International Journal of Pediatrics & Neonatal Care

Original Article Open Access

Effect of Anemia on Health Related Quality of Life in Pediatric Inflammatory Bowel Disease: Comparison of a Single Center Cohort to Published Data

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Abstract

Background: Health related quality of life (HRQL) is a key outcome measure, increasingly used to evaluate the efficacy of medical interventions. While anemia is the most common systemic complication of inflammatory bowel disease (IBD) in children, the literature is scarce on its effect on HRQL.

Aim: Evaluation of the association between anemia and HRQL in children with IBD.

Methods: PedsQL 4.0, a generic HRQL survey that assesses subjective perception of psychosocial and physical well-being from patient and parental perspective was administered to 30 children with IBD. Results were analyzed in patients with and without anemia, and with active and quiescent disease. Findings were compared to published data in pediatric IBD and healthy controls. Anemia was defined by WHO criteria. Active disease was defined by pediatric Crohn's disease or ulcerative colitis indices >10 and/or low albumin or elevated CRP.

Results: Within our cohort as a whole and among our patients in remission, anemia was associated with lower mean scores in multiple domains of the PedsQL 4.0 survey. Similarly, in these groups a higher proportion of patients had abnormal scores. Compared to published pediatric IBD data, our patients in remission with normal hemoglobin scored significantly higher in all HRQL domains, while there was no significant difference between the two cohorts as a whole. Compared to healthy controls our cohort as a whole and patients with anemia scored significantly lower in all parent-reported domains. In contrast, scores in patients with normal hemoglobin were not significantly different from healthy controls.

Conclusions: Anemia was associated with impaired HRQL in children with IBD including those in apparent remission.

Publication History:

Received: July 28, 2018
Accepted: August 28, 2018
Published: August 31, 2018

Keywords:

Anemia, Children, Crohn's Disease, Health Related Quality of Life, Inflammatory Bowel Disease, Ulcerative colitis

Introduction

Health related quality of life (HRQL) is recognized as one of the most important outcome measures in the assessment of the efficacy new treatment modalities in pediatric inflammatory bowel disease (IBD) [1]. The effects of gastrointestinal symptoms on HRQL are well studied [2,3] but despite of the high prevalence of anemia in children with IBD [4], its impact on HRQL is not well understood.

Our aim was to investigate whether there is an association between anemia and impaired HRQL in children with IBD. We have administered PedsQL 4.0 [5], a generic HRQL survey, to a cohort of children with IBD treated with infliximab. PedsQL 4.0 is validated in pediatric IBD and allows comparison with healthy controls [6]. We analyzed mean HRQL scores, and the prevalence of subjects with low scores, predicting poor HRQL, among patients with anemia and normal hemoglobin, in both active and quiescent disease. In addition we compared HRQL scores in our cohort with published data in pediatric IBD [3], as well as healthy controls [5].

Methods

Study overview

The study was conducted at the American Family Children's Hospital, University of Wisconsin, School of Medicine and Public Health between February of 2014 and August of 2016. Inclusion criteria were: age 18 years or less, diagnosis of Crohn's Disease (CD) or ulcerative colitis (UC) and treatment with infliximab. Data collection for disease activity indices, HRQL and laboratory studies were done on the same day. For comparisons with published literature in pediatric IBD and healthy controls, data were extracted from the report by Kunz et al. on PedsQL 4.0 scores in a large pediatric multicenter IBD cohort [3] and from the original validation study for the PedsQL 4.0 survey [5] respectively.

Laboratory studies

Hematology indices, albumin and C-reactive protein (CRP), were measured by routine methods in the hospital clinical laboratory. Anemia was defined according to general WHO criteria as Hemoglobin (Hb)< 11.5 g/dl in patients less than 11 years of age, <12 g/dl in females, and <13 g/dl in males above 11 years of age. Cut-off from normal albumin was 3.3 g/dl up to 8 years of age and 3.2 g/dl above 8 years of age. CRP up to 1 mg/dl was considered normal.

Assessment of disease activity and health-related quality of life

Disease activity was assessed with pediatric CD or UC activity indices, PCDAI [7] and PUCAI [8], respectively. Patients were considered in remission if they had PCDAI or PUCAI scores of 10 or less, plus normal serum albumin and CRP.

