



Anemia at Diagnosis of Pediatric Inflammatory Bowel Disease (IBD)

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Background Information

- Anemia is the most common systemic complication in IBD¹
- Anemia in children varies with age groups and sex.
- Anemia may affect physical health, emotional and cognitive functions, school attendance, hospitalization and health care costs.
- Iron Deficiency Anemia (IDA) is the most common anemia in IBD.
- Iron is an essential element for proliferation of pro-inflammatory intestinal microorganisms and its use to treat IDA may exacerbate colitis disease activity. Thus, overuse of iron may be a problem.
- Confirmation of a true iron deficiency associated with inflammation is of clinical importance to prevent unnecessary and potentially dangerous therapy.

- The gold standard for diagnosis of IDA would require an invasive and painful bone-marrow aspirate.
- Many indicators for iron deficiency (e.g. ferritin) are difficult to interpret in the presence of inflammation due to their acute nature of change.
- Newer tests such as high soluble transferrin receptor (sTfR) and a high ratio of sTfR to log ferritin (TfR-F) index have been identified for their utility to indicate true iron deficiency in the presence of inflammation.

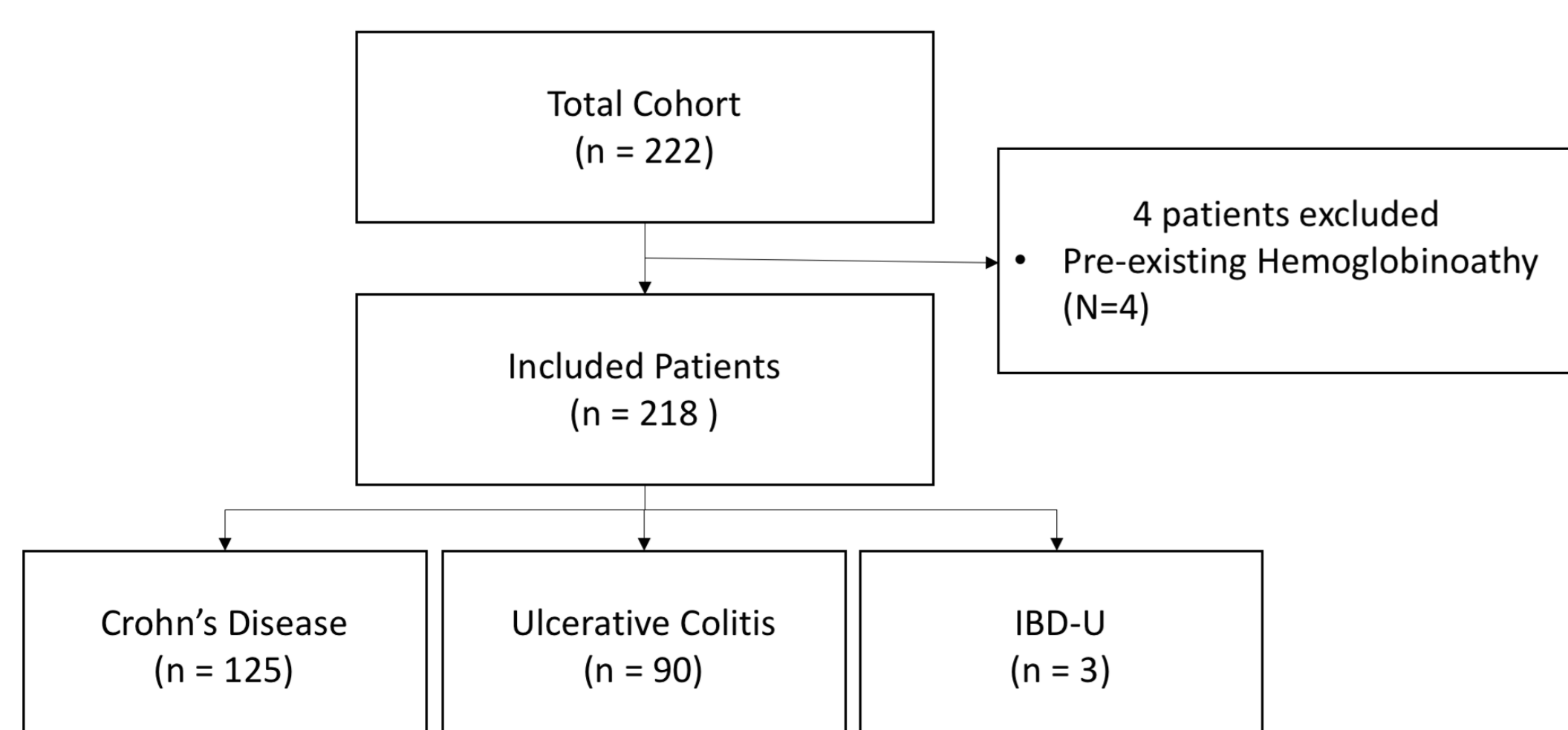
Objectives

- 1) Assess the utility of serum soluble transferrin receptor (sTfR) in the determination of iron deficiency and iron deficiency anemia.
- 2) Assess the utility of a calculated TfR-F ratio in the determination of iron deficiency and iron deficiency anemia.

