Published in final edited form as:

J Pediatr Gastroenterol Nutr. 2017 February ; 64(2): 286–291. doi:10.1097/MPG.0000000000001460.

Value of IgA tTG in Predicting Mucosal Recovery in Children with Celiac Disease on a Gluten Free Diet

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Abstract

Objective—Our objective was to determine the rate of mucosal recovery in pediatric patients with celiac disease on a gluten free diet. We also sought to determine whether IgA tissue transglutaminase (tTG) correlates with mucosal damage at the time of a repeat endoscopy with duodenal biopsy in these patients.

Methods—We performed a retrospective chart review of one-hundred and three pediatric patients, under 21 years of age, with a diagnosis of celiac disease defined as Marsh 3 histology, and who underwent a repeat endoscopy with duodenal biopsy at least twelve months after initiating a gluten free diet.

Results—We found that 19% of pediatric patients treated with a gluten free diet had persistent enteropathy. At the time of the repeat biopsy, tTG was elevated in 43% of cases with persistent enteropathy and 32% of cases in which there was mucosal recovery. Overall the positive predictive value of the autoantibody tissue transglutaminase was 25% and the negative predictive value was 83% in patients on a gluten free diet for a median of 2.4 years.

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Conflicts of Interest: The authors declare no conflict of interest.

Financial Disclosure Statement:

Alessio Fasano, MD: Alba Therapeutics: Co-founder and stock holder; Mead Johnson Nutrition: Sponsored research; Inova Diagnostics: Sponsored research; Regeneron: Sponsored research; Pfizer: Consultant. All other authors report no financial disclosures

Conclusions—Nearly one in five children with celiac disease in our population had persistent enteropathy despite maintaining a gluten free diet and IgA tTG was not an accurate marker of mucosal recovery. Neither the presence of symptoms nor positive serology were predictive of a patient's histology at the time of repeat biopsy. These findings suggest a revisitation of monitoring and management criteria of celiac disease in childhood.

Keywords

celiac; remission; serology; duodenal; pediatric

Introduction

Not long ago celiac disease (CD) was described as a childhood illness characterized by presentation with gastrointestinal symptoms, irritability, and poor growth (1). The development of a highly sensitive and specific diagnostic test for CD, the immunoglobulin A (IgA) tissue transglutaminase antibody (tTG) serology test, has allowed for minimally-invasive and cost-effective screening of at-risk individuals and groups (2). This has transformed our clinical appreciation of CD and how dietary adherence and mucosal recovery is monitored. Currently, children diagnosed with CD are followed in close collaboration with dietetic colleagues for counseling to educate and promote adherence to the gluten free diet (GFD). Growth and nutritional markers are monitored. In addition, current guidelines recommend follow-up serology both to assess dietary adherence and for use as a surrogate marker of mucosal recovery (3,4,5,6). In practice, antibody levels, usually the IgA tTG, are measured six months and then again one year after initiation of the GFD. When the level normalizes, it is presumed that mucosal recovery, attained through dietary adherence, has occurred. Adult patients with CD have similar follow-up with dietary counseling and the use of serologic markers. Studies evaluating mucosal healing in adults with CD on a GFD show that even after two years on a GFD, between one-third and two-thirds of patients have persistent mucosal damage, consistent with Marsh 3 criteria, (7,8) irrespective of IgA tTG levels. Recent data evaluating pediatric mucosal recovery is scarce, however, early data has suggested a more complete and faster healing time in children compared to adults (9). While not corroborated by evidence, anecdotally this has been explained by a decreased regenerative capacity of the adult intestine, resulting in slow and incomplete healing.

While current guidelines endorse and recommend the use of serology as a marker of dietary adherence and mucosal recovery, these serology tests have not been validated for this purpose. Our objective was to determine the rate of mucosal recovery in the pediatric population and to evaluate whether tTG correlates with mucosal damage at the time of a repeat endoscopy with duodenal biopsy in children with CD on a GFD.