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Citation: Danko I, Weidkamp M (2018) Effect of Anemia on Health Related Quality of Life in Pediatric Inflammatory Bowel Disease: Comparison of a Single Center Cohort to Published Data. Int J Pediatr Neonat Care 4: 142. doi: https://doi.org/10.15344/2455-2364/2018/142

HRQL reflects a patient's perception of the impact of a chronic illness on core dimensions of physical and social functioning and can be assessed with disease-specific or generic surveys [9]. The PedsQL 4.0 (Pediatric Quality of Life Inventory) Generic Core Scales [5,6] used in this study is a generic survey that assesses areas of physical and psychosocial functioning relevant for both healthy and ill populations [9], and normative data allow comparisons between patients with various diseases, or a particular disease and the general population. PedsQL 4.0 has been validated in pediatric IBD [1]. PedsQL 4.0 scores range from 0 to 100, higher scores indicate better HRQL. Results are reported as six consecutive numbers that represent child-reported psychosocial, physical and total (composite) scales followed by parent-reported values in the same order. Scores below 66.03, 72.98 and 69.71 for child self-report and 64.38, 63.28 and 65.42 for parent proxy-report are consistent with at risk status for poor HRQL [6] (henceforth referred to as "risk scores"). We have analyzed mean scores and the proportion of patients with risk scores as a function of anemia and/or active disease by dividing our study cohort into four subgroups: patients in remission with normal Hb, patients in remission with anemia, patients with active disease and normal Hb, and patients with active disease and anemia. HRQL scores in our cohort were then compared to scores published in pediatric IBD [3] and healthy controls [5]. In the final statistical analysis patients with active disease were treated as a single group regardless of the presence of anemia due to the very small number of patients with the unusual constellation of active disease and normal Hb.

Statistical analysis

Patient and parent reported HRQL scores were summarized in terms of means and standard deviations and compared between groups using a two-sample t-test. The Levene test was utilized to examine whether the variances in the HRQL scores differ between groups. Comparisons of the proportions of subjects with anemia, active disease and risk scores were conducted using Fisher's exact test. All p values are two-sided and $p<0.05$ was used for defining statistical significance. Statistical analyses were conducted using SAS software (SAS Institute Inc., Cary NC) version 9.4.

Results

Clinical characteristics

Table 1 shows summary of demographic and clinical data. All patients received infliximab for maintenance treatment. In addition, five patients took Prednisone at the time of the study. 17 patients representing almost half of those in remission and the majority of those with active disease had anemia. 12 patients representing the minority of those with normal Hb and more than half of those with anemia had active disease.

Detailed data of individual patients in our cohort are shown in Table 2. The groups with anemia (panels B+D) included all 3 patients with UC and 14 patients with CD. All 13 patients with normal Hb (panels A+C) had CD. All patients, regardless of the presence of anemia, were iron deficient (not shown). Folate and B12 levels within one year of enrollment were available for all except 2 patients and were all normal; none of the patients had mean corpuscular volume above 90 fl at the time of the study (not shown). All patients with active disease (panels C+D) had CD. Of the 18 patients in remission (panels A+B), 3 had UC and 15 had CD.

Statistical comparisons between mean laboratory values, disease activity indices and HRQL scores in various subgroups of our cohort along with published data in pediatric IBD and healthy controls are shown in tables 3, 4 and 5. Summary of the underlying data is shown in Supplemental Table 1. Henceforth the reader is referred to this table for mean values of various parameters that are discussed in the study.

Mean Hb was lower in patients with active disease compared to those in remission but the difference was not statistically significant (not shown). Patients in remission both with anemia and normal Hb had normal mean albumin, CRP and low mean PCDA/PUCAI scores; there was no statistically significant difference between the two subgroups in these variables (not shown).

Health-related quality of life in patients with anemia and active disease

Table 2 shows distribution of PedsQL 4.0 risk scores among individual patients as a function of anemia and/or active disease. There is obvious clustering of risk scores in the subgroups with anemia and/or active disease (panels B, C, D; risk scores are shown in bold).

