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ORIGINAL ARTICLE

A Multicenter Cross Sectional Study to Evaluate the Role of Duodenal Bulb Biopsy in the Diagnosis of Celiac Disease

MUHAMMAD AASIM KHAN[1], MOHAMMAD HANIF[2], KAPEEL RAJA[3], NAEEM ABBAS GILANI[4], AMANULLAH KHOKHAR[5], AMJAD ALI[6]
[1]*Assistant Professor Gastroenterology Department Gajju Khan Medical College, Swabi*
[2]*Assistant Professor Gastroenterology, Northwest General Hospital & Research Centre Hayatabad, Peshawar*
[3]*Associate Professor Department of Gastroenterology, Hepatology & Nutrition, Pir Abdul Qadir Shah Jilani Institute of Medical Science Gambat Khairpur, Sindh (Formerly known as Gambat Institute of Medical Science, Gambat*
[4]*Senior Registrar Gastroenterology and Hepatology, DHQ Teaching Hospital, Sargodha*
[5]*Assistant Professor Medicine, Al Tibri Medical College and Hospital, Malir Karachi/ Isra University Campus, Hyderabad*
[6]*Professor Medicine, BKMC / Mardan Medical Complex, Mardan*
Corresponding author: Mohammad Hanif, Email: mhanifdr@yahoo.com, Cell: +923009006267

ABSTRACT

Background and Aim: A systemic immune disorder elicited by dietary gluten in people who are genetically predisposed to it is referred to as a celiac disease. D1 had been ruled out as a biopsy site due to concerns about Brunner's glands, peptic duodenitis, gastric metaplasia, and presumed reduced villous height. Due to histological confounding factors, the duodenal bulb (D1) as a biopsy site was traditionally avoided. The present study aimed to assess the duodenal bulb biopsy role in the diagnosis of celiac disease.

Methodology: This multicenter cross sectional study was conducted on 108 celiac disease patients in the department of Gastroenterology, Bacha Khan Medical Complex, Swabi, North West General hospital Peshawar and Pir Abdul Qadir Shah Jilani Institute of Medical Science Gambat Khairpur, Sindh from September 2020 to July 2021. All the celiac disease patients were clinically symptomatic and had anti-tissue transglutaminase (anti TTG IgA) positive antibodies. Endoscopically, six mucosal biopsies were taken from each patient, four each from the distal duodenum and two additional biopsy separately labelled was taken from bulb. Modified Marsh grading was used for morphological grading.

Results: Of the total 108 Celiac disease patients, 60 (55.6%) were females and 48 (44.4%) were male patients. the overall mean age was 32.62±6.4 years. Prior to diagnosis of Celiac disease, symptoms median duration was 5.4 years with a range of 6 months to 40 years. The most prevalent clinical presentation were iron deficiency anemia 43% (n=46) and chronic diarrhea 32% (n=35) respectively. Other clinical presentation were chronic pain abdomen, infertility, short stature, and cirrhosis. Elevated TTG of 117.1 ± 49.82 U/ml was measured in all the patients with a range of 20 to 250 U/ml. The incidence of similar and different modified Marsh grade was in 66 (61.1%) and 42 (58.9%) respectively at both site. Out of 42 different modified March grade patients, higher mucosal atrophy in bulb and descending duodenum showed higher grade in 16 and 26 patients respectively. Isolated bulb involvement was seen in nine patients. Due to bulb biopsy, Celiac disease diagnosis was correctly done in these patients.

Conclusion: The present study supported the villous atrophy and intraepithelial lymphocytosis patchy nature in biopsy specimens of celiac disease. The diagnosis of celiac disease improved with inclusion of duodenal bulb biopsies in our sampling protocol. Celiac disease patchy nature and distribution demonstrated different Marsh grades in different biopsy sites. The celiac disease diagnostic yield is increased by combining the bulb and the descending duodenum biopsy.

Keywords: Celiac Disease, Duodenal bulb biopsy, Modified Marsh grade

INTRODUCTION

Celiac disease a systemic immune disorder elicited by dietary gluten in people who are genetically predisposed to it. The basic requirement for celiac disease diagnosis is the presence of biopsy specimen histological alterations classified based on Marsh grade taken from the descending duodenum [1, 2]. Gluten is the protein composite group found in barley, wheat, and rye. Celiac disease is distinguished by a various clinical manifestations, histologically small intestinal mucosa visible damage, and a specific serum antibody response [3]. Internationally, the prevalence of celiac disease ranges from 0.2 to 1.0% [4, 5]. Celiac disease, also known as gluten-sensitive enteropathy, can cause symptoms like diarrhea, bloating, fatigue, and symptomatic malabsorption. Intestinal lymphoma, deficiency of vitamin B12 and D, and iron deficiency anemia, hypocalcemic tatny , short stature and infertility could results if celiac disease is left untreated, emphasizing the importance of an accurate diagnosis [6, 7].