Methods

We performed a retrospective chart review at two hospitals and identified 103 pediatric patients who fulfilled our inclusion criteria described below. Study procedures were approved by the Partners Human Resource Committee (PHRC) and Institutional Review

Boards (IRB) at MassGeneral Hospital for Children (MGH/C) and Boston Children's Hospital (BCH).

Subjects

Data for patients seen between January 2012 and March 2015 were extracted from medical records at MGH/C. Patients were identified by ICD-9 code. Additional data were obtained for patients seen between January 2008 and December 2013 at BCH, identified using the BCH Celiac Database, a database of all children diagnosed with biopsy proven CD at that institution. 61 patients were identified at MGH/C and 42 patients were identified at BCH.

Inclusion Criteria

To be included in the study, patients were required to be 21 years or younger at the time of diagnosis of CD, must have had diagnostic endoscopy with Marsh 3 lesions, and have undergone a second endoscopy with duodenal biopsy at least twelve months after initiating a gluten free diet. All patients meeting these criteria were included in the study.

Setting

The Celiac Research Program at Harvard Medical School is a collaboration between Beth Israel Deaconess Medical Center, Boston Children's Hospital, and MassGeneral Hospital for Children, all located in Boston, MA, USA. These three hospitals serve as quaternary care centers and referral centers for children and adults with CD and gluten-related disorders. Patients from Beth Israel Deaconess Medical Center were not included in this study.

Data collection

Data extracted from medical records included predominant clinical symptoms, serology tests, and duodenal histology at the time of the diagnostic and repeat endoscopy. Serology tests reviewed included immunoglobulin A (IgA) level, IgA tissue transglutaminase (tTG), and anti-endomysial antibody (EMA) when available. Serological values collected within four months of the endoscopy were included in the analysis. We dichotomized serological values into positive/borderline or negative according to cut-off values defined by the laboratories which performed the tests. Mucosal changes were scored by more than one pathologist at each institution using the Marsh criteria as modified by Oberhuber (0 = normal; 1 = increased intraepithelial lymphocytes [$>25/100$ epithelial cells], normal crypts and villi; 2 = increased intraepithelial lymphocytes, normal villi, crypt hyperplasia; 3 = increased intraepithelial lymphocytes, villous atrophy, crypt hyperplasia) (10,11). If endoscopic evaluation revealed multiple Marsh scores, the most severe was used.

For analysis, subjects were evaluated by the presence or absence of symptoms and length of time on a gluten free diet. We also recorded whether subjects received any dietetic counseling, defined as a nutrition consultation with a Registered Dietician, during the interval between the initial endoscopy and the follow-up endoscopy. We reviewed the physician's and dietician's notes commenting on the subjects adherence to the GFD at the clinic visit prior to the repeat endoscopy and scored adherence using criteria modified from Leffler et al: (1) Excellent = patient never eats gluten intentionally and/or has rare exposure, (2) Good = inadvertent exposure once per month, (3) poor = exposure 1–2 times per week,

(4) noncompliant = not on a GFD, or (5) unable to assess GFD adherence from medical record (12).

Statistical Approach

Categorical data are presented as frequency (percentage) and group comparisons made with either the Pearson chi-squared statistic or Fisher's exact test when the expected cell count was <5. Continuous data are described as mean±SD if normally distributed and median (interquartile range; IQR) otherwise. Most continuous outcomes were right-skewed and therefore group comparisons were made with the Wilcoxon rank-sum test. Two-group comparisons of normally distributed variables were evaluated by Student's t-test. All tests of significance were two-sided with $\alpha = 0.05$, and all analysis performed with SAS (Cary, NC).

