International Journal of Medical Research Professionals
P-ISSN: 2454-6356; E-ISSN: 2454-6364
DOI: 10.21276/ijmrp

IJMRP

Original Research Article

Importance of Duodenal Bulb Biopsy in Pediatric Patients for Diagnosis of Celiac Disease

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ABSTRACT

Background: Celiac disease (CD) is a gluten-dependent enteropathy. It is a chronic gastrointestinal disorder in which ingestion of gluten, a protein present in wheat, rye and barley leads to damage of the small intestinal mucosa by an autoimmune mechanism in genetically susceptible individuals. The current standard for diagnosing CD involves obtaining 4 biopsy samples from the descending duodenum. It has been suggested that duodenal bulb biopsies may also be useful.

Objectives: To determine the role of the addition of duodenal bulb biopsies to distal duodenum (D2) biopsies in the diagnosis of celiac disease.

Material & Methods: We enrolled 50 children prospectively who underwent upper gastrointestinal endoscopy because of positive tissue transglutaminase antibodies and biopsy as the final evaluation for suspected CD. One to four biopsies were taken from the descending duodenum distal and duodenal bulb of each patient. The histologic lesions were classified according to the Modified Marsh Oberhuber grade.

Results: The diagnosis of CD was histologically confirmed in 96% (48/50) of the cases of biopsy samples obtained from the duodenal bulb and descending duodenum. In 28 patients (56%), histology was the same in the bulb and duodenum; in 7 (14%) cases, the grade of atrophy was higher in the bulb than the descending duodenum. 13 cases (26%) had a higher histological grade in the duodenum than in the bulb. Two patients had normal histology at both the sites. In none of the cases, the bulb biopsy was positive with negative distal duodenal biopsy for celiac disease.

Conclusion: It is concluded the diagnostic yield from bulb biopsy is as good as biopsy taken from distal duodenum and hence could be substituted for D2 biopsy in pediatric patients.

Keywords: Bulb Biopsy, Celiac Disease, Modified Marsh Grade, Pediatric Patients.

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Article History:

Received: 09-02-2017, **Revised:** 02-03-2017, **Accepted:** 12-03-2017

Access this article online	
Website: www.ijmrp.com	Quick Response code
DOI: 10.21276/ijmrp.2017.3.2.022	

INTRODUCTION

Celiac disease is a permanent condition of gluten intolerance in which exposure to gluten results in characteristic pathologic changes in the gastrointestinal tract, most notably in the small intestine. The diagnosis of CD requires recognition of characteristic pathologic changes in an intestinal biopsy, accompanied by clinical and/or histologic improvement on a gluten free diet. Positive serologic tests are supportive of the diagnosis but not necessary.[1]

The gluten sensitivity can produce a spectrum of morphologic abnormalities within the proximal small bowel mucosa, ranging from architecturally normal villi to complete flattening.[2] The development of CD is a dynamic process whereby mucosal damage to the small intestine develops in three subsequent phases: (a) infiltrative phase, characterized solely by an increased number of intraepithelial lymphocytes (IELs), (b) hyperplastic phase, characterized by crypt hypertrophy and raised IELs, and (c) destructive phase, which is characterized by progressive VA, crypt hypertrophy and raised IELs ultimately leading to the flattening of the mucosa.[3] It is generally believed that in CD, mucosal lesions may have a patchy distribution.[4,5]

In present study, we assessed whether the addition of duodenal bulb biopsies increased the diagnostic yield of celiac disease as compared to distal duodenum biopsies.

MATERIAL & METHODS

This was a prospective study of 50 cases, conducted in the Department of Pathology and Pediatric medicine of Sawai Man Singh Medical College and Hospital, Jaipur for the period of March 2015 to June, 2016. All patients underwent upper gastrointestinal tract endoscopy during which 1-4 mucosal biopsy samples were obtained from the duodenal bulb and descending duodenum of each patient.

Biopsy specimens were fixed in 10% formalin, histopathology slides were prepared and hematoxylin and eosin stain was done. Histomorphology analysed with Modified Marsh grade for the diagnosis of CD in the bulb and descending duodenal biopsies.

RESULTS

Among the 50 children enrolled in the study 21were boys and 29 were girls; age ranging from 2-20 years. All the patients were positive for anti-tissue transglutaminase antibodies IgA (>15AU/ml). Their main clinical sign and symptoms were iron-deficiency anemia (36%), chronic pain abdomen (24%), failure to thrive (16%), recurrent diarrhea (12%) and abdominal distention (6%).

The diagnosis of CD was histologically confirmed in 48/50 patients. Two patients had normal histology in both the bulb and the descending duodenum, despite the raised tTG levels explained by patchy villous involvement of the disease process; also the serology could also be false positive.