The considerable overlap between gastroenterological disorders and celiac disease delays the celiac disease diagnosis and becomes challenging regardless of ensuring the proper identification [8]. The celiac disease diagnosis includes with or without duodenal biopsy usage via tissue transglutaminase antibody (TTG-IgA) and serologic testing. Traditionally, biopsies were taken from the distal duodenum (i.e., sections duodenal stage 2 [D2] through D4). However, an increasing number of studies have evaluated biopsy of the duodenal bulb (sectionD1) for celiac disease diagnosis in adult and pediatric populations [9, 10]. Furthermore, peptic duodenitis and the possibility of gastric metaplasia at D1 complicate the histological diagnosis of Celiac disease [11]. However, a recent study suggested that D1 biopsies can be interpreted and might cause villous atrophy site in newly diagnosed Celiac disease [12]. However, the increased detection rate by including a D1 biopsy has not been proven in other studies [13]. The primary goal of this study was to assess the role of duodenal bulb biopsy in the diagnosis of celiac disease.

METHODOLOGY

This prospective study was conducted on 108 celiac disease patients in the department of Gastroenterology, Gajju Khan Medical College, Swabi, Northwest General hospital Peshawar and Pir Abdul Qadir Shah Jilani Institute of Medical Science Gambat Khairpur, Sindh from September 2020 to July 2021. All the celiac disease patients were clinically symptomatic and had anti-tissue transglutaminase (tTG) positive antibodies. Endoscopically, four mucosal biopsies were taken from distal duodenum and two biopsies from duodenal bulb in each patient. Modified Marsh grade was used for morphological grading. Patients with signs and symptoms of celiac disease (IgA anti-TTG >15 U/ml) and positive celiac serology (IgA anti-TTG >15 U/ml) with written consent were included. Patients who had previously been diagnosed with Celiac Disease were excluded from the study. Endoscopy was performed on the patients, and duodenal biopsies were obtained (two from duodenal bulb and four from descending duodenum). Patients were diagnosed with Celiac Disease if they had positive IgA TTG as well as histological evidence of increased crypt hyperplasia, intraepithelial lymphocytes (IELs), and villous atrophy (modified Marsh 3a–3c) in any of their biopsies.

The modified Marsh classification was used to evaluate and classify all histologic parameters: Type 0 represents normal mucosa; type 1 represents infiltrative (40 intraepithelial lymphocytes/100 epithelial cells); type 2 represents crypt hyperplasia; type 3A represents mild villous atrophy; type 3B represents marked villous flattening; and type 3C represents total villous atrophy. Fixed-effects models were used to determine effect size and 95 percent confidence intervals for duodenal bulb and distal duodenal biopsy data (CIs).

RESULTS

Of the total 108 Celiac disease patients, 60 (55.6%) were females and 48 (44.4%) were male patients. the overall mean age was 32.62±6.4 years. Prior to diagnosis of Celiac disease, symptoms median duration was 5.4 years with a range of 6 months to 40 years. The most prevalent clinical presentation were iron deficiency anemia 43% (n=46) and chronic diarrhea 32% (n=35) respectively. Other clinical presentation were chronic pain abdomen, infertility, short stature, and cirrhosis as shown in Figure-1. Elevated TTG of 117.1 ± 49.82 U/ml was measured in all the patients with a range of 20 to 250 U/ml. Figure-2 illustrate the gender distribution. The incidence of similar and different modified Marsh grade was in 66 (61.1%) and 42 (58.9%) respectively at both site. Out of 42 different modified March grade patients, higher mucosal atrophy in bulb and descending duodenum showed higher grade in 16 and 26 patients respectively. Isolated D1 involvement was null in Celiac disease patients. Due to bulb biopsy, Celiac disease diagnosis was correctly done in nine patients. Type 3 histology with intraepithelial lymphocytes >30/100 was the prevalent of modified Marsh grade in most of the biopsies. Villous atrophy either total, crypt hyperplasia, or altered villous of type 3C was prevalent in 44.4% patients. Villous atrophy is evidence by at least single site biopsy or descending duodenum in all celiac disease patients. Type 3C lesion of total villous atrophy was found in 44 (40.7%) bulb and 53 (49.1%) in descending duodenum. Raised IELs was showed and found uncommon in Type 1. Type 2 morphology was found in 17 (15.7%) patients as shown in Table-1.