Results

Subject Characteristics (Table 1)

At the time of data collection 103 subjects were identified for inclusion into the study. Subjects were 10.6±5.0 years of age at diagnosis and 60% were female. Consistent with the literature, tTG performed well at diagnosis with 89% of subjects with a positive IgA tTG. Eleven subjects had a negative tTG at diagnosis. Two subjects with a normal IgA tTG were asymptomatic at diagnosis. One of these subjects was IgA deficient, homozygous for DQ2, and had a family history of celiac disease. This patient underwent endoscopy to evaluate a gastric lesion and was found to have duodenal villous blunting. The second asymptomatic subject had a normal IgA tTG but an elevated IgA EMA and a family history of CD which prompted the endoscopy. The other nine patients had gastrointestinal complaints which prompted an evaluation by a gastroenterologist. Six out of nine individuals had HLA testing which confirmed genetic susceptibility for CD. One of these six patients had an elevated IgA EMA in the presence of a normal IgA tTG and one patient was IgA deficient. Of the three patients that had gastrointestinal complaints, normal IgA tTG, and no HLA testing, one patient had an elevated IgA EMA, one patient was under two years of age, and all three had improvement on a gluten free diet with subsequent resolution of villous atrophy upon repeat endoscopy.

Overall, the majority of subjects presented with gastrointestinal complaints such as abdominal pain and constipation. Approximately 14% of subjects were asymptomatic at diagnosis and identified via routine screening of high-risk populations. Additionally, 12% of subjects in our population had a comorbid autoimmune disease such as type 1 diabetes or thyroiditis. In line with the inclusion criteria, all subjects had intestinal enteropathy consistent with a Marsh 3 lesion at diagnosis.

Patient Characteristics at Repeat Biopsy (Table 2)

At the time of the repeat endoscopy, subjects had been following a GFD for a median of 2.4 years (IQR 1.4–4.0) with a range of 1–12 years. In most cases, patients had more than one indication for a repeat endoscopy. The most common indications for repeat endoscopy were due to persistent symptoms (43%) and new gastrointestinal symptoms (27%). Twenty-four subjects (34%) had persistently elevated serology at the time of the repeat biopsy. The

majority of subjects (91%) had excellent adherence to the GFD. One-hundred and one subjects (98%) saw a dietician. Only one subject had no record of seeing a dietician as the other subject had a sibling with CD and the family had previously seen a dietician. Thirty-four subjects (33%) were asymptomatic at the time of the repeat endoscopy. Twelve asymptomatic patients underwent a repeat endoscopy for follow-up of another disease (1 ulcer, 2 ulcerative colitis, 9 esophagitis). Eleven asymptomatic patients had a repeat endoscopy due to persistently elevated serology (two had both EOE and elevated serology). Four asymptomatic children underwent a repeat endoscopy to assess for mucosal recovery and confirm the diagnosis of celiac disease in the setting of seronegative CD. Finally seven asymptomatic patients underwent endoscopy to confirm that mucosal recovery was achieved. In total, 19% exhibited persistent enteropathy consistent with a Marsh 3 lesion at the time of the repeat endoscopy.

Predictive value of tTG in identifying Marsh 3 histology at repeat biopsy (Table 3)

In practice, IgA tTG was a poor predictor of Marsh 3 histology at repeat biopsy as sensitivity was 43%, specificity was 68%, the positive predictive value (PPV) was 25%, and the negative predictive value (NPV) was 83%. The poor predictability of IgA tTG was consistent regardless of whether subjects reported symptoms at the time of the repeat endoscopy or the duration of the GFD. Of note, repeat serology within 4 months of the repeat biopsy was available for 71 of the subjects. Subjects with serology obtained greater than 4 months from the time of the repeat biopsy were not included in this section of the analysis.

Concordance of IgA tTG with histology at repeat biopsy

At the time of the follow-up biopsy, tTG was elevated in 43% of subjects with persistent enteropathy and 32% of subjects with mucosal healing. The overall concordance of IgA tTG with histology at the time of the repeat biopsy is shown in table 4. These numbers are based on the 71 subjects that had an IgA tTG measured within 4 months of the repeat endoscopy.

Concordance of symptoms with histology at repeat scope (Table 5.)