Sex, n (%)			
	Male		18 (60)
	Female		12 (40)
Diagnosis, n (%)			
	CD		27 (90)
	UC		3 (10)
Age, years, mean (±SD)			
	At Diagnosis		10.9 (±3.1)
	At Enrollment		13.1 (±3.2)
Disease location, n (approx. %)			
CD	L1		1 (4)
	L2		5 (18)
	L3		10 (36)
	L1/4b		1 (4)
	L2/4a		1 (4)
	L3/4a		6 (22)
	L3/4b		1 (4)
	L3/4ab		1 (4)
	L4b		1 (4)
UC	E2		2 (67)
	E41		(33)
Anemia, n (%)			
	Entire Cohort	(n=30)	17 (57)
in	Pts in Remission	(n=18)	8 (44)
	Pts with Active Disease	(n=12)	9 (75)
Active disease, n (%)			
	Entire Cohort	(n=30)	12 (40)
in	Pts with Normal Hb	(n=13)	3 (23)
	Pts with Anemia	(n=17)	9 (53)

Table 1: Summary of Demographic and Clinical Data.
CD: Crohn's Disease, UC: Ulcerative Colitis, Hb: Hemoglobin, L, E: Paris class-ification categories for disease location in CD and UC, respectively, as follows: L1: ileal, L2: colonic, L3: ileocolonic, L1/4b: ileal with distal upper disease, L2/4a: colonic with proximal upper disease, L3/4a: ileocolonic with proximal upper disease, L3/4b: ileocolonic with distal upper disease, L3/4ab: ileocolonic with both proximal and distal upper disease, L4b: distal upper disease only, E2: UC with left sided colitis, E4: UC with pancolitis, Pts: Patients.

Patients with anemia had lower mean HRQL scores in all scales compared to patients with normal Hb; the difference was statistically significant in parent-reported physical and total scales (Table 3, Aa). The proportion of children with risk scores was higher in all scales among patients with anemia compared to those with normal Hb (Table 4, Aa vs Ab), but the difference was not statistically significant (Table 3, Ba).

Patients with active disease had lower mean scores in all scales compared to patients in remission but the differences were not statistically significant (Table 3, Ab). Similarly, the proportion of patients with risk scores was higher in all scales except the patient-reported psychosocial scale among patients with active disease compared to those in remission (Table 4, B vs C), however, the differences were not statistically significant (Table 3, Bb).