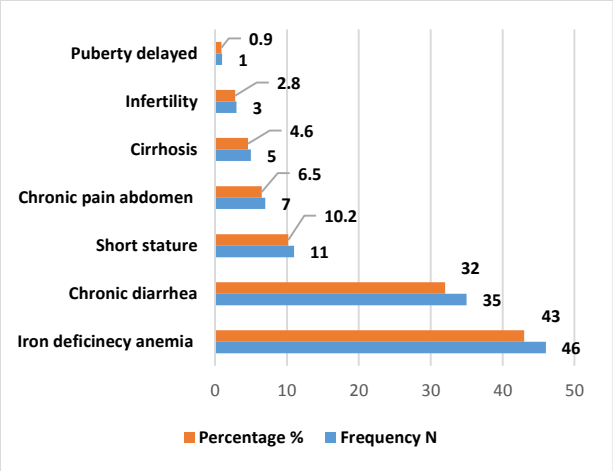

Figure-1: Celiac disease presenting symptoms

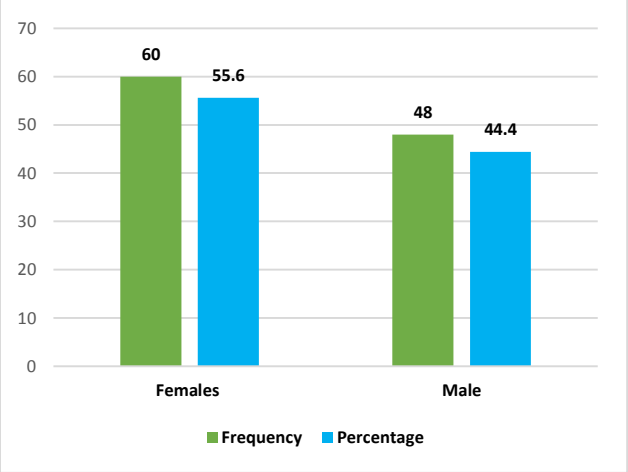

Figure-2: Gender distribution

Table-I: Biopsies from the duodenum bulb and descending duodenum were histologically graded using the modified Marsh criterion.

Modified Marsh Grades	1	2	3A	3B	3C
Duodenal bulb (D1)	4 (3.7%)	11 (10.2%)	13 (12%)	38 (35.2%)	42 (38.9%)
Descending Duodenum	0	6 (5.6%)	12 (11%)	36 (33.3%)	54 (50%)
Total	4 (1.9%)	17 (7.9%)	25 (11.6%)	74 (34.3%)	92 (42.6%)

DISCUSSION

The present study supported the evidence of villous atrophy and intraepithelial lymphocytosis patchy nature in celiac disease biopsy specimens. The diagnosis of celiac disease improved with inclusion of duodenal bulb biopsies in our sampling protocol. Celiac disease patchy nature and distribution demonstrated different Marsh grades in different biopsy sites. The celiac disease diagnostic yield is increased by combining the bulb and the descending duodenum biopsy. Patients with non-classical symptoms is mostly diagnosed with celiac disease. Previous research found that diarrhea was the prevalent symptoms in patients of celiac disease [14–16].

Recent studies conducted on adults and children revealed that non-classical celiac disease (NCCeD) was common in mostly patients [17, 18]. Similarly, NCCeD like symptoms were present in majority of patients in the present study. The prevalence of iron deficiency anemia, chronic diarrhea, short stature, abdomen chronic pain, puberty, and infertility was 43%, 32%, 10.2%, 0.9% and 2.83% respectively.

Recently, a few reports [19, 20] have identified isolated D1 involvement in Celiac disease patients with normal-appearing mucosa in the distal duodenum of pediatric and adult ages. However, no Celiac disease patient in our study had completely normal histology of isolated D1 involvement at the descending duodenum. The discrepancy in this finding could be explained by the fact that all of our patients were newly Celiac disease diagnosed. Vogelsang et al described that celiac disease could be diagnosed based on duodenum biopsy taken as a sample [21].

Previous research found similar results of biopsy sample taken from duodenum and jejunum in terms of quality and slight difference in forceps size [22]. The distal duodenum biopsy samples from these patients were normal. Tissue trans-glutaminase antibody titers increased among children and adults established villous atrophy and duodenal bulb biopsies patchy nature increased in diagnosed celiac disease patients [23, 24].

Multiple biopsy samples taken from duodenum recommended that patchy nature of celiac disease among children is not throughout duodenum but disease severity varies significantly. In the present study, collected samples from bulb biopsy were fewer compared to descending duodenum resulting to insignificant diagnosis higher rate among those bulb biopsy. The likelihood of adequate orientation and peptic injury avoidance could be increased with taking 5 or more samples from bulb

biopsy. A previous study conducted on non-oriented samples found that duodenal biopsy varies 25% and celiac disease were confirmed with 4 biopsy samples with 100% confidence [25].

The present study also verified the importance of histological variance in biopsy sites. Adequate samples of biopsy 54 patients with identical degree of atrophy between D2 and bulb. Additionally, histological variation were reported in duodenum samples based diagnosis of celiac disease. Few patients were newly diagnosed and undergone follow-up testing for diagnosis of celiac disease. Intraepithelial lymphocytosis estimation could be reduced by the gastric metaplasia presence in the samples. Also, majority of patients provides interference in villous atrophy evaluation.

CONCLUSION

The present study supported the villous atrophy and intraepithelial lymphocytosis patchy nature in biopsy specimens of celiac disease. The diagnosis of celiac disease improved with inclusion of duodenal bulb biopsies in our sampling protocol. Celiac disease patchy nature and distribution demonstrated different Marsh grades in different biopsy sites. The celiac disease diagnostic yield is increased by combining the bulb with descending duodenum biopsy.

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