OR "anemia of inflammation" OR "anemia of chronic disease" OR anemia OR anaemia OR "iron status")) AND

	TITLE-ABS-KEY((child* OR adolescent* OR pediatric* OR paediatric* OR teen* OR youth OR "young patient*" OR juvenile))
Web of Science	(inflammatory bowel disease OR Crohn* OR "ulcerative colitis" OR IBD) AND ("iron deficiency" OR "iron deficiency anemia" OR "iron-deficiency anaemia" OR "anemia of inflammation" OR "anemia of chronic disease" OR anemia OR anaemia OR "iron status") AND (child* OR adolescent* OR pediatric* OR paediatric* OR teen* OR youth OR "young patient" OR "young patients" OR juvenile*)
Cochrane Library	#1 [mh "Inflammatory Bowel Diseases"] OR [mh "Crohn Disease"] OR [mh "Colitis, Ulcerative"] OR "inflammatory bowel disease*" OR Crohn* OR "ulcerative colitis" OR IBD #2 [mh "Anemia"] OR [mh "Iron-Deficiency Anemia"] OR [mh "Anemia, Chronic Disease"] OR "iron deficiency" OR "iron deficiency anemia" OR "iron-deficiency anaemia" OR "anemia of inflammation" OR "anemia of chronic disease" OR anemia OR anaemia OR "iron status" #3 [mh Child] OR [mh Adolescent] OR [mh Infant] OR [mh Pediatrics] OR child* OR adolescent* OR pediatric* OR paediatric* OR teen* OR youth OR "young patient*" OR juvenile #4 #1 AND #2 AND #3

Figure 1. Search strings used for PubMed, Embase, Scopus, Cochrane Library, and Web of Science.

Inclusion criteria and data extraction

Specific inclusion and exclusion criteria were established to conduct this systematic review. Studies were eligible for inclusion if they met the following criteria:

1) **Study design:** Observational studies or interventional studies reporting prevalence data or association outcomes.
2) **Population:** Pediatric patients aged 0–18 years with a confirmed diagnosis of IBD (CD or UC);
3) **Assessment:** Studies that evaluated ID, IDA, or ACD based on biochemical markers or defined clinical criteria.
4) **Outcomes:** Studies that investigated the link between ID, IDA, or ACD and IBD in pediatric patients, including:
    a) the prevalence or incidence of ID, IDA, or ACD; and/or
    b) associations with disease course, remission, disease activity, quality of life, growth, or development.

Studies were excluded if they had an unclear IBD diagnosis, no distinction of prevalence estimates between pediatric and adults, preclinical studies, lack of relevant biomarkers, and non-English studies.

All search results were imported into Rayyan for screening [21]. After removal of duplicates, titles and abstracts were screened independently by two reviewers (RD and RNYY). Conflicts were resolved by a third reviewer (SA), who blindly reviewed the conflicting articles, through discussion

and consensus. Articles passing title and abstract screening were retrieved for full-text review. Full texts were screened independently by two reviewers to determine final eligibility. Reasons for exclusion were recorded for all full-text articles not included in the review. A PRISMA flow diagram was used to document the study selection process (Figure 1).

A narrative synthesis was conducted to summarize the prevalence and incidence of iron deficiency and anemia across studies, as well as reported associations with disease course, remission, disease activity, quality of life, and growth. Tables were used to organize study characteristics and findings.