Pt #	Demographics			Dx	Paris Classif.	Anemia	Disease Activity				PedsQL 4.0 Scores					
											Patient-reported			Parent-reported		
	Age at Dx	Age at Enrollment	M or F			Hb (g/dl)	CRP (mg/dL)	Alb (g/dL)	PCD AI	PUC AI	Ps	Phys	Total	Ps	Phys	Total
A	Patients in Remission with Normal Hemoglobin (n=10)															
1	7	14	M	CD	L1	13.1	0.2	3.3	7		71	**72[1]**	71	81	97	87
2	13	16	F	CD	L3	12.4	0.0	3.6	5		95	100	97	100	94	98
3	16	17	F	CD	L3/4a	13.4	0.5	3.7	5.0		68	88	75	75	84	78
4	14	15	F	CD	L3	12.6	0.0	3.7	0.0		100	91	97	92	78	87
5	11	14	M	CD	L3	13.9	0.0	4.2	0.0		97	94	96	93	94	93
6	14	15	M	CD	L2	14.6	0.0	3.5	5.0		90	94	91	85	94	88
7	13	15	F	CD	L3/4a	12.7	1.0	3.6	5.0		93	91	92	85	88	86
8	13	15	M	CD	L3/4b	13.3	0.0	3.6	1.3		82	97	87	83	100	89
9	13	15	M	CD	L3	13.3	0.0	4.2	0.0		67	100	78	75	91	80
10	13	16	M	CD	L3/4a	13.4	0.0	4.0	0.0		88	97	91	87	100	91
B	Patients in Remission with Anemia (n=8)															
1	9	15	M	CD	L2	12.9	0.0	4.0	10		77	84	79	**58[1]**	81	**61[1]**
2	11	13	F	UC	E2	11.9	0.0	3.2		5	**60[1]**	**72[1]**	**64[1]**	**33[1]**	**44[1]**	**37[1]**
3	13	17	F	CD	L3	10.0	0.0	3.2	7.5		**38[1]**	**63[1]**	**47[1]**	80	94	85
4	14	16	M	UC	E4	8.9	0.0	3.4		0	85	84	85	80	84	82
5	8	9	M	UC	E2	8.1	0.0	4.0		0	97	100	98	87	94	89
6	13	13	M	CD	L3	12.0	0.0	3.7	10.0		**58[1]**	**59[1]**	**59[1]**	**63[1]**	69	**65[1]**
7	17	17	F	CD	L3	11.8	0.0	3.2	5.0		67	**38[1]**	**57[1]**	**50[1]**	**50[1]**	**50[1]**
8	9	14	M	CD	L3	12.8	1.0	3.5	0.0		88	84	87	63[1]	59[1]	62[1]
C	Patients with Active Disease and Normal Hemoglobin (n=3)															
1	6	7	F	CD	L3/4a	11.7	1.0	2.5	35		67	**69[1]**	**67[1]**	**60[1]**	**63[1]**	**61[1]**
2	5	7	M	CD	L2	11.5	1.0	3.4	32.5		**63[1]**	**50[1]**	**59[1]**	**45[1]**	66	**52[1]**
3	12	14	M	CD	L3	13.6	1.2	4.3	0.0		72	78	74	77	91	82
D	Patients with Active Disease and Anemia (n=9)															
1	9	14	M	CD	L2	10.5	0.0	3.6	18		73	**69[1]**	72	**63[1]**	**63[1]**	**63[1]**
2	12	12	F	CD	L1/4b	11.9	2.0	2.7	10.0		92	84	89	78	84	80
3	7	8	F	CD	L3/4a	10.8	0.0	3.2	40.0		85	**72[1]**	80	85	69	79
4	9	11	M	CD	L2/4a	12.1	3.0	2.6	27.5		90	**66[1]**	82	87	**59[1]**	77
5	5	6	M	CD	L3/4ab	9.7	1.0	2.7	32.5		67	**69[1]**	**67[1]**	77	66	73
6	10	12	F	CD	L4b	11.3	1.0	2.4	40.0		87	81	85	**62[1]**	**53[1]**	**59[1]**
7	11	11	M	CD	L3	10.9	0.0	3.5	12.5		**58[1]**	**66[1]**	**61[1]**	**50[1]**	**63[1]**	**54[1]**
8	9	16	M	CD	L3/4a	12.9	1.0	3.2	12.5		82	100	88	82	97	87
9	10	10	F	CD	L2	9.3	1.0	3.7	12.5		98	100	99	87	88	87

Table 2: Detailed Demographics, Clinical Data and Distribution of Risk Scores.

[1]: risk scores; Pt: patient; Dx: diagnosis; M: male, F: female; Hb: Hemoglobin; CRP: C-reactive protein; Alb: albumin; PCDAI: pediatric Crohn's disease activity index; PUCAI: Pediatric ulcerative colitis activity index; Ps: psychosocial; Phys: physical; M: male; F: female; CD: Crohn's disease; UC: Ulcerative Colitis; L, E: Paris classification categories for disease location in CD and UC, respectively, see Table 1.

Patients in remission who had anemia had lower mean scores in all scales compared to patients in remission with normal Hb. Differences were statistically significant in all except the patient-reported psychosocial scale (Table 3, Ac). Similarly, in the group with quiescent disease the proportion of patients with risk scores was higher in all scales among those who had anemia (Table 4, Ca vs Cb). These differences were statistically significant in patient-reported total scales and parent-reported psychosocial and total scales (Table 3, Bc).

Comparisons to published data in children with IBD

Compared to the published multicenter pediatric IBD cohort [3], mean HRQL scores of our entire cohort were somewhat lower in all except the patient-reported psychosocial scale, but these differences were not statistically significant (Table 5, Aa). At the same time, mean scores were significantly lower in our patients with anemia in all parent reported scales (Table 5, Aai), in our patients with active disease in parent-reported physical scales (Table 5, Ab), and in our anemic patients in remission in parent-reported psychosocial and total scales (Table 5, Aci). In contrast, our patients in remission with normal Hb had significantly higher mean scores in all patient and parent reported scales (Table 5, Acii). This was remarkable considering the overall lower scores in our entire cohort.