Table 1: The Modified Marsh grades in bulb and distal duodenum-

Histology (Marsh grade)	Bulb histology (50 cases)	Distal duodenum (50cases)
Normal (M 0)	2 (4%)	2 (4%)
IELs >30/100 enterocytes (M1)	2 (4%)	1 (2%)
IELs+ crypt hyperplasia (M2)	-	-
IELs + Crypt hyperplasia +villous atrophy (M 3a/b/c)	46 (92%)	47 (94%)

Table 2: Bulb and distal duodenal biopsy shows different or same Marsh grades.

Marsh grade	No. of cases	%
Bulb = descending duodenum	28	56%
Bulb < descending duodenum	13	26%
Bulb > descending duodenum	7	14%

Table 3: Analysis of cases in which the bulb and distal duodenal biospies showed different Marsh grades.

No of cases	Marsh grade (D2)	Marsh grade (D1)
8	3c	3b
4	3b	3c
4	3b	3a
3	3a	3b
1	3a	1

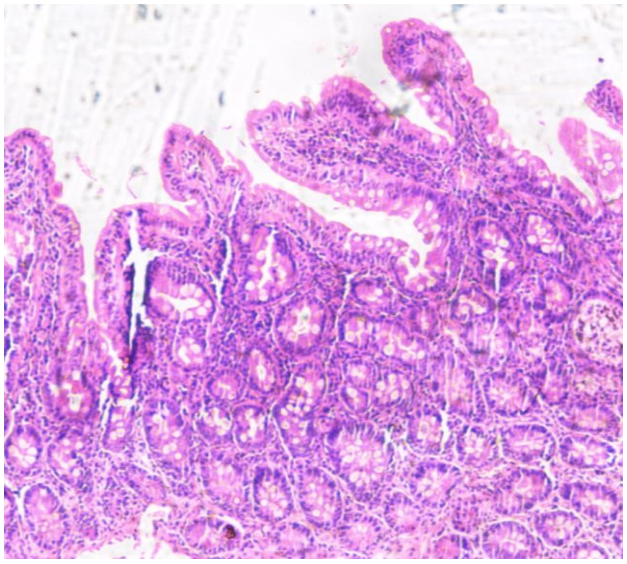

Fig 1: Micrograph shows Partial villous atrophy, crypt hyperplasia and raised IELs (H & E sectioned 100x)

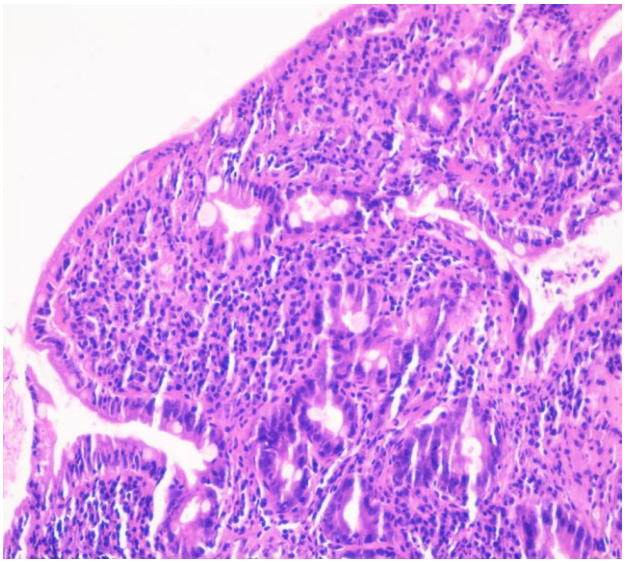

Fig 2: Subtotal villous atrophy with dense lymphoplasmacytic infiltrate in the lamina propria (H &E sectioned, 400x)

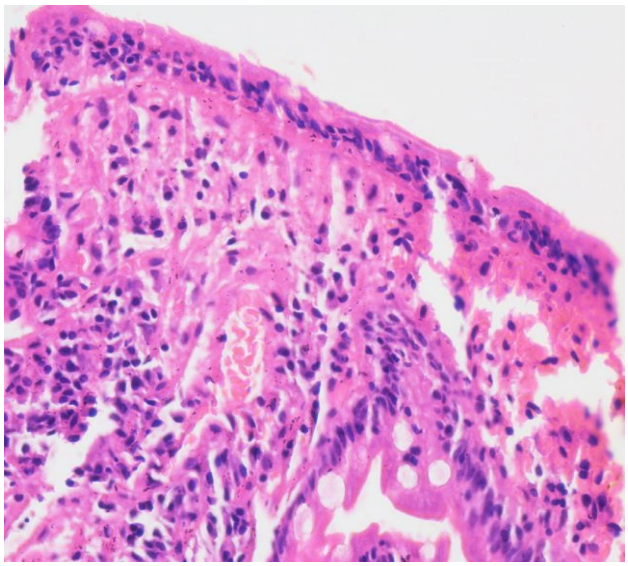

Fig 3: Total villous atrophy, raised IELs, lymphoplasmacytic infiltrate in the lamina propria (H&E sectioned, 400x)

Histological patterns in the descending duodenum in patients with positive serology for CD