Methods

- Data IBD patients followed at CHEO from September 2012 to June 2016 were retrospectively collected.
- Crohn's disease (CD) and Ulcerative colitis (UC) diagnosis was made by standard clinical, biochemical, endoscopic, radiologic and histological criteria.
- Disease severity was determined by Pediatric Crohn's Disease Activity Index for Crohn's Disease (PCDAI) or Pediatric Ulcerative Colitis Activity Index for Ulcerative Colitis (PUCAI)⁵.
- Hemoglobin reference values for age and sex¹ were utilized.
- TfR-F index was calculated by calculating the sTfR/(log Ferritin)
- Basic demographic characteristics were expressed as means with standard deviation.
- Comparative statistics between CD and UC patients utilized t-tests
- Difference between laboratory results in anemic and non-anemic IBD patients were evaluated using X² test and Fisher's exact test.
- p<0.05 was considered significant for all tests.

Figure 1: Flowchart of Study Cohort



Results

Table 1: Patient Characteristics

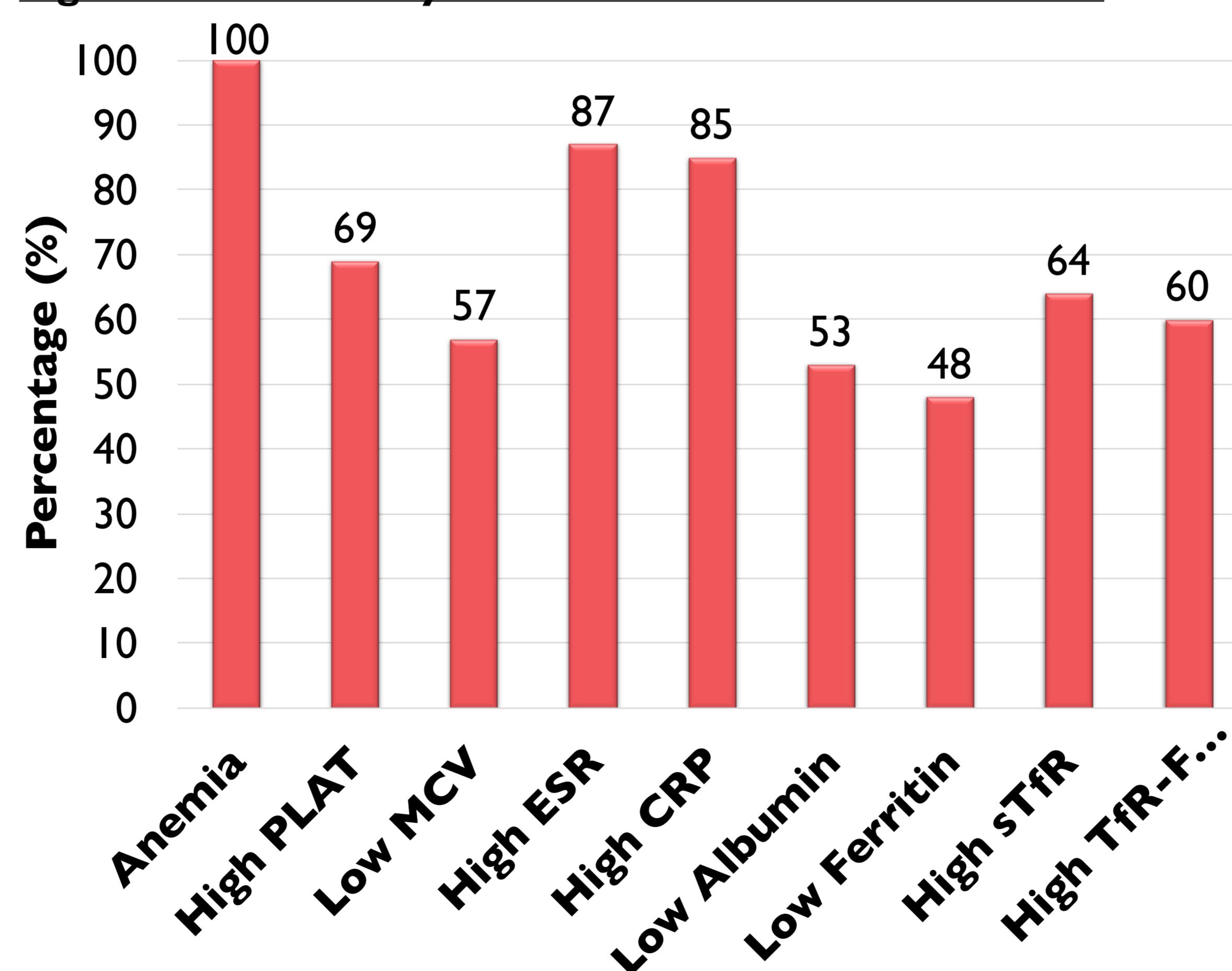
Total Cohort		Crohn's disease Patients	
Patients included	218		
Male: n (%)	118 (54)		
Age at Diagnosis			
Age at Diagnosis: years (SD)	13.1 (3.6)	0-9.9 yrs: n (%)	16 (13)
		10-16.9 yrs: n (%)	105 (84)
		>17yrs: n (%)	4 (3)
Crohn's disease: n (% of all IBD)	125 (57)	Disease Location*	
Ulcerative colitis: n (% of all IBD)	90 (42)	Distal 1/3 ileum: n	38
IBD-Unclassified: n (% of all IBD)	3 (1)	Colonic only: n	31
		Ileocolonic: n	53
		Upper GI disease: n	35
		Jejunal/Ileal disease: n	11
		Biological Behavior*	
		Non-stricturing, non-penetrating: n (% all CD)	107 (86)
		Stricturing: n (% all CD)	13 (10)
		Penetrating: n (% all CD)	7 (6)
		p: Perianal: n (% all CD)	31 (25)
Ulcerative colitis Patients			
Disease Location			
Proctitis: n (% of all UC patients)	3 (3)		
Distal to Splenic Flexure: n (% of all UC patients)	16 (18)		
Distal to Hepatic Flexure: n (% of all UC patients)	8 (9)		
Pancolitis: n (% of all UC patients)	63 (70)		

