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Adherence to the New Zealand Pediatric Guideline for the Assessment and Diagnosis of Inflammatory Bowel Disease

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ABSTRACT

Background: New Zealand (NZ) guidelines for the approach to diagnosis and management of inflammatory bowel disease (IBD) in children were developed in 2014.
Objectives: This study aimed to assess the application of the guidelines in a group of children diagnosed with IBD in regards to baseline investigations.
Methods: This retrospective observational study analyzed the application of recommended baseline investigations included in the NZ guidelines in a group of children aged <16 years diagnosed consecutively with IBD at the 2 NZ tertiary pediatric gastroenterology centers.
Results: Fifty children were included from each center. Seventy-two were diagnosed with Crohn's disease (CD), 15 with ulcerative colitis (UC), and 13 were with IBD unclassified. The children with CD had a mean Pediatric Crohn's Disease Activity Index score of 31 and almost half had ileocolonic involvement (47%). The 15 children with UC had a mean PUCAI score of 42, and 13 had pancolonic involvement. All 100 children underwent upper and lower gastrointestinal endoscopy with biopsies, and 92% had magnetic resonance enterography at diagnosis. Iron studies, folate, and vitamin B12 were measured in >70 children. Serum zinc, magnesium, and phosphate were infrequently measured. Current anthropometry was recorded in all children but historical growth data were variably recorded. Vaccination status was also inconsistently recorded.
Conclusion: Most of this group of children diagnosed with IBD in 2 NZ centers underwent key recommended investigations at diagnosis including gastrointestinal endoscopy and small bowel imaging. Other baseline assessments, including measurement of micronutrient levels, were completed variably. Measures to enhance consistent baseline assessments are required.

Key Words: children, inflammatory bowel disease, Crohn's disease, ulcerative colitis, diagnosis, nutrition

What Is Known

- Rates of inflammatory bowel disease (IBD) are increasing in New Zealand (NZ).
- Most children diagnosed with IBD in NZ have Crohn's disease.
- Active IBD can impact adversely upon growth and nutrition in children.

What Is New

- All of this group of children diagnosed with IBD in NZ underwent upper and lower endoscopic assessments and had a recording of current anthropometry.
- Many of this group of children had a measurement of key micronutrients (iron, vitamin B12, vitamin D, and folate), but other micronutrients were assessed infrequently.
- Variable recording of past growth data, pubertal status, and vaccination status was conducted.

INTRODUCTION

Crohn's disease (CD) and ulcerative colitis (UC) are collectively termed inflammatory bowel diseases (IBDs).[1] Previous reports have delineated the typical phenotype of children diagnosed with IBD in New Zealand (NZ) and have shown high prevalence.[2,3,4] Furthermore, a longitudinal study conducted over 20 years to 2015 demonstrated increasing incidence in the Canterbury region of NZ.[3] Annual incidence increased from 2.88/100 000 children <16 years in 1996 to 13.06/100 000 children <16 years in 2015.[3]

A consensus national guideline for the diagnostic approach to pediatric IBD was developed in 2014 and has since been available online to NZ practitioners.[4] The guideline was formulated with input from physicians at both NZ tertiary pediatric gastroenterology units (Christchurch Hospital, Christchurch and Starship Child Health, Auckland) and outlines the investigations required to establish a diagnosis of IBD, along with further baseline assessments and investigations recommended at the time of diagnosis of IBD.[4] The application of these recommendations has not previously been established.

The primary aim of this study was to characterize the baseline assessments and investigations conducted in a cohort of children diagnosed with IBD at NZ's 2 pediatric tertiary gastroenterology centers. Additional aims were to describe the results of these assessments and to characterize the cohort of children.