Compared to published patients with active disease mean scores in physical scales were lower in our patients with active disease but the difference was not statistically significant (not shown). Compared to published patients in remission mean scores in physical scales were slightly lower in our patients in remission but the difference was not statistically significant (not shown). No published scores in other scales were available for comparisons.

Comparisons to healthy controls

In patient-reported physical scales our patients with normal Hb scored slightly higher, and patients in remission with normal Hb scored significantly higher (Table 5, Bcii) compared to healthy controls. In the other subgroups and remaining scales, mean patient-reported scores were lower but not significantly different (Table 5, B, patient-reported columns).

At the same time, mean scores were significantly lower in all parent-reported scales in our entire study cohort (Table 5, Ba), in our patients with anemia (Table 5, Bai), in our patients with active disease (Table 5, Bb) and in our patients in remission who had anemia (Table 5, B ci). In the entire group of our patients in remission, mean parent-reported scores were also significantly lower in all except the physical scales (Table 5, Bc). In contrast, there was no significant decrease in mean parent-reported scores compared to healthy controls in patients with normal Hb in the entire cohort, and among those with normal Hb in remission (Table5, Baii and Bcii, respectively).

Discussion

To our knowledge, this is the first study to analyze HRQL in children with IBD as a function of anemia with comparisons to published data in pediatric IBD cohorts and healthy controls. This is also the first study that examines HRQL scores in the context of validated cut-off levels below which subjects are at risk for poor HRQL. Relating HRQL scores to such cut-off values provides clues to their true clinical significance.

We have found that a sizable proportion of patients had scores consistent with poor HRQL in all areas of the PedsQL 4.0 survey except those who were both in remission and had no anemia. The association of anemia with impaired HRQL was also supported by the comparisons of our patients to unselected IBD cohorts and healthy controls. Our study demonstrated divergence of patient and parental assessments, underscoring the importance of obtaining both perspectives when evaluating HRQL in these children.

HRQL scores in our patients in remission were higher compared to those with active disease. Although the differences did not reach statistical significance these findings are consistent with published data on the negative impact of disease activity on HRQL in IBD [10,11].

Our most intriguing finding was the association of anemia with lower HRQL scores in patients with apparently quiescent disease. This association was less prominent in our cohort as a whole, likely due to the confounding effect of disease activity. A limitation of our study is that we do not have endoscopic or fecal calprotectin data to further confirm disease remission. In some children anemia may have been an indicator of occult disease activity missed by traditional clinical assessments and conventional laboratory markers, similar to elevated fecal calprotectin reported in clinically inactive patients [12]. In either case, anemia in children in apparent remission appears to be an important red flag that should alert physicians to the need for optimization of treatment for anemia, inflammation, or both.

Authors' Contributions

Istvan Danko:
Conception and design of the work, acquisition, analysis, interpretation of data for the work.
Drafting the work and revising it critically for important intellectual content.
Final approval of the version to be published.
Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Marcy Weidkamp:

Acquisition of data.
Critical review of the work.
Final approval of the version to be published.
Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Acknowledgments

The authors greatly appreciate the help with statistical analysis by Jens C. Eickhoff, PhD, Department of Biostatistics & Medical Informatics, University of Wisconsin, Madison.

Funding

The research was supported from research and development funds of the Department of Pediatrics, University of Wisconsin, School of Medicine and Public Health.

Compared Patient Subgroups					P values					
					Patient-reported			Parent-reported		
					Ps	Phys	Total	Ps	Phys	Total
A					Mean HRQL Scores					
a. Anemia[1]	(n=17)	to	Normal Hb	(n=13)	0.439	0.086	0.235	0.084	**0.006**[1]	**0.024**[1]
b. Act.	(n=12)	to	Rem.	(n=18)	0.848	0.168	0.493	0.407	0.069	0.222
c. Rem. + Anemia[1]	(n=8)	to	Rem. + Normal Hb	(n=10)	0.083	**0.011**[1]	**0.030**[1]	**0.004**[1]	**0.008**[1]	**0.003**[1]
B					Proportion of Patients with Risk Scores					
a. Anemia	(n=17)	to	Normal Hb	(n=13)	0.350	0.140	0.410	0.120	0.092	0.120
b. Act.	(n=12)	to	Rem.	(n=18)	0.990	0.140	0.680	0.460	0.210	0.460
c. Rem. + Anemia[1]	(n=8)	to	Rem. + Normal Hb	(n=10)	0.069	0.118	**0.023**[1]	**0.007**[1]	0.069	**0.007**[1]