*CD Location and Behaviour does not add up to n = 125 as patients may have one or more attributes

Table 2: Clinical Disease Severity

	Crohn's disease n (%)	Ulcerative colitis n (%)	Total n (%)
Remission	7 (6)	3 (3)	10 (5)
Mild	14 (11)	17 (19)	31 (14)
Moderate	59 (47)	41 (46)	100 (46)
Severe	45 (36)	29 (32)	74 (34)

Figure 2: Laboratory Parameters in Anemic Patients



- Severe CD patients are more likely to have anemia (p=0.0073)
- Severe UC patients are not more likely to have anemia (p=0.2438).
- Anemic IBD patients have elevated platelets (p<0.0001).
- Anemic IBD patients are more likely to have abnormal mean corpuscular volume (MCV) (p<0.0001).
- Anemic IBD patients have elevated ESR (p<0.0001).
- Anemic IBD patients have elevated C-reactive protein (p=0.0002).
- Anemic IBD patients have low albumin (p < 0.0001).

*There were only 3/144 patients with low vitamin B12.

Table 3: Laboratory Testing in all IBD Patients by Disease Subtype

	CD n (%)	UC n (%)	Total IBD Cohort n (%)	p-Value
Low Hgb	61* (49)	36* (40)	97 (45)	0.2008*
Low MCV	58* (46)	19* (21)	77 (35)	<0.001*
High ESR	105* (84)	52* (58)	157 (73)	<0.0001*
High CRP	110* (88)	45* (50)	155 (72)	<0.0001*
Ferritin				
High	26 (23)	3 (4)	29 (15)	<0.0001*
Normal	62 (55)	27 (34)	89 (46)	
Low	25* (22)	49* (62)	74 (39)	
sTfR				
High	45* (41)	39* (53)	84 (46)	0.2923*
Normal	62 (56)	34 (46)	96 (52)	
Low	3 (3)	1 (1)	4 (2)	
TfR-F Ratio				
High	29* (28)	42* (60)	71 (41)	0.0002*
Normal	41 (40)	15 (21)	56 (33)	
Low	32 (31)	13 (19)	45 (26)	

Note: "*" Denotes values used for p-value calculation

- 49% of CD patients and 40% of UC patients had low hemoglobin (Hgb) at the time of diagnosis.
- The incidence of anemia is the same for CD and UC (p=0.2008) at the time of diagnosis but a low MCV was more likely in CD (p<0.001).
- CD patients were more likely to have elevated ESR (p<0.0001) and CRP (p<0.0001) than UC patients.
- UC patients are more likely than CD patients to have low ferritin (p<0.0001) and high TfR-F ratio (p=0.0002).
- There was no difference in sTfR between CD and UC (p=0.2923)
- Only 20 of 218 (9%) of patients on iron supplement at baseline.

Conclusions

- In our IBD cohort, we found high prevalence (45%) of anemia.
- There was a correlation between the incidence of anemia with clinical and biochemical parameters of disease activity.
- Prevalence of low ferritin inversely correlated to elevated ESR & CRP.
- Indirect testing of iron deficiency using elevated sTfR may have most utility in identifying IDA in IBD patients.

Future Directions

- Determine whether abnormal iron markers are associated with markers of inflammation and disease activity using linear regression analysis controlling for confounding factors such as age, sex, time since diagnosis, and site of disease.
- Assess indirect serology testing following response in follow-up of those receiving iron supplementation.

References

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