METHODS

Study Population

In this retrospective, observational study, children aged <16 years who had been diagnosed consecutively with IBD before a set date were identified retrospectively at the 2 NZ hospitals with a pediatric gastroenterology service: Starship Child Health in

Auckland and Christchurch Hospital in Christchurch. A convenience sample of the 50 most recently diagnosed children with IBD at each of the 2 centers was included up to the date of March 31, 2019. The inclusion criteria were children <16 years of age with a new diagnosis of IBD (CD, UC, or IBD unclassified), as confirmed by a pediatric gastroenterologist and consistent with widely-accepted criteria.[5]

Cases were identified by pediatric gastroenterologists at NZ's 2 tertiary pediatric gastroenterology services, which provide care for all children with IBD in NZ. Starship Child Health has 5 pediatric gastroenterologists and provides care for all children with IBD in the North Island of NZ, which has a population of 3.9 million people.[6] Christchurch Hospital has 1 pediatric gastroenterologist who provides all IBD care in the South Island of NZ, which has a population of 1.2 million people.[6]

Data Collection and Analysis

Clinical data collected for each subject included demographics, anthropometry, and disease classification. Disease phenotype was described using the Paris classification.[7] Baseline disease activity scores were derived for each subject. The Pediatric Crohn's Disease Activity Index (PCDAI), a well-established tool that includes assessment of symptoms, growth parameters, and key laboratory results with a maximum score of 100 (highest disease activity) was calculated for the children with CD.[8] The Pediatric Ulcerative Colitis Activity Index (PUCAI) was utilized for children with UC: this tool stratifies disease activity by assessing gastrointestinal symptoms and activity restriction and has a maximum score of 85.[9]

The occurrence and the results of all assessments and investigations recommended at diagnosis of IBD in the NZ guideline were recorded. These included upper and lower GI endoscopy, biopsies and small bowel imaging, recommended laboratory tests, and clinical data (Supplemental Digital Content Table, http://links.lww.com/PG9/A94). The number and percentage of children who had each recommended investigation or assessment were analyzed. In addition, the results of investigations were noted.

Statistical Methods

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 25 (Armonk, NY). The proportion of children with IBD disease type, location, phenotype, Upper GI, perianal disease, and extraintestinal manifestations was reported. In the analysis of results of recommended investigations completed, the number and proportion of children receiving the investigation and those with missing investigations were reported. In the analysis of continuous variables including body mass index (BMI) z score, PUCAI, and PCDAI scores at diagnosis and laboratory investigations obtained, mean and standard deviation were reported. The range of continuous variables was also included. The proportion of children with abnormal laboratory results at diagnosis was also reported. An independent samples t test was used to compare BMI z-score in children with CD to the combined group of children with UC and IBDU. A 2-sided P value was reported, with a P-value of <0.05 considered significant.

Ethical Considerations

Ethical approval was obtained from the University of Otago Human Research Ethics Committee, reference HD 18/036.

RESULTS

Cohort Characteristics

Fifty children were included from each center, giving a total cohort of 100 children who had been diagnosed consecutively with IBD. The children from the North Island were diagnosed between February 2016 and March 2019, while the 50 children from the South Island were diagnosed between September 2017 and March 2019.

The median age at diagnosis overall was 11.7 years (interquartile range 9.1–13.8 years) (Table 1). Male children comprised 63% of the cohort. There were 72 children with CD, 15 with UC, and 13 with IBDU. Two of the children with IBDU (both girls) had Very Early Onset-IBD, diagnosed at 9 and 11 months of age, respectively. The ethnicity of children diagnosed with IBD was 78% NZ European, 5% other European, 9% Asian or Indian, 2% Māori, and 6% other (2 Middle Eastern, 2 South African, 1 North African, and 1 Russian).

Documented Information at Diagnosis

Disease Location and Characteristics

Disease location for each child in the cohort was documented in their endoscopy report and/or in the initial clinical letter following diagnosis. The phenotype was not reported but has been determined for this study cohort as descriptive data (Table 2). The most frequent disease location in the children with CD was ileocolonic (47%) while almost all children with UC had pancolonic involvement. Only 1 of the children with CD had non-inflammatory disease (penetrating) at diagnosis. Overall, 15 of the children had an extraintestinal manifestation present at diagnosis: oral ulceration was seen most frequently.

Disease Activity

The mean PCDAI score of children with CD was 31.4, while the children diagnosed with UC had a mean PUCAI score of 42.

Details of Patient History

Just over half (52%–56%) of the children had a record of their vaccination status, TB exposure risk, and past medical history documented in the clinical notes. A higher proportion (63%) had a family history of IBD recorded.

Growth and Development

All children had records of their current anthropometry, with BMI values derived from weight and height values. Overall, the mean BMI z-score of the cohort at diagnosis was −0.68 (SD ± 1.12) (Table 1). The children with CD had lower BMI z scores than the children in the other 2 groups combined (mean −0.88 versus −0.15, difference −0.73, 95% confidence interval −1.21 to −0.26, P = 0.03). The number of children with BMI z scores <−2.0 did not differ between groups (P > 0.05).