Table 3: Statistical Comparison of HRQL Scores and Proportion of Patients with Risk Scores between Subgroups.
A: P values from two-sample t tests; B: P values from Fisher's exact test; Act.: Active Disease; Rem.: Remission; [1]:Groups with more abnormal values (lower HRQL scores, higher proportion of patients with risk scores) reaching statistical significance and corresponding P values; Ps: psychosocial; Phys: physical.

Patient Groups			Patient-reported			Parent-reported		
			Ps	Phys	Total	Ps	Phys	Total
A Entire Study Cohort		(n=30)	17%	40%	27%	33%	27%	33%
	a. Anemic	(n=17)	24%	53%	35%	47%	41%	47%
	b. Normal Hb	(n=13)	8%	23%	15%	15%	8%	15%
B Active Disease		(n=12)	17%	58%	33%	42%	42%	42%
C Remission		(n=18)	17%	28%	22%	28%	17%	28%
	a. Anemic	(n=8)	38%	50%	50%	63%	38%	63%
	b. Normal Hb	(n=10)	0%	10%	0%	0%	0%	0%

Table 4. Proportion of Patients with Risk Scores in various PedsQL 4.0 Scales.
Ps: psychosocial; Phys: physical

Patient Groups		P values					
		Patient-reported			Parent-reported		
		Ps	Phys	Total	Ps	Phys	Total
A	Compared to	IBD (n=136)					
a. Entire Study Cohort	(n=30)	0.774	0.321	0.777	0.160	0.284	0.134
i. Anemic	(n=17)	0.970	0.160	0.580	**0.048**[1]	**0.026**[1]	**0.021**[1]
ii. Normal Hb	(n=13)	0.260	0.350	0.280	0.730	0.130	0.480
b. Active Disease	(n=12)	0.720	0.150	0.660	0.120	**0.037**[1]	0.046
c. Remission	(n=18)	0.550	0.690	0.600	0.600	0.790	0.720
i. Anemic	(n=8)	0.455	0.195	0.303	**0.031**[1]	0.156	**0.043**[1]
ii. Normal Hb	(n=10)	**0.036**[2]	**0.001**[2]	**0.006**[2]	**0.011**[2]	**< 0.001**[2]	**< 0.001**[2]
B	Compared to	Healthy Controls (n=399-717)[3]					
a. Entire Study Cohort	(n=30)	0.081	0.070	0.054	**< 0.001**[1]	**< 0.001**[1]	**< 0.001**[1]
i. Anemic	(n=17)	0.17	0.051	0.094	**< 0.001**[1]	**< 0.001**[1]	**< 0.001**[1]
ii. Normal Hb	(n=13)	0.720	0.670	0.940	0.120	0.640	0.170
b. Active Disease	(n=12)	0.250	0.054	0.120	**0.004**[1]	**0.001**[1]	**< 0.001**[1]
c. Remission	(n=18)	0.410	0.880	0.530	**0.017**[1]	0.140	**0.027**[1]
i. Anemic	(n=8)	0.105	0.098	0.082	**< 0.001**[1]	**0.012**[1]	**0.001**[1]
ii. Normal Hb	(n=10)	0.497	**0.004**[2]	0.144	0.691	0.244	0.992

Table 5: Statistical Comparison of Mean HRQL Scores to Published Data.
P values from two-sample t tests; Ps: psychosocial; Phys: physical; [1]: significantly lower scores in our cohort; [2]: significantly higher scores in our cohort; [3]: for detailed sample sizes see footnote to Supplemental Table 1.

Competing Interests

The authors declare that no competing interests is present.