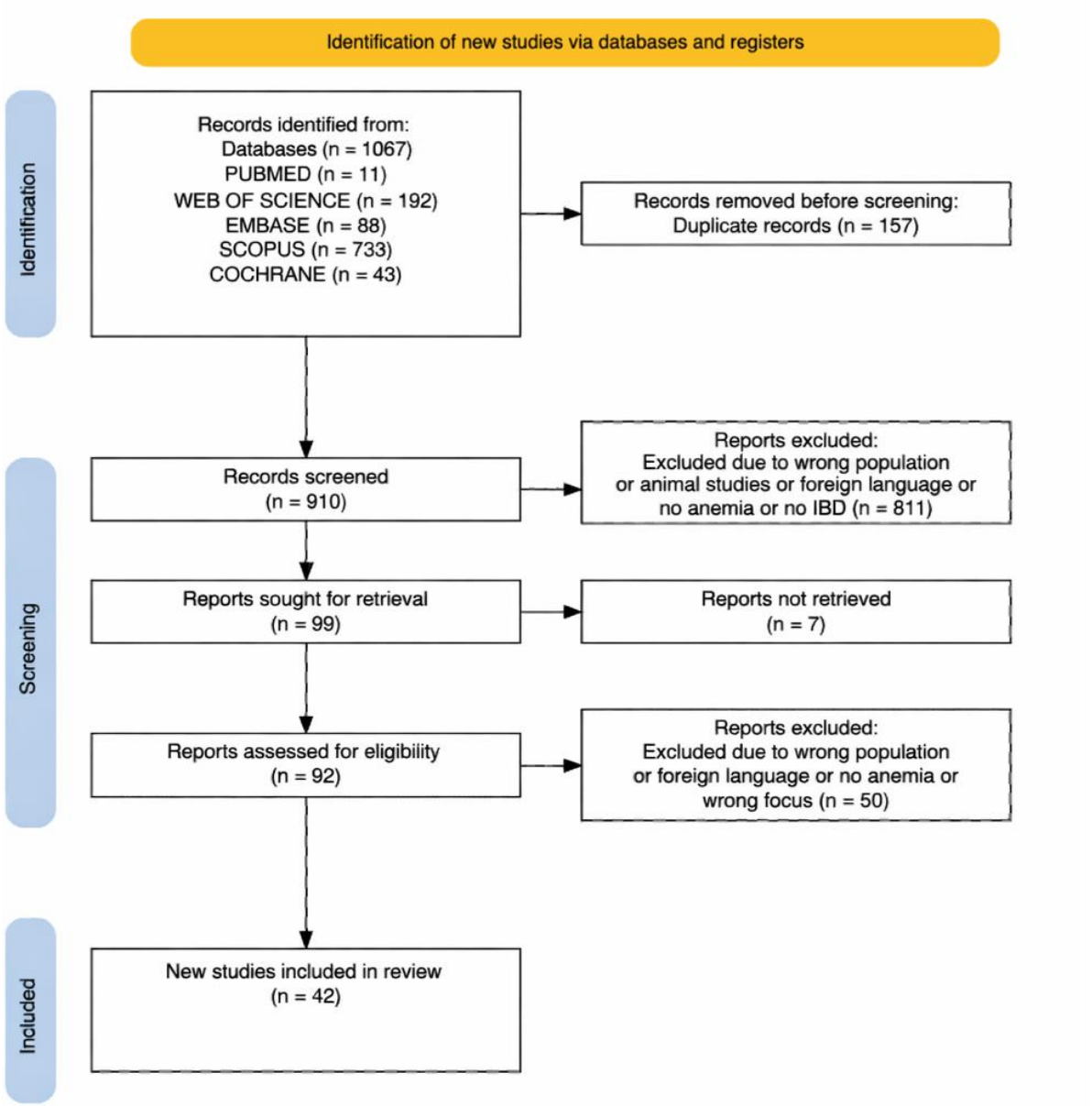

Figure 2. Flow diagram of the study selection process

Risk of Bias Assessment

The quality and risk of bias of included studies were assessed using the Newcastle–Ottawa Scale (NOS) [22]. Each study was evaluated for selection of participants, comparability of study groups, and ascertainment of outcomes. Assessment was performed independently by two reviewers (SA and RD), with disagreements resolved through discussion. The scale addresses the risk of bias in three domains: selection, comparability, and outcome (cohort and cross-sectional studies) or exposure (case control studies). Summarizing these domains, a score from 0 to 9 was presented for each study, with scores of ≥7: low risk, 6-4: moderate risk, and ≤3: high risk.

Results

Study selection process

A systematic database search yielded 1,067 results, of which 157 were duplicates and 910 articles entered the screening process. After screening of titles and abstracts, 811 records were excluded. The reasons for exclusion were incorrect population, animal studies, foreign language, no anemia or no IBD. Another 50 records were excluded after full-text screening due to no pediatric distinction in results, incorrect population, language or exposure. An additional 7 records were excluded due to missing full-text versions.

Characteristics of the Study

The studies, detailed in Table 1, spanned 20 countries and comprised 23 cohort studies [1,23–44] , 11 cross-sectional [45–55], 2 case-control[56,57], 3 case series [58–60], 2 QI-intervention [61,62], and a diagnostic accuracy study [63]. The studies were subject to the risk of bias in varying degrees (Table 2). Twenty-five studies had low risk [1,23,26,28,29,31,33,34,37,38,41,43–55,61], 15 had moderate risk [24,25,27,30,32,36,39,42,56–60,62,63] and 2 had high risk [35,40].

The sample sizes ranged from 16 participants to large nationwide registries of more than 5,000 children. Diagnostic criteria of anemia and ID also varied, with approximately half using WHO criteria, while others applied specific laboratory cut-offs and hemoglobin thresholds.

Table 1: Anemia Prevalence in Pediatric Patients with Inflammatory Bowel Disease.

Author, year	Country	Study design	Participants	Definition of anemia	Disease Type	Prevalence
Miller et al., 2019 [23]	United States	Retrospective cohort study	2,446 pediatric IBD-patients (1-21 years)	WHO criteria	CD: 1,560 (63.8%) UC: 886 (36.2%)	Anemia: CD 51% (676/1328) UC 43% (308/718) ID among anemic: CD: 84% (119/142) UC: 86% (50/58)
Isa et al., 2023 [45]	Bahrain	Retrospective cross-sectional study	117 pediatric IBD-patients (<18 years)	Hgb <11 g/dL (6mo-5yrs) <11.5 g/dL (5-11yrs) <12 g/dL (12-13yrs) <13 g/dL men, <12 g/dL non-pregnant women	CD: 66 (56.4%) UC: 51 (43.6%)	Anemia: 68.1% (79/116) ID: 83.1% (64/77) IDA: 89.8% (53/59)
Chu et al., 2013 [24]	Singapore	Retrospective cohort study	32 pediatric IBD patients (5-17 years)	Not specified	CD: 30 (94%), UC: 2 (6%)	Anemia: 78.1% (25/32)
Smith et al., 2022 [61]	United States	QI intervention study	298 pediatric IBD-patients (1-21 years)	ECCO guidelines ID: Ferritin < 30 µg/L	CD: 200 (67%) UC: 86 (29%) IC: 12 (4%)	ID or IDA: 88% (205/232) IDA: 65% (151/232) ID : 23% (54/232)
Aljomah et al. 2018 [25]	United States	Retrospective cohort study	153 pediatric IBD- patients (<18 years)	WHO criteria	CD: 92 (60.1%) UC: 49 (32%) IC: 12 (7.8%)	Anemia: 67.3% → of these: 28.9% had IDA or IDA+ACD; 38.5% had ACD alone. IDA or (IDA + ACD): CD: 39.39% (13/33) UC: 13.33% (2/15) ACD: CD: 42.42% (14/33) UC: 26.67% (4/15)