Records of historical growth data were poorly recorded (40%), and parental heights were not noted for any child. Pubertal status (Tanner stage) was noted for 2 children.

Adherence to Baseline Investigations and Assessments

Establishing a Diagnosis

As stated in the NZ guidelines,[4] investigations required to establish a diagnosis of IBD include upper gastrointestinal endoscopy and biopsies, ileocolonoscopy and biopsies, and small bowel imaging (eg, magnetic resonance enterography [MRE]) (Supplemental Digital Content Table, http://links.lww.com/PG9/A94). All 100 children in the study cohort underwent upper GI endoscopy and ileocolonoscopy at diagnosis. Furthermore, almost all children (92%) had small bowel imaging at diagnosis with MRE. A further 5 children had small bowel ultrasound scanning as MRE was contraindicated due to anxiety or young age, while 2 had delayed MRE (due to non-attendance on 1 occasion and unknown on the other). The final child did not have small bowel imaging due to disease location with isolated proctitis.

TABLE 1. Demographics, body mass index, and disease activity in 100 children diagnosed with inflammatory bowel disease (IBD)

	CD (n = 72)	UC (n = 15)	IBDU (n = 13)	All IBD (n = 100)
Age, median (IQR)	12.0 (9.9–13.8)	10 (9.3–12.8)	8.5 (5.2–13.3)	11.7 (9.1–13.8)
Male sex, N (%)	49 (68.1%)	7 (46.7%)	7 (53.8%)	63 (63%)
BMI *z* score, mean (SD)	−0.88 (0.99)*	−0.37 (1.15)	0.09 (1.42)	−0.68 (1.12)
BMI <−2 SD, N (%)	12 (16.7%)	2 (13.3%)	1 (7.7%)	15 (15%)
Disease activity score, mean (SD)	PCDAI 31.4 (11.3)	PUCAI 42 (17)		

BMI = body mass index; CD = Crohn's disease; IBDU = IBD unclassified; IQR = interquartile range; PCDAI = Pediatric CD Activity Index; PUCAI = Pediatric UC Activity Index; SD = standard deviation; UC = ulcerative colitis.

*Children with CD had lower BMI *z* scores than the other children: p = 0.03.

Baseline Laboratory Markers

Guideline Adherence

Of the assessments to be carried out at the time of IBD diagnosis according to the guidelines, iron studies, folate, vitamin B12, and creatinine were measured in between 71 and 82 of the 100 children (Table 3). Vitamin D levels were recorded in 73 children, with an additional 2 children described as having normal Vitamin D levels. Calcium and urea levels were both measured in almost two-thirds of the children. Serum levels of magnesium, phosphate, and zinc were measured in less than half of the children. Most children (≥90%) had albumin, erythrocyte sedimentation rate, varicella serology, thiopurine methyltransferase activity, fecal calprotectin, and fecal microbiology performed. In addition, liver chemistry was assessed in all children.

Results of Investigations

All but 2 of the 95 children with calprotectin results had elevated levels of this stool biomarker (Table 3). Furthermore, most of those tested had low albumin (61%), high CRP (62%), or high ESR (60%). Twenty-one (23%) of the 90 children with documented status were not immune to varicella. Twenty-three (25%) of the 93 children who had been assessed were shown to have abnormal thiopurine methyltransferase activity or genotype. Ten (10%) of the 100 children had abnormal liver chemistry.

Micronutrient deficiency was commonly seen at diagnosis (Table 3). Fifty-two (71%) of 73 children with measurement of iron had low levels, while 16 of 81 children had low ferritin. Of the 75 children with known vitamin D status, 17 (23%) were deficient. Although only measured in 13 children, zinc levels were low in 3.

DISCUSSION

This report focused on the baseline assessments of 100 children recently and consecutively diagnosed with IBD at NZ's 2 tertiary gastroenterology centers. In line with the NZ IBD guidelines, key disease-defining assessments (small bowel imaging, and upper and lower GI endoscopy) were performed at diagnosis in almost every case. A number of investigations (such as levels of micronutrients) were investigated infrequently. The vaccination status of the children was recorded inconsistently. Furthermore, although the current anthropometric status of all children was noted, other aspects of growth and nutrition (past growth data, pubertal status, and parental height) were variably recorded.