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Supplemental Table

Patient Groups		Hb (g/dl)	Albumin (g/dl)	CRP (mg/dl)	PCDAI	PUCAI	Health-Related Quality of Life Scores					
							Patient-reported			Parent-reported		
							Ps	Phys	Total	Ps	Phys	Total
A. Entire Study Cohort	n=30	11.9 ± 1.6	3.4 ± 0.5	0.5 ± 0.7	12.3 ± 13.1 (27)	1.7 ± 2.9 (3)	77.30 ± 15.35	78.81 ± 16.21	77.79 ± 14.22	73.73 ± 16.38	78.26 ± 16.66	75.01 ± 15.53
a. Anemic	n=17 (57%)	11.0 ± 1.5	3.3 ± 0.5	0.6 ± 0.9	17.0 ± 12.8 (14)	1.7 ± 2.9 (3)	76.58 ± 16.50	75.94 ± 16.28	76.41 ± 15.05	69.70 ± 15.95	71.58 ± 16.58	70.00 ± 15.07
b. Normal Hb	n=13 (43%)	13.0 ± 0.9	3.7 ± 0.5	0.4 ± 0.5	7.4 ± 12.0 (13)	N/A	81.0 ± 13.40	86.2 ± 14.89	82.7 ± 12.67	79.8 ± 14.44	87.7 ± 11.97	82.4 ± 12.77
B. Active Disease	n=12 (40%)	11.4 ± 1.2	3.2 ± 0.6	1.0 ± 0.9	22.7 ± 13.4 (12)	N/A	77.83 ± 12.84	75.33 ± 14.39	76.92 ± 12.29	71.08 ± 14.56	71.83 ± 14.27	71.17 ± 12.71
C. Remission	n=18 (60%)	12.3 ± 1.7	3.6 ± 0.3	0.2 ± 0.3	4 ± 3.6 (15)	1.7 ± 2.9 (3)	78.94 ± 16.85	83.78 ± 16.96	80.62 ± 15.50	76.09 ± 16.83	83.06 ± 16.94	78.18 ± 16.44
a. Anemic	n=8 (44%)	11.1 ± 1.8	3.5 ± 0.3	0.1 ± 0.4	6.5 ± 4.2 (5)	1.7 ± 2.9 (3)	71.25 ± 19.24	73.00 ± 19.32	72.00 ± 17.74	64.25 ± 17.87	71.88 ± 19.42	66.38 ± 18.06
b. Normal Hb	n=10 (56%)	13.3 ± 0.6	3.7 ± 0.3	0.2 ± 0.3	2.8 ± 2.8 (10)	N/A	85.10 ± 12.40	92.40 ± 8.18	87.52 ± 9.49	85.57 ± 7.88	92.00 ± 7.01	87.63 ± 5.81
D. Published IBD Cohort[1]	n=136						76.42 ± 13.88	82.07 ± 16.24	78.59 ± 13.27	78.33 ± 15.16	81.91 ± 17.64	79.67 ± 14.35
a. Active Disease	n=42 (35%)			n/a			n/a	78.57 ± 17.99	n/a	n/a	76.65 ± 19.45	n/a
b. Remission	n=79 (65%)							86.67 ± 13.31			85.68 ± 16.09	
E. Published Healthy Controls	n=399-717[2]		n/a		N/A	N/A	82.38 ± 15.51	84.41 ± 17.26	83.00 ± 14.79	86.58 ± 12.79	89.32 ± 16.35	87.61 ± 12.33

Supplemental Table 1. Serum Hemoglobin, Disease Activity Indicators and HRQL Scores.
Data shown as mean ± SD (n); Hb: Hemoglobin, CRP: C-reactive protein, PCDAI: Pediatric Crohn's Disease Activity Index, PUCAI: Pediatric Ulcerative Colitis Activity Index; Ps: psychosocial; Phys: physical N/A: not applicable, n/a: data not available; [1]:In the published IBD sample the respective number (%) of patients with Crohn's, ulcerative and indeterminate colitis was 100 (73.5), 34 (25) and 2 (1.5), (see Kunz et al., Ref. #3). [2]: Sample sizes for healthy controls were: 399, 400, 401 in respective patient reported scales, and 717 in all parent-reported scales (see Varni et al., Ref. #5).