Table 1: *Cont.*

Akkermans et al., 2017 [46]	Netherlands	Observational/cross-sectional study	59 pediatric IBD-patients (1-18 years)	Absolute ID: WHO criteria IDA = absolute ID + anemia; functional ID defined as ZPP > 70 µmol/mol Hb and/or RDW > 14%; ACD = functional ID + anemia.	CD: 42 (71.2%) UC: 14 (23.7%) IBD-U: 3 (5.1%)	Absolute ID: 32.2% (19/59) CD: 31.0% (13/42) UC: 42.9% (6/14) IDA: 27.1% (16/59) CD: 26.2% (11/42) UC: 35.7% (5/14) Functional ID: 80% (32/40) CD: 50.0% (21/42) UC: 57.1% (8/14) IBD-U: 100% (3/3) ACD: 20% (8/40) CD: 19% (8/42) UC: 0% (0/14)
Syed et al., 2017 [47]	United States	Cross-sectional/observational study	62 pediatric IBD-patients (5-18 years)	Hb < 11.5g/dL (5–11.99 yrs) Hb < 12.0 g/dL (12–14.99 yrs) Hb < 12.0 g/dL (≥15.0 yrs female) Hb < 13.0 g/dL (≥15.0 yrs male)	CD: 43 (69%) UC: 19 (31%)	Anemia: 32% (20/62) ID adjusted for inflammation: 68%(42/62) IDA: 27% (17/62)
Sjöberg et al., 2014 [26]	Sweden	Population-based cohort study	72 pediatric IBD patients (<17 years)	WHO criteria	CD: 254 (33.9%) UC: 495 (66.1%)	Anemia: IBD: 54.9% (45/82) CD: 63.6% (28/44) UC: 44.7% (17/38)
Wiskin. et al., 2012 [27]	United Kingdom	Retrospective cohort study	80 pediatric IBD-patients (4-16 years)	WHO criteria. ID: transferrin saturation < 16% serum ferritin < 30 µg/l (for CRP >10 mg/l)	CD: 46 (57.5%) UC: 34 (42.5%)	Anemia: 75% (60/80) ID: CD: 90% UC: 95%
D'Arcangelo et al., 2025 [28]	Italy	Register-based cohort study	1,634 pediatric IBD-patients (<18 years)	WHO criteria	CD: 748 (45.8%)	Anemia: IBD: 36% (589/1634) CD: 39% (295/748)

Table 1: *Cont.*

					UC: 886 (54.2%)	UC: 33% (294/886) IDA 87.7% (471/537) ACD 12.3% (66/537)
Tanpowpong et al., 2024 [29]	Thailand	Retrospective cohort study	72 pediatric IBD-patients (<19 years)	Hemoglobin < 11 g/dL if aged < 5 years, < 11.5 g/dL if aged 5–11 years < 12 g/dL in adolescent females < 13 g/dL in adolescent males	CD: 35 (48.6%) UC: 36 (50%) IBD-U 1 (1.4%)	Anemia: IBD: 74.7% CD: 74.3% UC: 75%
Olczyk et al., 2024 [30]	Poland	Retrospective cohort study	80 pediatric IBD-patients (4-18 years)	Not specified	CD: 27 (33.75%) UC: 53 (66.25%)	Anemia: IBD: 62.5% (50/80) CD: 77.8% (21/27) UC: 54.7% (29/53)
Pawłowska et al., 2023 [48]	Poland	Cross-sectional observational study	70 pediatric IBD-patients (5-18 years)	WHO criteria	CD: 41 (58.6%) UC: 29 (41.4%)	Anemia: CD: 62.5% (25/40) UC: 65.5% (19/29)
Klamt et al., 2023 [31]	Germany	Retrospective registry cohort study	1,172 pediatric CD-patients (<18 years)	Not specified	CD	Anemia: 24.1% (283/1172)
Breton et al., 2021 [62]	United States	QI intervention study	1,343 pediatric IBD-patients (11.5-19.9 years)	WHO criteria	CD: 911 (67.8%) UC: 242 (18%) IBD-U: 190 (14.2%)	Anemia: 35.8% (345/963)
Shentova-Eneva et al., 2021 [32]	Bulgaria	Retrospective cohort study	80 pediatric IBD-patients (2-17 years)	WHO criteria	CD: 35 (43.75%) UC: 45 (56.25%)	Anemia: IBD:67.5% (54/80) CD: 77.1% (27/35) UC: 60.0% (27/45) ID in anemic patients:

Table 1: *Cont.*

						CD 77.8% (21/27) UC 74.1% (20/27)
Rempel et al., 2021 [1]	Canada	Longitudinal cohort study	165 pediatric IBD-patients (<18 years)	WHO criteria	CD: 87 (52.7%) UC 78 (47.3%)	Anemia: IBD: 57% (94/165) - at diagnosis CD: 62% (54/87) UC: 51% (40/78) ID: CD: 56% UC: 42%
Krawiec et al., 2020 [49]	Poland	Observational cross-sectional study	75 pediatric IBD-patients (3.5-18 years)	WHO criteria	CD: 29 (38.7%) UC: 46 (61.3%)	ID: 66.7% (50/75) CD: 58.6% (17/29) UC: 71.7% (33/46) Among these: Anemia: 44% (33/75)
Marcil. et al., 2019 [50]	Canada	Cross-sectional comparative study	203 pediatric IBD-patients (<16 years)	Not specified	CD: 179 (88%) UC: 4 (2%) IBD-U: 20 (10%)	Anemia: 59.1% (120/203) CD: 60.9% (109/179) UC: 75% (3/4) IBDU: 40% (8/20)
Krawiec et al., 2019 [51]	Poland	Cross-sectional observational study	75 pediatric IBD-patients (8-16 years)	Anemia : WHO criteria IDA: ferritin <30 ng/ml and satTf <20% ACD: ferritin >100 ng/ml and satTf < 20% ACD with ID: Serum ferritin 30-100 ng/ml with satTf < 20%	CD: 29 (38.7%) UC: 46 (61.3%)	Anemia: 51% 38/75 IDA: 36% (27/75) ACD with ID: 8% (6/75) ACD: 7% (5/75)
Carvalho et al., 2017 [33]	Portugal	Retrospective cohort study	69 pediatric IBD-patients (1-17 years)	WHO criteria	CD: 49 (71%) UC: 20	Anemia: IBD: 52% (36/69) CD: 46.9% (23/49) UC: 65% (13/20)

Table 1: *Cont.*

					(29%)	ID: IBD: 76.8% (53/69) CD: 69.4% (34/49) UC: 95% (19/20) IDA: IBD: 43.5% (30/69) CD: 34.7% (17/49) UC: 65% (13/20)
Syed et al., 2017 [52]	United States	Cross-sectional observational study	69 pediatric IBD-patients (5-18 years)	Anemia: WHO criteriaID: inflammation-corrected ferritin < 15 µg/L or soluble transferrin receptor (sTfR) > 8.3 mg/L	CD: 49 (71%) UC: 20 (29%)	Anemia: 36% (25/69) ID: 67% (46/69) IDA: 28% (19/69)
de Laffolie et al., 2017 [34]	Germany & Austria	Registry-based pediatric IBD cohort	2756 pediatric IBD-patients (0-18 years)	Hemoglobin below the 3rd percentile for age and gender based on recent population-based pediatric reference values from the KiGGS Study in Germany	CD: 1753 (63.6%) UC: 882 (32%) IBD-U: 121 (4.4%)	Anemia: IBD:63.2%(1743/2756) CD: 65.2% (1142/1753) UC: 60.2% (531/882) IBD-U: 61.8% (75/121)
Martinelli et al., 2016 [53]	Italy	Comparative, cross-sectional, single-centre study (2-18 years)	50 pediatric IBD-patients (4-18) 45 Coeliac patient (2–14) 50 HC(3.2–18)	WHO criteria	CD: 22 (44%) UC: 28 (56%)	Anemia: 34% (17/50) IDA: 17.6% (3/17) ACD: 11.7% (2/17) IDA + ACD: 70.5% (12/17) Coeliac patient :11.1% (5/45) HC: 0% (0/50)
Saadah et al., 2015 [35]	Saudi Arabia	Retrospective cohort study (0.2-18 years)	330 pediatric IBD-patients	Not specified	CD	Anemia: 57.9% (191/330)
Al-Saleem et al., 2015 [36]	Saudi Arabia	Retrospective cohort study	188 pediatric UC-patients (<18 years)	Not specified	UC	Anemia: 75% (141/188)

Table 1: *Cont.*

Gerasimidis et al., 2013 [37]	United Kingdom	Observational cohort study	184 pediatric IBD patients (1.2-17.3 years)	Gender- and age-specific hemoglobin cutoffs were used	CD: 122 (66%) UC: 51 (28%) IBD-U: 11 (6%)	Anemia: at diagnosis IBD: 72% (132/184) CD: 77% UC: 79%
Wang et al., 2013 [38]	China	Retrospective cohort study	153 pediatric IBD-patients (0-18 years)	Not specified	CD: 82 (53.6%) UC: 71 (46.4%)	Anemia: IBD: 52.3% (80/153) CD: 59.8% (49/82) UC: 43.7% (31/71)
Saadah, 2012 [39]	Saudi Arabia	Retrospective cohort study	96 pediatric CD patients (0.12-17.6 years)	Not specified	CD	Anemia: 84.4% (81/96)
Goodhand et al., 2012 [54]	United Kingdom	Observational cross-sectional study	113 pediatric IBD patients 59 children (3-17 years) 54 adolescents (16-26 years)	WHO criteria	Children: CD: 37 (63%) UC: 19 (32%) IBDU: 3 (5%) Adolescents: CD: 36 (67%) UC: 12 (22%) IBDU 6 (11%)	<u>Anemia:</u> Children 70% (41/59) Adolescents 42% (24/54) <u>ID among anemic:</u> Children 88% (36/41) Adolescents 83% (20/24)
Ahmaida A., Al-Shaikhi S., 2009 [60]	Libya	Retrospective case-series	16 pediatric IBD patients (<15 years)	Not specified	CD: 9 (56%) UC:6 (38%) IC: 1 (6%)	Anemia: 43.75% (7/16)
Jose et al., 2009 [40]	United States	Retrospective cohort study	387 pediatric IBD patients who developed EIMs (0-17 years)	Not specified	CD:1007 (61%) UC: 471 (29%)	Anemia: 13.4% (52/387)