Consistent with the Revised Porto criteria,[5] the NZ guidelines recommend that all children should undergo both upper GI endoscopy and ileocolonoscopy at diagnosis, and that small bowel imaging is indicated in most settings. All children included in the current study cohort underwent complete endoscopic assessment and almost all had MRE at the time of diagnosis.

TABLE 2. Disease characteristics (location, phenotype, and extraintestinal manifestations) of children diagnosed with Crohn's disease (CD) and ulcerative colitis (UC)

IBD type	Characteristics at diagnosis	N (%)
CD (n = 72)	Location	
	L1	18 (25%)
	L2	18 (25%
	L3	34 (47%)
	L4	37 (51%)*
	P	18 (15%)†
	Phenotype	
	B1	71 (99%)
	B2	0
	B3	1 (1%)
	EIM	
	Oral ulceration	5
	OFG	2
	Erythema nodosum	3
	Pancreatitis	1
	Arthritis	2
	Penile	1
UC (N = 15)	Location	
	E1	0
	E2	1 (7%)
	E3	1 (7%)
	E4	13 (87%)
	Severity	
	S0	12 (80%)
	S1	3 (20%)
	EIM	
	IALD	2 (13%)

Disease features defined according to Paris classification.[7] EIM = extraintestinal manifestations; IALD = inflammatory bowel disease-associated liver disease; IBD = inflammatory bowel disease; OFG = orofacial granulomatosis.

*One child had isolated upper gut disease.

†One child had isolated perianal disease.

Whilst there is no direct comparative data, it appears that NZ practitioners are fulfilling these key recommendations more than noted historically. In an earlier report involving 51 children from

TABLE 3. The proportion of 100 included children who received investigations, and results of investigations recommended in the New Zealand guidelines at diagnosis of inflammatory bowel disease[4]

Recommended investigation	Percentage performed (N = 100)	Normal level	Mean (SD, range)	Abnormal results n/N (%)
25-OH vitamin D	73%	<50 nmol/L	70.3 (25.5, 22–140)	17/73 (23)
Iron	73%	<8 μmol/L	6.8 (4.9, 2–24)	52/73 (71)
Ferritin	81%	16–150 μg/L	62.2 (90.6, 3–663)	81/222* (27)
Vitamin B12	71%	250–650 pmol/L	576 (242, 233–1383)	30/71† (42)
Corrected calcium	63%	>2.6 mmol/L	2.5 (0.12, 2.25–2.79)	6/63 (10)
Magnesium	37%	>1.2 mmol/L	0.91 (0.18, 0.7–1.6)	2/37 (5)
Phosphate	46%	0.8–1.5 mmol/l	1.43 (0.27, 0.78–1.97)	1/46‡ (2)
Zinc	13%	<10 μmol/L	11.6 (2.4, 8.1–16.0)	3/13 (23)
Urea	64%	>5.7 mmol/L	3.8 (1.3, 1.5–7.1)	5/64 (8)
Creatinine	79%	>80μmol/L	54.6 (14.9, 20–84)	2/79 (3)
Calprotectin	94%	≥50 μg/g	*Variable reporting*	93/95 (98)
Albumin (g/L)	97%	<35 g/L	31.8 (6.8, 14–44)	59/97 (61)
C-reactive protein	88%	>5 mg/L	29.7 (39.1, 1–173)	58/94 (62)
Erythrocyte sedimentation rate	91%	>15 mm/hour	27.6 (24.0, 1–105)	55/91 (60)
Folate	82%	<8 nmol/L		1/81 (1)
Liver chemistry	100%			10/100§ (10)
TPMT activity or genotype	93%			23/93‖ (25)
Stool culture	90%			1/90¶ (1)
Varicella serology	90%			21/90 (23) non-immune

TPMT = thiopurine methyl transferase.
*16 low, 6 high.
†2 low, 28 high.
‡A 4-year-old child with low phosphate (0.78 mmol/L).
§6 elevated transaminases (>2 times normal range), 4 slightly elevated transaminases (up to 2 times normal range).
‖abnormal activity or abnormal genotype (heterozygous or homozygous).
¶1 *Aeromonas hydrophila* infection.

