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ORIGINAL ARTICLE

Histopathological Practices of Handling, Processing and Interpretation of Small Intestinal Biopsies for Diagnosis and Management of Celiac Disease

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ABSTRACT

Aim: Evaluate the histological findings of celiac disease and to analyze the variations that occurred in biopsies. We aimed to execute the GFD method which helps us in diagnosing and managing celiac disease during follow-up.
Methodology: This retrospective study was conducted at the Rawalpindi Medical University hospital from September 2020 to September 2021. Standard bioptic forceps and flexible endoscopes were used to perform upper GIT endoscopy and biopsies. For every patient, we collected 4 biopsy specimens from the duodenum. We cut 3µm thick sections from each block and stained them in a hematoxylin compound. We counted intraepithelial lymphocytes using anti-CD3 immuno histochemical staining.
Results: We recruited 69 celiac patients with a total of 2,760 power fields. Out of these 69 patients, 52 were (76%) females and 17 (24%) were males. Patients from the age range 14 to 69 were recruited. The mean age of patients was reported as 39 ± 15 years. By the EF method, we observed improvement in histological patterns of 8 patients, and one remain unchanged. Only 2 cases reported worsened histological outcomes.
Conclusion: Interpretation of duodenal biopsies demands different methods of analysis based on the clinical settings to address the presence of atrophy and improvements in CD patients.
Keywords: Celiac disease, Marsh-Oberhuber scale, endoscopy

INTRODUCTION

Celiac disease is one of the most common autoimmune small intestine disorders which arises due to gluten ingestion and is triggered by genetically susceptible subjects[1]. Celiac disease has a variety of symptoms ranging from severe malabsorption or subclinical or silent symptoms only observed during screening[2]. The diagnosis of Celiac disease (CD) is based on the detection of anti-transglutaminase type 2 IgA autoimmune antibodies and histological findings of duodenal. Mucosal findings including damage to the enterocyte surface, increase intraepithelial lymphocytes (IELs), crypt hyperplasia, and villous atrophy plays a fundamental role in diagnosing celiac disorders[4] however, these alterations are not only completely specific to CD. Therefore, histology is considered as the golden standard for diagnosing CD in adults[3].

We aimed to execute the GFD method which helps us in diagnosing and managing celiac disease during follow-up.

METHODOLOGY

This retrospective study was conducted at the Rawalpindi Medical University hospital from the September 2020 to September 2021 after permission from Ethical Review Board. All the patients attending the centre for the prevention and diagnosis of celiac disease from the year 2019 to 2020 were recruited. All the patients with duodenal histology who followed the gluten-containing diet and those who were on GFD for at least one year were included. We excluded all the patients with IgA deficiency. For this research, we categorized celiac disorder as a classical and non-classical category associated with dermatitis herpetiformis presence. In the classical category, we classified patients with symptoms of diarrhea, weight loss, and longitudinal growth retardation. On the other hand, in the non classical category, we categorized patients with symptoms of dyspepsia, anemia, hypertransaminasemia, and osteopenia. Our studies were conducted after attaining ethical consent from the ethic and research committee of the institution. Written consents were obtained from each participant Standard bioptic forceps and flexible endoscopes were used to perform upper gastrointestinal endoscopy and biopsies. For every patient, we collected four biopsy specimens from the duodenum. We used SPSS 23.0 for statistical analysis.

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RESULTS

For this clinical and histological study, we recruited 69 Celiac patients with a total of 2,760 power fields.

Table 1: Demographic and clinical manifestations

Variables	N (%)
Mean age	39 ± 15 years
Male	17 (24 %)
Female	52 (76 %)
Associated autoimmune disease	12 (17 %)
Hashimoto's thyroiditis	9/12
Alopecia	2/12
Sjogren's disease	1/12
Classical onset	34 (50 %)
Non- classical	25 (36 %)
Dermatitis herpetiformis	3 (4%)
Familial screening	7 (10 %)

Table 2: Celiac patients with or without duodenal atrophy

Variables	**celiac patients with duodenal atrophy(n= 37)**	**celiac patients without duodenal atrophy(n= 32)**
Mean age	39 ± 17	33 ± 12
Male	9 (24.3%)	8 (25%)
Female	28(75.6%)	24 (75%)

P value 0.089

Table 3: Histological evaluation of duodenal biopsies of Celiac patients using EF method

Variables	**Gluten free diet (Treated)**	**Gluten containing diet (Untreated)**
Marsh0	0	29(42%)
Marsh1	1(1.4%)	1(1.4%)
Marsh2	1(1.4%)	3(4.3%)
Marsh3a	18(26%)	25(36.2%)
Marsh3b	17(24.6%)	20(33,3%)
Marsh3c	8(11.5%)	60(86.9%)

Table 4: Histological evaluation of duodenal biopsies of Coeliac Patients

Marsh-Oberhuber grade	**During Gluten-free diet**	**At diagnosis**
Grade 3c	8 (11%)	49 (72%)
Grade 3b	12 (17%)	10 (14%)
Grade 3a	17 (25%)	10 (14%)
Grade 2	1 (1%)	0 (0%)
Grade 1	11 (17%)	0 (0%)
Grade 0	20 (29%)	0 (0%)

Table 5: Histological evaluation of duodenal biopsies of Celiac patients using Marsh-Oberhuber grading