Table 1: *Cont.*

					BD-U: 171 (10%)	
Castro et al., 2008 [41]	Italy	Registry-based cohort study	1576 pediatric IBD-patients (<18 years)	Not specified	CD: 635 (40%) UC: 810 (51%) IC: 131 (9%)	Anemia: CD: 23.8% (151/635) UC: 17.6% (142/810) IBD-U: 13.6% (18/131)
Goel & Shanks R, 1973 [42]	United Kingdom	Retrospective cohort study	25 pediatric UC-patients (2.7-13 years)	Hb <9 0 g/100 ml	UC	IDA: 36% (9/25)
Maćków et al., 2024 [57]	Poland	Prospective case-control study	118 pediatric IBD-patients (4-18 years)	Not specified	IBD-U	Anemia: 25.4% (30/118)
Altaş & Ertem D , 2024 [43]	Turkiye	Retrospective cohort study	78 pediatric IBD-patients (5-18 years)	WHO criteria	CD: 36 (46%) UC: 42 (54%)	Anemia: CD: 76.5% (26/34) UC: 76.7% (23/30)
Alrashidi et al., 2023 [59]	Saudi Arabia	Retrospective case series	56 pediatric IBD patients (0-14 years)	Hemoglobin <12 g/dL	CD: 11 (20%) UC: 45 (80%)	Anemia: 66% (37/56)
Güven et al., 2022 [63]	Turkiye	Retrospective diagnostic accuracy study	20 pediatric IBD-patients (0-18 years)	Hb < −2 SD for age/gender for the entire population.	CD: 8 (40%) UC: 12 (60%)	Anemia: 20% (4/20)

Table 1: *Cont.*

Correa et al., 2021 [56]	Brazil	Case-control study	81 pediatric IBD patients 35 HC (2-20 years)	WHO criteria.	IBD-U	Anemia (at baseline): Conventional therapy (CT): 61% (11/18) Infliximab group (pre-treatment) 50% (10/20) Remission: 18.6% (8/43)
El Mouzan et al., 2020 [44]	Saudi Arabia	Retrospective cohort study	456 pediatric IBD-patients (0-17 years)	Not specified	CD: 309 (68%) UC: 147 (32%)	Anemia: CD Central: 46.3% CD Western: 54.7% CD Eastern: 77.6% UC Central: 57.4% UC Western: 55.6% UC Eastern: 90.9%
Dotson et al., 2015 [55]	United States	Cross-sectional study	5,782 pediatric CD-patients (13-18 years)	Not specified	CD	Anemia: 26.8% (1552/5782)
Leković et al., 2011 [58]	Serbia	Retrospective case-series	17 pediatric idiopathic ulcerative colitis (IUC) (3.8-17.5 years)	Hb<115 g/l	UC	Anemia: 35.3% (6/17)

IDA:Iron Deficiency Anemia; ID:Iron Deficiency; ACD Anaemia of Chronic Disease; CD:Chron`s Disease; UC: Ulcerative Colitis; IUC:Idiopathic Ulcerative Colitis; IC:Indeterminate colitis; Hb:Hemoglobin; EIMs: Extraintestinal manifestations; HC:Healthy controls

Table 2: Risk of bias assessment (Newcastle–Ottawa Quality Assessment Scale criteria)

	Selection (max 4)				**Comparability (max 2)**		**Exposure/outcome (max 3)**			**Total (max 9)**
Cohort studies	Exposed representativeness	Non-exposed representativeness	Exposure assessment	Outcome of interest	Adjusts for age	Adjusts for additional factors	Outcome assessment	Follow-up length	Follow-up adequacy	
Miller et al. [23]	1	1	1	0	1	0	1	1	1	7
Chu et al. [24]	1	1	1	0	0	0	1	0	1	5
Aljomah et al. [25,26]	1	1	1	0	0	0	1	1	1	6
Sjöberg et al. [26]	1	1	1	0	1	0	1	1	1	7
Wiskin. et al. [27]	1	1	1	0	0	0	1	1	1	6
D'Arcangelo et al. [28]	1	1	1	0	1	0	1	1	1	7
Tanpowpong et al. [29]	1	1	1	0	1	1	1	1	1	8
Olczyk et al. [30]	1	1	1	0	0	0	1	0	1	5
Klamt et al. [31]	1	1	1	0	1	1	1	1	1	8

Table 2: *Cont.*

Shentova-Eneva et al. [32]	1	1	1	0	1	0	1	0	1	6
Rempel et al. [1]	1	1	1	0	1	1	1	1	1	8
Carvalho et al. [33]	1	1	1	0	1	1	1	1	1	8
de Laffolie et al. [34]	1	1	1	0	1	0	1	1	1	7
Saadah et al. [35]	0	0	0	0	0	0	0	0	1	1
Al-Saleem et al. [36]	1	0	0	0	0	0	1	1	1	4
Gerasimidis et al. [37]	1	1	1	0	1	1	1	1	1	8
Wang et al. [38]	1	1	1	0	1	1	1	1	1	8
Saadah.[39]	1	1	0	0	0	0	0	1	1	4
Jose et al. [40]	0	0	1	0	0	0	0	1	1	3
Castro et al. [41]	1	1	0	0	1	1	1	1	1	7
Goel & Shanks R. [42]	1	1	1	0	0	0	1	1	1	6