NZ diagnosed in 2002 and 2003, ileocolonoscopy was conducted in 91% and upper GI endoscopy in 76%.[10] Sixty-eight percent of that cohort had imaging of their small bowel (barium meal and follow-through or small bowel enema). Another NZ report noted colonoscopy had been performed in 100% of 161 children over a 20-year period, with upper endoscopy in 74.1% of the group.[3] In an international clinical practice 80% of the centers reported fulfilling the Porto Criteria for ≥80% of patients.[11] However, this report did not provide the specific rates of completion of upper endoscopy in the centers.

A key rationale to complete an upper GI endoscopy at diagnosis is the pattern of distribution of disease in childhood, with high rates of upper gastrointestinal tract involvement.[12,13] More than half of the children diagnosed with CD in the current study were shown to have upper GI involvement. Previous reports from NZ have indicated upper gut involvement in between 56% and 76.5% of the children diagnosed with CD.[2,3,10]

Aspects relating to growth and nutrition were included in the NZ guidelines as many children with IBD (especially those with CD) have presenting features of nutritional compromise, with weight loss or linear growth impairment.[14-17] Altered nutritional status may also impact adversely upon pubertal growth. Key aspects of assessing the impact of active IBD upon nutrition include current anthropometry, historical growth patterns, pubertal status, and parental height. In the current study, all children had recording of current weight and height, from which BMI scores were calculated. Inconsistent recording of other aspects of growth and growth history were noted however.

In comparison to the 15% of children in the current study noted to have BMI <−2SD at diagnosis, a French study of 261 children with pediatric-onset CD found 32% had BMI -2SD at diagnosis.[14] Management of the nutritional aspects of IBD relies upon adequate information; this is an item requiring ongoing emphasis for clinicians in NZ caring for children with IBD.

The vaccination status of the children in the current study was also documented inconsistently, although varicella serology was tested in a majority of the included children. This is particularly relevant in NZ as routine varicella vaccination was added as a routine vaccination on the national schedule only in 2017, meaning that most children were not vaccinated before this. Documenting vaccination status is an important baseline and monitoring step in the management of children diagnosed with IBD given the frequent use of immune suppressant therapies for management.[18] A number of previous reports have also shown low rates of vaccine awareness in children with IBD.[19,20] A recent report on an Australian initiative demonstrated the impact of referral of children with IBD to a specialist immunization clinic; this process enhanced vaccine rates and ensured delivery of additional coverage.[21]

Micronutrient deficiencies occur frequently in IBD. These include iron, B12, folic acid, zinc, magnesium, calcium, selenium, and fat-soluble vitamin deficiencies.[15,17,22] This was, therefore, an important consideration during the development of the NZ guidelines regarding baseline testing at diagnosis. Previous studies have reported zinc deficiency in 40%–50%, vitamin B12 deficiency in 48%, and folic acid deficiency in 54%–67% of people with CD.[17]

Although many children (71%–82%) in the current cohort had the assessment of iron studies, folate, vitamin D, or vitamin B12 status at diagnosis, low numbers of children had the assessment of other micronutrients or minerals. In addition, micronutrient deficiencies in these children included high rates of iron deficiency and a number with vitamin D deficiency. Similar to the assessment of vaccination status, this is also an aspect requiring greater attention.

The current report included a representative cross-sectional assessment of practice with inclusion of all consecutively diagnosed patients from NZ's 2 tertiary pediatric gastroenterology units. Further, the cohort was broadly similar to previous NZ cohorts in terms of features such as sex, ethnicity, and disease patterns.[3,4,10] The study is, however, limited by the retrospective design with reliance upon available clinical notes. Although this provided an evaluation of standard clinical care, a prospective evaluation would likely ensure accuracy. In addition, this report did not include any benchmarking or institute any formal quality improvement principles, which have clearly been demonstrated to enhance consistency and improve patient outcomes.[23]

In conclusion, this is the first study to evaluate adherence to pediatric guidelines for recommended assessments and investigations at diagnosis of IBD in children in NZ.

Most of the children included in the current study underwent the investigations and assessments recommended in the national guideline, although poor adherence to the guidelines was noted in regards to the measurement of micronutrients and collection of important background information such as historical growth patterns. Future prospective research would allow a quantitative evaluation assessing clinician knowledge and adherence to guidelines, with specific quality improvement methodology and goals to enhance clinical practice.

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