In 2 of the 50 cases, biopsy specimens from the descending duodenum were negative for CD (M 0). Among the 48 children in whom the diagnosis of CD was confirmed from descending duodenal biopsy samples, 1 showed only intraepithelial lymphocytes (IELs) (corresponding to M 1), in the remaining 47 cases, the diagnosis was based on IELs plus crypt hyperplasia and villous atrophy (M 3a,b,c). (Table 1)

Histological patterns in the duodenal bulb in patients with positive serology for CD

In 2 of the 50 cases, biopsy specimens from the duodenal bulb were negative for CD (M 0). Among the 48 children in whom the diagnosis of CD was confirmed from descending duodenal biopsy samples, 2 showed only intraepithelial lymphocytes (IELs) (corresponding to M 1), in the remaining 46 cases, the diagnosis was based on IELs plus HCs and villous atrophy (M 3a,b,c). (Table 1)

Comparison of descending duodenum and duodenal bulb biopsy specimens in patients with positive serology for CD

Twenty eight patients (56%) had the same histology in the bulb and descending duodenum: 1 patient had M 1(3.5%), 5 had M 3a (17.8%), 8 had M 3b (28.5%), and 14 had M 3c (50%). Two patients had normal histology at both the sites.

In 20 cases histological findings differed in the bulb and descending duodenum.

Among the 20 patients, 13 patients had higher histological grade in the descending than bulb and 7 patients had higher grade in the bulb.

There was none of the cases, the bulb biopsy was positive with negative distal duodenal biopsy for celiac disease.

DISCUSSION

Considering that mucosal specimens from the distal duodenal or jejunal mucosa are strongly correlated, that these biopsy specimens provide adequate material for histological interpretation, and that studies on the usefulness of bulbar biopsies in the diagnosis of CD have been inconclusive, we decided to compare bulbar and duodenal histology in patients with suspected CD.

Benedetto et al[6] studied 47 patients, 23.4% had a higher grade of histological atrophy in the bulb than in the descending duodenum and 10.6% did not show histological signs of CD on biopsy samples from the descending duodenum, although bulb biopsy samples were positive for CD. If no bulb biopsy samples had been taken from this latter group, it would not have been possible to make the diagnosis of CD correctly. In our study 14% patients had higher grade in bulb than descending duodenum and such a finding where bulb show histological changes and descending duodenum being normal was not observed in any case.

Vogelsang et al[5] after finding 2 cases of CD in which biopsy samples from the duodenal bulb were diagnostic, retrospectively analyzed biopsy samples from the descending duodenum and duodenal bulb of 51 patients with suspected or diagnosed CD. The number of IELs was on average higher in the descending part of the duodenum, although the difference was not statistically significant, and the conclusion was that most patients with CD showed similar mucosal changes in biopsy samples from the descending duodenum and from the bulb. In present study, intraepithelial lymphocytes >30/100 enterocytes were seen in most of the patients. There was a difference in morphologic grades at both the sites; however the difference was not significant. Prasad et al[7] studied 52 children in whom bulbar and descending duodenum biopsy samples were taken. No significant differences were found between the histology in the 2 sites, leading to the conclusion that the diagnosis of CD can be made even if biopsy samples are taken from the duodenal bulb rather than the distal duodenum. This is similar to our present study.

Mohsin Rashid et al[8] studied 35 patients, in 31 patient had abnormal distal duodenal biopsies (1 Marsh type1, 1 Marsh type 2 and 29 Marsh type 3 lesion) and 4 patient had normal distal duodenal biopsies but abnormal bulb biopsies (1 Marsh type 2, Marsh type 3 lesion). The distal duodenum was also grossly normal in these 4 patients. The histologic diagnosis of celiac disease would not have been possible in these 4 cases with distal duodenal biopsies only. They concluded that the lesion in children can be patchy with duodenal bulb mucosa being the only area showing histologic change. Regarding the site of biopsies, it should be revised to include biopsies not only from distal duodenum but also from bulb to improve diagnostic yield.

Weir et al[9] published the results of their study, reporting on 101 children from whom biopsy samples were taken from both the duodenal bulb and the second portion of the duodenum; in only10 cases (9.9%), only the duodenal bulb biopsy samples were diagnostic of CD. In our study 48 cases were diagnostic for CD. In our study most of the patients (96%) had the bulb biopsy is diagnostic.

CONCLUSION

It is concluded that biopsy from both sites (D1&D2) are mutually exclusive and biopsy can be done from either bulb or descending duodenum. Diagnostic yield from D1 is as good as biopsy taken from distal duodenum and hence could be substituted in pediatric patients. This conclusion is limited by however the small number of cases in our study. More studies needed to substantiate our conclusion.

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Source of Support: Nil. **Conflict of Interest:** None Declared.

Cite this article as: Arpita Jindal, Pushpa Bairwa, Ranjana Solanki, R. K. Gupta, Hema Udawat. Importance of Duodenal Bulb Biopsy in Pediatric Patients for Diagnosis of Celiac Disease. Int J Med Res Prof. 2017; 3(2):107-10.
DOI:10.21276/ijmrp.2017.3.2.022