Table 2: *Cont.*

Altaş & Ertem D [43]	1	1	1	0	1	1	1	1	1	8
El Mouzan et al. [44]	1	1	1	0	1	1	1	1	1	8
Case-control studies	Case definition	Case representativeness	Control selection	Control definition	Adjusts for age	Adjusts for additional factors	Exposure assessment	Same for cases and controls	Non-response rate	
Maćków et al. [57]	1	1	0	0	0	0	1	1	1	5
Correa et al. [56]	1	1	0	0	0	0	1	1	1	5
Cross-sectional studies	Sample representativeness	Sample size	Nonrespondents	Exposure assessment	Adjusts for confounders		Outcome assessment	Appropriate statistical method		
Isa et al. [45]	1	0	0	2	1		2	1		7
Smith et al.[61]	1	0	1	2	0		2	1		8
Akkermans et al. [46]	1	0	0	2	1		2	1		7
Syed et al. [47]	1	0	0	2	1		2	1		7
Pawłowska et al. [48]	1	0	0	2	1		2	1		7

Table 2: *Cont.*

Breton et al. [62]	1	0	0	2	0		2	1	6
Krawiec et al. [49]	1	0	1	2	0		2	1	7
Marcil. et al. [50]	1	1	1	2	1		2	1	9
Krawiec et al. [51,52]	1	0	1	2	0		2	1	7
Syed et al. [52]	1	0	0	2	1		2	1	7
Martinelli et al. [53]	1	1	1	2	1		2	1	9
Goodhand et al. [54]	1	0	1	2	1		1	1	7
Ahmaida A., Al-Shaikhi S. [60]	1	0	0	2	0		2	1	6
Alrashidi et al. [59]	0	0	0	2	1		2	1	6
Güven et al. [63]	1	0	0	2	0		2	1	6
Dotson et al. [55]	1	1	1	0	1		2	1	7
Leković et al. [58]	1	0	0	2	0		2	0	5

Prevalence of Anemia, Iron Deficiency, and Iron Deficiency Anemia

Across 42 studies from 20 different countries, the prevalence of anemia in pediatric patients with IBD varied significantly, ranging from 20% to more than 80%.

Prevalence estimates were often higher when evaluated at diagnosis or during active disease.

Several single-center cohorts reported anemia rates exceeding 70%, including those from Sweden[26], the United Kingdom [27], Poland [30,48], Saudi Arabia[36,59], and Thailand [29], where 63-75% of children were anemic at presentation. Similarly high rates were observed in Singapore [24] and UK cohorts [37] with 78% and 72% respectively.

Conversely, prevalence estimates were often lower, although still clinically significant, in large registry-based cohorts. This includes a cohort by Miller et al. of more than 2,400 children, reporting anemia in 51% of CD patients and 43% of UC patients [23], as well as D'Arcangelo et al. reporting 36% anemia from 1,600 patients [28]. Additionally, other registry-based studies, e.g. those from Germany [31], Austria [34] and Canada [1,50], generally reported anemia in 25-60% of pediatric IBD cohorts.

Overall, most studies found prevalence rates between 40-70%, making it one of the most prominent extraintestinal manifestations of pediatric IBD.

Likewise, ID was remarkably common, with prevalence typically exceeding 60-90%, especially in anemic subgroups.

Isa et al. reported that over 83% anemic patients had ID and nearly 90% met criteria for IDA [45]. Additionally, cohort studies from Portugal [33] and the UK [27,54] reported ID in 76-95% of affected children, while D'Arcangelo et al. showed that nearly 88% of anemic children had IDA, with only 12% meeting criteria for ACD [28]. IDA estimates generally ranged widely from 27% to almost 90%, with the highest rates reported among patients with active disease or newly diagnosed IBD.

Studies using biomarkers such as ferritin and transferrin saturation reported similarly high rates. In a cohort by Akkermans et al., 80% of evaluated patients had functional ID, 32% with absolute ID while ACD accounted for only 20% of anemia cases [46].

Prevalence by IBD Subtype

Twenty studies reported prevalence rates for CD and UC separately [1,23,25–30,32–34,37,38,41,43,44,46,48–50]. Overall, studies indicate higher prevalence of anemia and ID among CD patients than UC. Cohorts from Sweden [26], Poland [30], United States [23] and Bulgaria [32] consistently showed 10-20% higher anemia rates in CD than UC. However, this wasn't universal, with several studies demonstrating similar estimates in CD and UC. Tanpowpong et al. reported anemia in 74.3% of patients with CD and 75% of patients with UC [29], while a Polish cohort found anemia in 62.5% of patients with CD and 65.5% of patients with UC [48]. A minority observed higher prevalence in UC, e.g. a cohort from Saudi Arabia reporting up to 20% higher prevalence in UC across Central, Western and Eastern regions [44].