Marsh-Oberhuber grade (%)											
At diagnosis				During GFD							Outcomes
IELs %	3c	3b	3a	IELs %	3c	3b	3a	2	1	0	
31%	100%	0	0%	48%	85%	0%	15%	0%	0%	0%	Improved
42%	0%	30%	70%	46%	0%	80%	20%	0%	0%	0%	Improved
23%	100%	0	0%	45%	15%	35%	50%	0%	0%	0%	Improved
55%	100%	0%	0%	32%	60%	30%	0%	0%	10%	0%	Improved
47%	0%	90%	10%	64%	5%	95%	0%	0%	0%	0%	Worsened
45%	100%	0%	0%	38%	60%	40%	0%	0%	0%	0%	Improved
49%	100%	0%	0%	31%	30%	0%	0%	0%	20%	50%	Improved
56%	100%	0%	0%	61%	75%	20%	0%	5%	0%	0%	Improved
4%	0%	0%	100%	12%	0%	0%	75%	5%	0%	20%	Improved
27%	60%	40%	0%	34%	100%	0%	0%	0%	0%	0%	Worsened
53%	0%	100%	0%	35%	0%	100%	0%	0%	0%	0%	Unchanged

DISCUSSION

We observed that the novel approach (EF method) causes significant changes in histological reports and reported evolution outcomes of injury. This approach also assists us in differentiating the duodenal injuries instead of the classical MO method. Different methods have been proposed to classify the duodenal injury in CD patients including the Marsh method[6] and its modification by Oberhuber[4]. Past study of Laffer[7] reported the IELs variations with the correlation of gluten intake. Furthermore, these studies also focused on the villus area, its depth, and ratio and associate them with the gluten intake. However, these parameters are difficult to apply in clinical settings. These parameters are not enough to build correlation with Marsh grade and need a modified grading system. Our study did not find any significant difference in duodenal histology of CD patients with or without GFD because our main focus was to detect the atrophy. We summarized these patterns in the Marsh-Oberhuber classification. However, the effects of GFD can be used in the interpretation of further diagnosis. We observed slow and absent histological responses in adult patients who were on a strict GFD regimen. We did not observe complete or partial normalization of mucosal atrophy in these patients[5]. These results are persistent with the previous endoscopic studies in which they observed similar macroscopic signs of intestinal atrophy[8].

During the Gluten-free diet, we observed a successful association of serological tests (anti-tissue transglutaminase IgA) with clinical responses but at the same time, both of these were not correlated with mucosal healings (histological improvement). The gap between serological findings and histological improvements causes severe obstacles in managing the persistent cases of mucosal atrophy. The recent study of Kaukinen et al[9] also reported the same results in which they observed no association between gluten ingestion and increased amount of anti-transglutaminase IgA titers. Involvement of the small bowel is highly observed in autoptic studies in which they reported a decrease in mucosal injury from proximal to the distal tract of the small intestine[10].

To examine the complete picture of involvement, at least 4 duodenal endoscopic biopsies are highly recommended by our side. For complete understanding, our patients underwent complete endoscopic investigation before and after GFD. This complete analysis highlights the questions related to incomplete normalization of the intestinal mucosa and future risks of CD complications. Somehow, we observed a correlation between the mucosa damage and CD complications but we recommend that serological findings should be needed for patient management. The k test value of our study reported good agreement between the interpretations of both pathologists still we recommend it to use in tertiary settings by expert pathologists.

CONCLUSION

Interpretation of duodenal biopsies demands different methods of analysis based on the clinical settings to address the presence of atrophy and improvements in CD patients.

Conflict of interest: Nil

REFERENCES

1. Elli L, Discepolo V, Bardella MT et al. Does Gluten Intake Influence the development of celiac disease-associated complications? J Clin Gastroenterol. 2014;48(1):13–20.
2. Fasano A, Catassi C. Clinical practice. Celiac disease. N Engl J Med. 2012;367(25):2419–26.
3. Jamma S, Rubio-Tapia A, Kelly CP et al. Celiac crisis is a rare but serious complication of celiac disease in adults. Clin Gastroenterol Hepatol. 2010;8(7):587–90.
4. Oberhuber G, Granditsch G, Vogelsang H. The histopathology of celiac disease: time for a standardized report scheme for pathologists. Eur J Gastroenterol Hepatol. 1999;11(10):1185–94.
5. Bardella MT, Velio P, Cesana BM et al. Coeliac disease: a histological follow-up study. Histopathol. 2007;50(4):465–71.
6. Marsh MN. Gluten, major histocompatibility complex, and the small intestine. A molecular and immunobiologic approach to the spectrum of gluten sensitivity ('celiac sprue'). Gastroenterol. 1992;102(1):330–54.
7. Leffler D, Schuppan D, Pallav K et al. Kinetics of the histological, serological and symptomatic responses to gluten challenge in adults with celiac disease. Gut. 2013;62(7):996–1004.
8. Lanzini A, Lanzarotto F, Villanacci V et al. Complete recovery of intestinal mucosa occurs very rarely in adult celiac patients despite adherence to gluten-free diet. Aliment Pharmacol Ther. 2009;29(12):1299–308.
9. Kaukinen K, Sulkanen S, Maki M et al. IgA-class transglutaminase antibodies in evaluating the efficacy of gluten-free diet in celiac disease. Eur J Gastroenterol Hepatol. 2002;14(3):311–5.
10. Macdonald WC, Brandborg LL, Flick AL et al. Studies of celiac sprue. Iv. the Response of the Whole Length of the Small Bowel to a Gluten-Free Diet. Gastroenterology. 1964;47:573–89.