

APPROCCIO MULTIDISCIPLINARE ALL'ANEMIA SIDEROPENICA: UNA PATOLOGIA FREQUENTE E CURABILE



Patologie infiammatorie intestinali: da un regime trasfusionale ad uno infusionale

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IBD DEFINITION



- Immunomediated, inflammatory disorders
- Chronic and relapsing course
- Mucosal ulcerations and bleeding
- Systemic diseases with extraintestinal manifestations



ANAEMIA IS THE SECOND MOST COMMON EXTRAINTESTINAL MANIFESTATION OF INFLAMMATORY BOWEL DISEASE (IBD)



Ott C & Scholmerich J. Nat Rev Gastroenterol Hepatol 2013



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Filmann N et al. Inflamm Bowel Dis 2014



CLINICAL BURDEN OF ANAEMIA IN INFLAMMATORY BOWEL DISEASE: ROLE OF IRON DEFICIENCY AND IRON REPLACEMENT THERAPY, OBSERVATIONAL STUDY (RIDART) 1

Recruiting sites: 28; registered patients: 5433; anaemia prevalence 13.7%





ANAEMIA IS A RELEVANT CAUSE OF REDUCED QUALITY OF LIFE AND HIGH MORTALITY IN IBD PATIENTS



PREDICTORS OF QUALITY OF LIFE IN 615 PTS

(Regression Analysis)					
VARIABLES	F VALUE	P VALUE			
IBD severity score	113.10	<0.0001			
Arthritis	54.53	<0.0001			
Hearth disease	12.77	0.0004			
Age	8.4 6	0.0039			
Anemia	6.93	0.0089			
Back/shoulder pain	6.00	0.0149			
Hypertension	4.41	0.0367			

CAUSES OF DEATH IN IBD

(Proportional Mortality Rate, PMR)						
COMORBIDITIES	PMR	95% CI				
Suppurative peritonitis	20.6	15.4-25.8				
Malnutrition	19.9	13.5-26.3				
Surgical complications	17.9	9.5-25.0				
Hypoalbuminemia	9.3	3.5-15.1				
Anemia	6.9	2.4-11.4				
Sepsis	6.9	4.7-9.1				
Shock	2.9	2.4-3.3				

Cucino C & Sonnenberg A. Inflamm Bowel Dis 2001



PREVALENCE OF ANAEMIA ACCORDING TO IBD TYPE, AGE, SEX AND CORRELATION WITH DISEASE ACTIVITY)







Bergamaschi G et al. Haematologica 2010





VARIABLES	ANAEMIC GROUP	NON- ANAEMIC GROUP	p-VALUE
Age (years) Mean, range	46.2, 18-87	46.3, 18-92	NS
Gender Male (n, %) Female (n, %)	298 (47.4) 331 (52.6)	2391 (56.9) 1811 (43.1)	<0.0002
Duration of IBD (years): Median, range	11.9, 0-50	12.1, 0-67	NS

NS, not significant.



CORRELATIONS BETWEEN LAB TESTS & DISEASE ACTIVITY INDEXES AND HAEMGLOBIN IN ANAEMIC PTS (RIDART I)



PARAMETERS	CASES (n)	CORRELATION COEFFICIENT r	P-VALUE
Hb – CDAI	211	-0.302	<0.0001
Hb – CAI	138	-0.190	0.0256
Hb – PLT	246	-0.296	<0.0001
Hb – albumin	116	0.236	0.0107
Hb – asthenia	387	-0.238	<0.0001
Hb – IBDQ	398	0.163	0.0008

CAI, clinical activity index; CDAI, Crohn's disease activity index. No corelation was observed between Hb and ESR,CRP or BMI.



British IBD guidelines statements on PREOPERATIVE ANAEMIA



Increases the risk of postoperative intra-abdominal sepsis

- . risk of intestinal obstruction and haemorrhage,
- . postoperative perforation
- pulmonary oedema and septic complications such as pneumonia and
- . wound infection

Perioperative red cell transfusion before ileocaecal resection

- . increased risk of postoperative ileus and intra-abdominal abscess
- . wound dehiscence and thrombotic events
- . "avoiding blood transfusion where possible"



8.0-9.4 g/dl

<8 g/dl

0

>=9.5 g/dl



PATHOGENESIS OF ANAEMIA (RIDART I)





ANAEMIA SCREENING AND TREATMENT IN INFLAMMATORY BOWEL DISEASES



Table 1. Summary of the 17 studies on prevalence and treatment of anemia among children with IBD

2		8		
Author; Location	Year	No. of pediatric IBD patients	Prevalence of anemia among screened patients	Prevalence of Fe treatm
Miller; United States*	2018	CD n=1,560*	CD 49%*	CD IV Fe 4%*
		UC n=886*	UC 43%*	UC IV Fe 3%*
Wikholm; Sweden	2016	CD n=28	46%†	Oral Fe 40% [†]
		UC n=45		Oral + IV Fe 4%†
		IBDU n=17		IV Fe 3% [†]
Sjöberg; Sweden	2014	CD n=44	55% [†]	Not reported
		UC n=38		
Van Biervliet; Belgium	2014	CD n=83	CD 61%	CD Oral Fe 12%
				CD IV Fe 4%
Gerasimidis; United Kingdom	2013	CD n=122	CD 72%	CD Oral Fe 34%
		UC n=51	UC 69%	UC Oral Fe 58%
		IBDU n=11	IBDU 66%	
Goodhand; United Kingdom	2012	CD n=73	57% [†]	Oral Fe 20% [†]
		UC n=31		IV Fe 10% [†]
		IBDU n=9		
Wiskin; United Kingdom	2012	CD n=46	75% [†]	Not reported
		UC n=34		
White; United States	2008	CD n=860	20% [†]	Not reported
		UC n=409		
		IBDU n=137		
Mack; United States and Canada	2007	CD n=392	CD 69%	Not reported
		UC n=134	UC 36%	
Howarth; United Kingdom	2007	n=32 [†]	63% [†]	Not reported
Thayu; United States	2005	CD n=78	CD 77%	Not reported
Khan; United States	2002	UC n=51	CD 41%	Not reported
		CD n=39	UC 41%	
Revel-Vilk; Israel	2000	CD n=50	41% [†]	Not reported
		UC n=13		
Gryboski; United States	1994	CD n=40	CD 75%	Not reported
		UC n=38	UC 84%	
Thomas; United States	1989	CD n=24	CD 71%	Not reported
Burbige; United States	1979	CD n=58	CD 50%	Not reported
Beeken; United States	1975	CD n=11	CD 73%	Not reported