Four studies reported estimates for IBD-U [34,41,46,50] but generally showed intermediate prevalence with wide variability due to small sample sizes. An Italian cohort reported anemia in 13.6% of IBD-U patients [41], while a Canadian cross-sectional study found a prevalence of 40% [50]. The studies consisted of 131 and 20 IBD-U patients respectively.

Anemia and Disease Activity

Seventeen studies reported on the association between anemia or ID and disease activity [1,23,25–28,32,34,37,46,47,49,50,53,54,56,62]. Studies generally showed a higher prevalence of anemia in active disease and correlated with markers of systemic inflammation, including elevated CRP and erythrocyte sedimentation rate (ESR), as well as high disease activity using Paediatric

Crohn's Disease Activity Index (PCDAI), and Paediatric Ulcerative Colitis Activity Index (PUCAI)-scores.

Cohort studies from the US [23,25] , Canada [1] , Poland [51] and UK [27] demonstrated a positive correlation between the prevalence of anemia and inflammatory markers. Miller et al. found that 60% of anemic patients had elevated CRP vs. only 27% of non-anemic patients [23]. Likewise, Wiskin et al. reported an improvement in prevalence relative to decreased median CRP [27]. The Canadian cohort also found a significant association between anemia and ESR (>10 mm/h) at diagnosis ($p = 0.012$) [1]. Additionally, a case-control study from Brazil [56] reported anemia prevalence of 61% in active disease, and 18.6% in remission, while a Bulgarian cohort [32] found that anemia was less common in patients with mild disease compared with moderate to severe and severe disease (22.2 vs. 77.8%, $p < 0.001$ in UC and 25.9% vs. 74.1%, $p < 0.001$ in CD). Furthermore, an Italian cross-sectional study found a positive correlation between hepcidin levels and disease activity ($p = 0.02$),

as well as a significant inverse correlation between hepcidin levels and iron absorption ($p = 0.002$) [53].

In contrast, several other studies reported no association between anemia and clinical measures of disease activity. A Polish cross-sectional study found that ID was present in 70.4% of patients with active phase IBD and 57.1% of patients in IBD remission, although this difference was not found to be statistically significant ($\chi 2 = 1.19$; $p = 0.27$) [49]. Likewise, Akkermans et al. [46] and a US cohort [25] did not find an elevated PCDAI or PUCAI to be significantly associated with ID or IDA (PCDAI $p = 0.050$; PUCAI $p = 0.393$), although the latter did find a significant association with inflammatory markers such as ESR and CRP ($p = <.0001$). Meanwhile, a Polish cross-sectional study examined soluble transferrin receptors in relation to disease activity indexes but did not find any correlation ($p = 0.76$) [51].

Anemia and Quality of Life

Only 1 study reported on quality of life in relation to anemia or ID [34] .

Despite limited data and non-quantifiable measurements, findings suggested a significant impact on quality of life. In a German and Austrian cohort, anemic patients with both CD and UC assessed their own well-being significantly worse than CD and UC patients without anemia ($p < 0.0001$). Likewise, similar significant differences were found in anemic vs. non-anemic IBD-U patients ($p < 0.001$) [34].

Growth and Development

Seventeen studies reported on IBD in relation to growth and development in children[1,24,31,35,37–39,41–43,48,50,52,55,57,60,62].

Children with IBD, particularly those with CD, were more likely to demonstrate low height-for-age, weight-for-age, and abnormal body mass index (BMI) z-scores. Studies from Singapore [24], China [38], and Germany [31], and Canada [1] reported increased rates of growth impairment or retardation, ranging from 13% to 34%. Saadah et al. reported low weight-for-age and height-for-age in 32.7% and 20.3% of children, respectively, but suggested multiple possible causes such as anorexia, malabsorption, intestinal inflammation, and corticosteroid usage [35]. Two studies examined the association between anemia and growth impairment [37,48]. A UK cohort reported that a high risk of undernutrition, reflected by weight loss and low BMI z-score, differentiated anemic from nonanemic CD patients and correlated with hemoglobin concentration [37]. However, the study did not find this to be statistically significant ($p = 0.129$). Likewise, Pawłowska et al. found that children

with anemia presented with a lower BMI z-score than those without anemia, although this also wasn't statistically significant ($p = 0.062$)[48]. Meanwhile, Wang X-q et al. found that weight loss and growth failure were more common in patients with CD than UC, with growth failure occurring in 34.0% CD patients and only 0.7% of UC patients [38].
Most studies did not directly examine the association between anemia or ID and growth impairment but focusing instead on the broader nutritional deficiencies secondary to IBD.

Discussion

We systematically reviewed the evidence on prevalence of ID and IDA in pediatric patients with IBD, after which, 42 eligible studies were identified and included.
The results suggest a high prevalence of anemia among pediatric IBD patients, as well as significant association with disease activity, growth and impact on quality of life.

The prevalence of anemia in pediatric IBD ranged widely from 20-80%, with the majority of studies reporting prevalences between 40 and 70%. ID showed even higher prevalence, often presenting in more than 60-90% of pediatric patients, with a higher frequency in anemic subgroups. ID was also found to be the most dominant cause of anemia, regardless of geography or study design. IDA was present in more than 80% of anemic children, whereas ACD only accounted for a small percentage.