We examined the concordance between symptoms and mucosal recovery in the entire cohort (n=103) strictly by the presence or absence of symptoms at the time of the repeat endoscopy. We found that the majority of patients with complaints that may be related to CD had mucosal recovery 84%) (Marsh 0–2). However, 45% of patients with persistent enteropathy were asymptomatic. Twenty-six percent of the 23 asymptomatic patients who underwent repeat endoscopy to follow-up another disease (12), to assess for mucosal recovery due to seronegativity at diagnosis (4), or to assess for mucosal recovery (7), had persistent enteropathy. Twenty-seven percent of the 11 asymptomatic patients who underwent repeat endoscopy due to an elevated tTG had persistent enteropathy.

Comparison of select characteristics by Marsh severity at repeat endoscopy

We found no significant characteristics predictive of persistent enteropathy. Sex, age at diagnosis, presence of a positive tTG within four months of the repeat endoscopy, and self-reported adherence to a GFD were not significantly different in subjects with persistent

enteropathy compared to those in remission. Additionally, there was no significant difference in frequency of persistent enteropathy when comparing subjects maintaining a GFD for more than two years compared to those maintaining a GFD for less than two years. Finally, there was no difference in Marsh severity between subjects that reported symptoms at the time of the repeat endoscopy compared to those who did not.

Discussion

Historically, making the diagnosis of CD required three phases and three biopsies (13). The current protocol, which requires only one biopsy, relies upon the assumption that the vast majority of children with CD experience complete mucosal recovery after one year of a GFD. (14,15). These guidelines, drafted over 25 years ago were based on clinical evidence. However, over the past several decades there has been a shift to an older age at onset of CD and milder enteropathy at diagnosis. These findings along with the transformation in clinical presentation from almost exclusively gastrointestinal symptoms to a more diverse, systemic presentation provide further evidence that pediatric CD has changed (16,17,18,19,20). Despite this, the need for a follow-up biopsy has not been revisited and the need for an initial biopsy to confirm the disease in pediatric patients has been questioned. Data from adult patients with CD suggest the persistence of enteropathy in more than 33% of patients on a GFD, irrespective of symptoms or positive serology (7,8). This persistent enteropathy in adults has been associated with an increased risk of lymphoma, low bone density, and fracture (21,22,23). To date there is no clear understanding of the risk of mortality. In children, the long-term consequences of suboptimal healing are also unclear. However, malabsorption and ongoing inflammation in children may have negative repercussions on physical and cognitive development.

In our population, 19% of pediatric patients on a GFD had persistent enteropathy despite treatment on a GFD for at least one year. Forty-five percent of patients with persistent enteropathy were asymptomatic at the time of the repeat endoscopy. The majority of asymptomatic patients with CD who underwent a repeat endoscopy did so to assess mucosal recovery due to a different gastrointestinal disorder (ulcer, EOE, UC) and duodenal biopsies were taken for completeness. Four patients with seronegative CD at diagnosis underwent a repeat endoscopy to confirm CD remission, 7 others were evaluated to confirm remission of CD and the remaining asymptomatic patients underwent a repeat endoscopy due to persistently elevated tTG. The frequency of persistent enteropathy noted is similar to findings from Ghazzawi et al. who found that 15% of pediatric patients with CD had persistent enteropathy on a GFD. The frequency of persistent enteropathy in our work is higher than Bannister et al. and Vecsei et al. who reported persistent enteropathy in 5% and 9% of pediatric patients with CD on a GFD respectively (24,25,26). We found that 15.9% of patients with symptoms at the time of the repeat endoscopy had persistent enteropathy while 26% of asymptomatic patients had persistent enteropathy at repeat endoscopy. Characteristics including presence of symptoms at the time of the repeat endoscopy, persistently elevated tTG, and following the GFD for less than two years were not predictive of persistent enteropathy. Poor adherence, particularly in teenagers could be a potential reason for persistent enteropathy especially in patients that do not report symptoms. However, in this group of patients who underwent repeat endoscopy, adherence to the GFD

was evaluated by a dietician or gastroenterologist and 91% of subjects were found to have excellent adherence to the GFD. This high level of adherence may not reflect our general patient population however. Patients with symptoms or persistently elevated IgA TTG and clearly identified nonadherence/ongoing gluten exposure are unlikely to undergo repeat endoscopy as often as children without clear gluten exposure and would therefore not be included in this analysis.