Miller et al Pediatr Gastroenterol Hepatol Nutr. 2019 Mar;22(2):152-161



ANAEMIA SCREENING IN INFLAMMATORY BOWEL DISEASES





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ANAEMIA SCREENING IN INFLAMMATORY BOWEL DISEASES



Table 3. Anemia Screening, Prevalence, and Treatment by Age and Sex Among Children with IBD

Characteristics	Age (y)	CD (%)		Age <i>p</i> -value	UC (%)		Age <i>p</i> -value
		Male	Female		Male	Female	_
Screening	1-4	87.5	77.8	0.71	91.0	100.0	0.25
	5-11	87.8	86.5	0.52	82.2	84.9	0.39
	12-13	75.9	83.8	0.05	84.4	70.0	0.48
	14-21	85.9	85.2	Reference	84.4	77.4	Reference
	Sex p-value	0.99			0.02		
Anemia prevalence	1-4	50.0	50.0	0.98	14.3	0.0	0.09
	5-11	43.8	45.5	0.31	33.3	46.0	0.59
	12-13	50.9	57.4	0.32	42.9	80.0	0.03
	14-21	42.4	56.3	Reference	37.3	48.3	Reference
	Sex p-value	<0.01			<0.01		
Treatment	1-4	0.0	0.0	0.98	0.0	0.0	0.99
	5-11	2.4	6.3	0.36	2.2	1.5	0.13
	12-13	3.5	1.5	0.12	2.7	0.0	0.22
	14-21	4.3	7.4	Reference	4.1	6.2	Reference
	Sex p-value	0.02			0.32		

Results are presented here of % patients screened for anemia, % patients with anemia, and % patients treated for anemia broken down by IBD subtype, age, and sex. The *p*-values were generated from logistic regression models; age is adjusted for sex and vice versa. The *p*-values are provided to 2 decimal places. CD: Crohn's disease, UC: ulcerative colitis, IBD: inflammatory bowel disease.

Only 10%-20% of IDA patients receive iron supplementation



ANAEMIA TREATMENT IN INFLAMMATORY BOWEL DISEASES



TABLE 5. Iron Treatment Among Anemic Patients

		I	IBD		Non-IBD		
		No.	%		No.	%	Р
Had oral iron during follow-up?	Yes	635	36.71	\leftarrow	377	22.05	< 0.001
	No	1095	63.29		1333	77.95	
	Total	1730	100.00		1710	100.00	
Had IV iron during follow-up?	Yes	49	2.83	\leftarrow	10	0.58	< 0.001
с .	No	1681	97.17		1700	99.42	
	Total	1730	100.00		1710	100.00	



HAEMOGLOBIN VARIATIONS DURING FOLLOW-UP (RIDART I)





COMPARISON OF IRON SUPPLEMENTATION VS NO SUPPLEMENTATION IN DIFFERENT TYPES OF ANAEMIA (RIDART I)



	Iron (N)	No iron (N)	р
Total anaemias	129	106	0.0013
IDA	111	71	0.0137
Other anaemias	18	35	NS



Hemoglobin variations and HRQL following iv Fe supplementation



(A) psychosocial; (B) emotional; (C) social; (D) school; (E) physical; and (F) total.
Hb, hemoglobin; HRQL, health-related quality of life. Hb; HRQL.



MULTIPLE REGRESSION MODEL FOR PREDICTION OF FATIGUE (RIDART I)



Iron deficiency as a risk factor for fatigue (Lamb CA, et al. Gut 2019;68:s1–s10)

Multiple regression (N=233)	df	F	р
Active disease	1	8.8216	0.0033
Hb	1	7.3828	0.0071
Tf saturation	1	5.6576	0.0182
Model	3	10.8387	<0.0001

Tf saturation is a predictor of fatigue independent from disease activity and Hb (studio RIDART I)



Anaemia Therapy in IBD



IDA and ID deserve to be treated

Iron supplementation suggested even in the presence of inflammation IV iron is to be preferred for supplementation in IBD

- IV iron is more effective (due to oral iron malabsorption and GI side effects)
- Oral iron has pro-inflammatory effects on the GI mucosa and may change GI microbiota

Response to IV iron can be increased by addition of ESA if inflammation is present

Oral iron reserved for mild anaemia with quiescent disease

IDA frequently relapses if the underlying disease is not controlled



IV vs oral iron supplementation (meta-analysis)



Response rate (Hb increase at least 2 g/dL)

Treatment discontinuation

Serious adverse events







65.6% in IV iron groups, 52.1% in oral iron groups, OR 1.58 2.5% in the IV iron groups,10.9% in the oral irongroups, OR 0.25

4.2% in the IV iron groups (19 events), 1 in the oral iron groups (0.4%)



IV vs oral iron supplementation in ID/A





IV iron reduced hospitalizations (37% vs 48%)



Anaemia Therapy in IBD



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IDA Therapeutic Flow Chart