These findings suggest that, even in the presence of chronic inflammation, absolute ID is the predominant mechanism in pediatric IBD.
Contrarily, Akkermans et al., while using more comprehensive biomarkers such as ferritin, transferrin saturation, and soluble transferrin receptor, found that 80% of patients had functional ID. This subtype of ID is frequently caused by inflammation-induced hepcidin increase [64], which lends credence to the theory that anemia in IBD is caused by both malabsorption and impaired iron utilization.

The large variance in anemia prevalence likely reflects differences in disease activity, diagnostic thresholds, and sample size, with higher prevalence rates being observed in smaller cohorts. Additionally, the prevalence seems to be somewhat correlated with the origin of the population, with higher prevalences occurring predominantly in developing countries, and lower prevalences in Western regions. However, the combined results continue to show that ID and IDA are significant clinical issues in pediatric IBD.

Anemia is a major concern in both disease subtypes, but it is slightly more pronounced in CD. An explanation of this could be CD's more frequent involvement of the small intestine, where iron absorption occurs, and its association with deeper mucosal ulceration and more extensive inflammation [65,66].

Nonetheless, several studies reported comparable rates between CD and UC, and some even found higher anemia prevalence in UC. These disparities most likely result from population differences, small sample sizes, or regional variation in disease severity.

Several cohorts demonstrated improvement in anemia prevalence following reduction in inflammatory markers or successful remission induction. Prevalence tended to be highest at disease onset and during periods of active inflammation, often exceeding 70%. This is consistent with the physiological mechanisms of chronic blood loss from mucosal ulceration, while inflammatory cytokines increase hepcidin production, restricting iron absorption and release from stores [64]. Therefore, the presence of anemia could not only be an indication of nutritional deficiency but also as an indicator of ongoing inflammation. However, not all studies found this association statistically significant. A few cohorts [25,46,49,51] reported no direct correlation between anemia and clinical disease activity. This disparity may reflect the limitations of clinical scoring systems or the impact of subclinical inflammation. Other IBD studies suggest a potential time delay between changes in disease activity and hematologic recovery. A US cohort examining changes in hepcidin and hemoglobin following anti-TNF-alpha treatment, found that despite increases in hemoglobin, 90% of patients remained anemic even after 10 weeks of treatment [67]. Nonetheless, most studies indicate that anemia is more prevalent and severe during periods of active inflammation.

Only a singular study examined the clinical consequences of anemia and ID beyond laboratory measures. This study did, however, find a significant impact on quality of life in anemic vs. non-anemic CD, UC, and IBD-U patients. This gap in the literature may be due to the fact that anemia has only recently emerged as a significant concern in pediatric IBD. Despite this, several adult studies indicate that anemia affects fatigue, well-being, work, and psychosocial function [68,69]. Additionally, other studies also showed improvements in patient-reported outcomes following effective diagnosis and treatment of anemia [70], suggesting a significant contribution to functional impairment. Growth and developmental outcomes were more frequently reported, although only two studies directly associated this with anemia. Gerasimidis et al. and Pawłowska et al. both found that anemic CD patients had a higher risk of undernutrition compared to non-anemic CD patients.

However, the majority of studies suggest that children with IBD have increased rates of growth delay, weight loss, and reduced BMI z-scores. This is likely due to the poor nutrient absorption as a result of inflammation [71]. Since IBD doesn't solely affect iron absorption, it is perhaps difficult to differentiate growth impairment caused by anemia as opposed to other nutritional deficiencies. This could be the point of investigation for future studies.

This systematic review was conducted based on a large number of high-quality studies and is the first to evaluate the prevalence of anemia in pediatric IBD patients. It covered multiple major databases and included a wide range of study designs, geographic regions, and clinical settings. Independent screening and risk-of-bias assessment also reduced the likelihood of selection bias, allowing for more generalizable results.

Nevertheless, the review has some limitations. Notably, included studies differed in their definitions of anemia, some following WHO criteria, others applying age- and sex-specific national guidelines, and some not specifying thresholds at all. ID definitions also varied, with inconsistent use of ferritin, transferrin saturation and CRP markers. Since ferritin acts like an acute-phase reactant, relying on this value alone risks underestimating ID during active disease [18]. In contrast, using non-adjusted transferrin saturation can overestimate ID [72]. This heterogeneity complicates direct comparison of prevalence estimates and may partly explain the wide range observed. The lack of pediatric-specific guidelines is also a significant hindrance to consistent reporting and highlights an important target for future research.

Additionally, most of the included studies were retrospective, which further limits the interpretability of results. Missing data, inconsistent testing and follow-up, limit the ability to draw conclusions on the relationships between anemia, disease activity, and other outcomes. Twenty-three of the studies were also cohorts whose primary aims usually weren't to assess anemia prevalence. As a result, the measurement and reporting of anemia were inconsistent or incomplete, with some studies not characterizing the specific type of anemia. For these studies, it is therefore difficult to determine whether the anemia is caused by ID or perhaps B12- or folic acid deficiency.

Conclusion:

In conclusion, with consistent findings across countries, study designs, and healthcare settings along with results suggesting a population-based variance, this systematic review strengthens the position

that anemia and ID are highly prevalent among children and present a significant challenge in pediatric IBD. Their strong association with inflammation and disease activity, combined with reported impacts on well-being and development, emphasizes the need for standardized diagnostic approaches. Improving recognition and management of anemia and ID may therefore represent an important opportunity to improve overall patient outcomes.

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