IgA tTG was not an accurate measure of mucosal recovery in this population of pediatric patients with CD on a GFD. The NPV of IgA tTG was highest at 87% in patients treated with a GFD for more than two years however PPV was poor at 36%. Additionally, the NPV of tTG was not improved when correlated with the presence or absence of symptoms at the repeat endoscopy. Overall at the time of the follow-up biopsy, tTG was elevated in 43% of subjects with persistent enteropathy and 32% of subjects with mucosal healing. Specifically in subjects that were symptomatic at the time of the repeat endoscopy, 84% had mucosal recovery upon repeat biopsy. Only 55% of patients with persistent enteropathy at the time of the repeat endoscopy were symptomatic. Therefore, in our population, neither the presence of symptoms nor a positive tTG could be relied upon as a measure of mucosal recovery in patients with CD on a GFD.

Despite the clinical practice and endorsement of using serological tests as markers of dietary adherence and mucosal recovery in pediatric patients with CD on a GFD, these serology tests have not been validated for this purpose. Our findings raise concerns about this monitoring approach. Identifying the frequency of persistent enteropathy in children is important to begin to understand term consequences that may be associated with it. Furthermore identifying minimally invasive accurate surrogate endpoints for patients is of utmost importance to identify patients that may benefit from potential for new therapeutic agents that may serve as adjuvant medications to the GFD(27). Our work is in agreement with previous research that supports a lower accuracy of serological studies at the time of follow-up endoscopy compared to at diagnosis in patients with CD on a GFD. Bannister et. al evaluated 150 pediatric patients (mean age 7.5 years) diagnosed with CD who had been on a GFD for a mean of 1.4 years (25). They found that 5% of patients had persistent mucosal damage defined as Marsh 3 histology. In this study, IgA tTG and IgG deamidated gliadin peptides (DGP) were measured and used in combination at the time of the repeat endoscopy resulting in a sensitivity of 65% and specificity of 85%, a positive predictive value (PPV) of 22% and negative predictive value (NPV) of 98% (25). When the statistical approach was repeated with any equivocal values regarded as “positive” the NPV improved to 100% but the specificity dropped to 68%. While this combined approach resulted in a higher NPV, accuracy overall compared to diagnosis was sub-optimal. A separate study evaluated 53 children with CD (mean age 11.3 years) who underwent repeat endoscopy after approximately 2.2 years on a GFD (26). This study found that 9% of patients had persistent mucosal damage defined as Marsh 3 histology at the time of follow-up. In this study, the sensitivity of IgA tTG was 83% and specificity was 87% (26). These studies provide further evidence that current serological tests used as surrogate endpoints for mucosal recovery need further investigation. IgA tTG in combination with IgG DGP may provide a more accurate measure of mucosal recovery at the time of the repeat endoscopy. The negative predictive value of these tests when used in combination may be quite powerful.

The utility of IgG DGP as a marker of mucosal disease in patients with CD on a GFD was corroborated in a recent comprehensive study evaluating twelve serological tests at the time of follow-up endoscopy in adult patients with CD on a GFD (28). This study used retrospective samples to examine 100 adult patients with CD who underwent a repeat biopsy after an average of 4.5 years on a GFD. In addition to finding that the manufacturer cutoff levels created for the diagnosis of CD are sub-optimal for patients with CD on a GFD, this study also showed that the IgG DGP correlated with residual intestinal damage as measured by a follow-up small intestinal biopsy in adult patients (28).

While we did not identify predictors of persistent mucosal damage in this pediatric population, Lebwohl et al. evaluated 7648 children and adults over an 8 year period in order to determine what factors may be predictive of persistent villous atrophy. In this study, 31% of patients had persistent villous atrophy at the time of the follow-up endoscopy which occurred at a median time of 1.3 years (29). Persistent villous blunting was more common in older patients and males, and less common in patients with higher educational attainment (29).

The limitations of our study include that the IgA tTG assay was run in multiple laboratories due to the retrospective nature. While not ideal, all laboratories were CLIA certified. For this reason and the purposes of the study, IgA tTG was dichotomized as positive or negative according to the cut off levels supplied by the laboratory performing the test. Additionally, we included only serology tests run within 4 months of the repeat endoscopy which reduced our sample size to 71 subjects for part of the analysis. Since both Boston Children's Hospital and MassGeneral Hospital *for* Children are quaternary care centers, the results may not be generalizable to other institutions. Studies have suggested that patients referred to specialized centers were three times more likely to have non-responsive celiac disease (NRCD) than those initially followed at the quaternary care center (30). Furthermore, the use of centralized pathology reading, standard biopsy procedures including standardized locations and numbers of biopsies, and evaluating the mucosa for villous height to crypt depth ratio would provide a more accurate measure of mucosal recovery. Additionally, there was a wide range of time during which the repeat endoscopy was performed which does not allow us to comment on the natural history of mucosal recovery in pediatric CD. Finally, while all patients were advised about the GFD by a knowledgeable dietician, their adherence assessment was based on physician and or dietician report at the time of the clinic visit in this study.

We found that 19% of pediatric patients with CD on a GFD may have persistent enteropathy. While the long term effects are not known, persistent enteropathy may predispose pediatric patients with CD to future complications and suboptimal growth. Evidence in adult patients with CD is accumulating that not only is persistent enteropathy common but that the presence of symptoms is not predictive of enteropathy. Additionally, IgA tTG, while accurate at diagnosis, is a poor predictor of persistent enteropathy in children with CD on a GFD irrespective of whether symptoms are present. While current guidelines do not suggest a repeat endoscopy to assess for mucosal recovery, it is the only way to confirm it. Given the mounting evidence in adults, our concern for persistent enteropathy, particularly in growing children led to this retrospective study. Due to the retrospective nature, we cannot comment

on the natural history of mucosal recovery in patients with CD on a GFD as patients did not undergo repeat endoscopy at a pre-determined time point. Therefore, these findings must be confirmed prospectively and systematically in order to evaluate the natural history of mucosal recovery in pediatric patients with CD on a GFD. Long term complications including growth trajectory must be monitored and further study evaluating available treatment options beyond the GFD and timing of subsequent endoscopies in patients found to have persistent enteropathy must be established. Our findings, show that nearly one in five children with CD may have persistent enteropathy despite maintaining a strict GFD (based on self-report and provider assessment) and that IgA tTG is not an accurate marker of mucosal healing. These findings suggest the need not only for a baseline endoscopy to confirm the diagnosis of CD, but consideration of a repeat endoscopy to confirm remission. These findings suggest that prospective studies which include objective measurements of dietary transgression are needed to establish whether the management criteria of CD in childhood should be revisited.

Acknowledgments

Funding:

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was conducted with support from the Harvard Digestive Disease Center HDDC (NIH/NIDDK, 5 P30 DK34854) and the Harvard Catalyst | The Harvard Clinical and Translational Science Center (NCRR and NCATS, NIH Award UL1 TR001102) and financial contributions from Harvard University and its affiliated academic health care centers.

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1. WHAT IS KNOWN

- Over 90% of pediatric patients with celiac disease achieve mucosal recovery after one year on a gluten free diet.
- Current guidelines recommend follow-up serology both to assess dietary adherence and for use as a surrogate marker of mucosal recovery

2. WHAT IS NEW

- 1 in 5 children with celiac disease may have persistent enteropathy despite adherence to a GFD
- IgA tTG may not be accurate marker of mucosal recovery in these patients
- We did not identify characteristics predictive of persistent enteropathy in this population

Table 1

Subject characteristics at diagnosis of celiac disease (n=103).

Characteristic	Statistic
Female sex	62 (60.2%)
Age at diagnosis (y)	
Mean $\pm$ SD	10.6 $\pm$ 5.0
Other autoimmune disorder	12 (11.7%)
¹ Positive or borderline serology at diagnosis	91 (89.2%)
² Symptoms at diagnosis	88 (85.4%)
Abdominal pain	52 (59.1%)
Constipation	26 (29.6%)
Weight loss; poor weight gain	21 (23.9%)
Diarrhea	20 (23.0%)
Nausea and/or vomiting	19 (21.6%)
Abdominal distention	17 (19.3%)
Fatigue	12 (13.6%)
Short stature; poor growth	10 (11.4%)
Loss of appetite	7 (8.0%)
Reflux	6 (6.8%)
Arthralgia; arthritis; joint problems	5 (5.8%)
Neurologic	5 (5.7%)
Gassiness	4 (4.6%)
Rash	4 (4.6%)
Marsh 3 at initial biopsy	103 (100%)

¹ Serology data from the time of diagnosis unavailable for 1/103 subjects.² Symptoms ascertained from medical chart review.

Table 2

Subject characteristics at repeat endoscopy (n=103).

Characteristic	Statistic
Symptomatic	
Yes	69 (67.0%)
No	34 (33.0%)
Reason for repeat endoscopy *	
Persistent symptoms	44 (42.7%)
New symptoms	28 (27.2%)
Esophagitis follow-up	14 (13.6%)
Confirm CD resolution only **	11 (10.7%)
New/additional diagnosis suspected	10 (9.7%)
Other endoscopic finding follow-up	2 (1.9%)
Months from start of GFD to repeat scope	
Median (IQR)	29.0 (16.8, 48.1)
Range	12.0 – 144.0
Dietetic counseling	101 (98.1%)
Adherence to GFD	
Excellent	94 (91.3%)
Good	5 (4.9%)
Fair	1 (1.0%)
Non-compliant	2 (1.9%)
Unable to assess from medical record	1 (1.0%)
Repeat serology positive or borderline ***	24 (33.8%)
Marsh score at repeat biopsy	
0	63 (61.2%)
1	14 (13.6%)
2	6 (5.8%)
3	20 (19.4%)

* Patients had more than one reason for a repeat endoscopy. Reason was determined by chart review and therefore is >100%.

** Seven patients were asymptomatic and repeat endoscopy was performed to confirm CD resolution, four patients had seronegative CD at diagnosis and repeat endoscopy was performed to confirm CD resolution.

*** Repeat serology was only included if it was measured within 4 months of the date of repeat endoscopy (N=71).

Table 3

Test performance of IgA tTG in predicting marsh 3 histology at repeat biopsy

Group	N	Se	Sp	PPV	NPV	Accuracy
Overall	71	0.43	0.68	0.25	0.83	0.63
Symptomatic at repeat biopsy						
Yes	49	0.25	0.73	0.15	0.83	0.65
No	22	0.67	0.56	0.36	0.82	0.59
Months on GFD						
<24	30	0.20	0.52	0.08	0.76	0.47
≥24	41	0.56	0.81	0.45	0.87	0.76

* Repeat serology was only included if it was measured within 4 months of the date of repeat endoscopy (N=71).

Table 4

Concordance of IgA tTG with histology at repeat biopsy

Marsh Score	Frequency (%)	tTG Positive (%)
0	41 (57.8)	11/41 (26.8)
1	11 (15.5)	6/11 (54.5)
2	5 (7.0)	1/5 (20)
3	14 (19.7)	6/14 (42.9)

* Repeat serology was only included if it was measured within 4 months of the date of repeat endoscopy (N=71).

Table 5

Concordance of symptoms with histology at repeat biopsy

Marsh Score	Frequency (%)	Symptoms Present (%)
0	63 (61.2)	43/63 (68.3%)
1	14 (13.6)	11/14 (78.6%)
2	6 (5.8)	4/6 (66.7%)
3	20 (19.4)	11/20 (55.0%)

*
Reported for all patients (N=103).