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ORIGINAL ARTICLE

Celiac Disease Diagnosis Via Histopathological Correlation of Duodenal Biopsies in Children

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ABSTRACT

Aim: The purpose of this study is to compare the diagnostic accuracy of duodenal bulb biopsies to distal duodenal biopsies in patients suspected of having celiac disease.

Study Design: Cross-sectional study

Place and Duration: This study was conducted at Department of Pathology, The children's hospital & The institute of child health, Multan during the period from April, 2022 to September, 2022.

Methods: Total 86 children of celiac disease were presented in this study. Informed written consent provided by parents of children for the collection of detailed demographic data. Under general anaesthesia, a duodenal bulb sample and four distal duodenum samples were collected during an upper gastrointestinal endoscopy. Histological alterations indicative with CD were identified. Histological diagnosis and grading were performed using a modification of the Marsh-Oberhuber classification. The entire data set was analyzed by using SPSS 20.0.

Results: Forty nine (56.97%) patients were females and 37 (43.03%) cases were males. Children's mean age was 6.4±3.27 years with mean weight 15.9±6.19 kg. Mean height of the cases was 94.7±10.42 cm. There were 51 (59.3%) children had urban residency. According to marsh grading, 50 (58.1%) cases had grade IIIC. We found that frequency of crypt hyperplasia, influx of immune cells in lamina propria and enterocytes change in both duodenal bulb and distal part biopsies were equal while only frequency of villous atrophy and intraepithelial lymphocytes were different in both biopsies. 96.5% patients reported a high level of correlation, while only 3.5% reported no correlation.

Conclusion: Both biopsy sites agree strongly. We may now suggest duodenal bulb biopsy alone. Since the endoscopic method of distal duodenum is laborious and requires more knowledge and time, obtaining biopsies from the proximal section is easier and requires less experience, therefore this strategy may be used even at facilities with junior paediatric gastroenterologists.

Keywords: Celiac disease, Children, Histopathology, Duodenal bulb, Distal duodenum

INTRODUCTION

dividuals with the HLA type II DQ2 and/or DQ8 haplotypes are predisposed to develop coeliac disease (CD), an autoimmune disorder affecting the small intestine that is triggered by the ingestion of gluten [1-3]. Screening programmes have revealed a spectrum of CD symptoms, from severe malabsorption to subclinical or silent signs. Common features of CD include the presence of specific auto-antibodies (anti-transglutaminase type 2 IgA), as well as duodenal histological abnormalities such as surface enterocyte damage, increased intraepithelial lymphocytes (IELs), crypt hyperplasia, and villous atrophy [4, 5].

Even though the aforementioned mucosal abnormalities are seen in other conditions as well [5], histology remains the gold standard for diagnosing CD in adults. Clinical and pathological experts need to work closely together and use a standardised categorization system to make reliable diagnoses that can be compared. According to Marsh [6]'s 1990 classification of GI lesions, type 1 lesions are characterised by an increased number of IELs and crypt hyperplasia, type 2 lesions by the same, type 3 lesions by the above lesions plus villous atrophy, and type 4 lesions by a normal number of IELs and crypts and the absence of villi. Subtypes 3a (mild atrophy), 3b (moderate atrophy), and 3c (total atrophy) were assigned to the atrophic type 3 lesion after the 1999 modification of the Marsh criteria published by Oberhuber et al. [7]. Typed according to the Marsh-Oberhuber system. A alternative classification approach classifies CD damage as either atrophic or non-atrophic [8].

The ESPGHAN and the NAPGHAN have significant sway in shaping the field of paediatric gastroenterology with their respective philosophies and policies (NASPGHAN). Up until 2012, both of these related organisations published recommendations for CD diagnosis that were essentially identical. Patients with a serum immunoglobulin A anti-tissue transglutaminase antibody titer more than 10 times the upper limit of normal (>10x ULN) now have the option of a "no-biopsy" diagnostic approach, thanks to updated recommendations published by ESPGHAN in 2012 [9]. Examination of existing clinical data, professional medical opinion, and preliminary clinical trial outcomes across a spectrum of illnesses provided support for this revised perspective [10].

Recently, it has been questioned whether all patients with increased anti-tTG antibody titers require a duodenal biopsy to establish a diagnosis of CD. It has been suggested that such individuals might still acquire an appropriate diagnosis of CD without having such invasive procedures. This is especially important for youngsters because not all hospitals have paediatric endoscopic facilities for sick kids who need surgery [11]. With anti-tTG antibody titers 10 times the upper limit of normal (ULN), a positive EMA, and a good response to a gluten-free diet, the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) suggested in 2012 that a diagnosis of CD can be established without small intestine biopsy in symptomatic, genetically predisposed children (GFD). There is a shortage of information from India, particularly for children, about the correlation between serum anti-tTG antibody levels and duodenal histological damage and whether or not this test has a high enough PPV to be utilised exclusively in the diagnosis of CD [12].

The researchers wanted to examine the prevalence of lesions in the bulb mucosa and the sporadic distribution of histological abnormalities in the local population. Duodenal bulb biopsy alone may be indicated if agreement between the two biopsy locations is high.

MATERIALA AND METHODS

This cross-sectional study was conducted at Department of Pathology, The children's hospital & The institute of child health, Multan during the Period from April, 2022 to September, 2022. and comprised of 86 children. Female and male children with celiac disease symptoms and a positive tissue transglutaminase IgA

antibody test were included. It was also taken into account whether or not they are healthy enough to have a duodenal biopsy performed under general anaesthesia. We didn't include children above 12 or who weren't yet weaned. Children on a gluten-free diet were also not included.

After thoroughly describing the study to the parents, we obtained their signed agreement to participate. The proforma contained information on demographics and outcome factors. One sample was collected from the duodenal bulb region, and four were taken from the distal duodenum during a general anaesthetic upper gastrointestinal endoscopy. CD agreement was reported based on the presence or absence of histological alterations associated with CD. In order to diagnose and grade histological conditions, we used a modified version of the Marsh Oberhuber classification.

SPSS 20 was used to input data and conduct statistical analysis. Quantitative factors, such as age, were used to compute means and standard deviations. The frequency and proportion of qualitative characteristics like gender were computed. Stratification was used to manage any confounding factors, such as age and gender. The kappa statistic was utilized to evaluate the level of concordance between duodenal bulb and distal portion biopsies used to diagnose CD.

RESULTS

Among all, forty nine (56.97%) patients were females and 37 (43.03%) cases were males. Children's mean age was 6.4±3.27 years with mean weight 15.9±6.19 kg. Mean height of the cases was 94.7±10.42 cm. There were 51 (59.3%) children had urban residency.(table 1)

Table-1: Demographic information of the enrolled cases

Variables	Frequency	Percentage
Mean age (years)	6.4±3.27	
Mean weight (kg)	15.9±6.19	
Mean height (cm)	94.7±10.42	
Gender		
Male	49	56.97
Female	37	43.03
Living Area		
Urban	51	59.3
Rural	35	40.7

According to marsh grading, majority of the cases 50 (58.1%) had grade IIIC, 2 (2.3%) cases had grade I, 4 (4.7%) cases had grade II, 6 (6.97%) cases had grade IIIA and 24 (27.1%) cases had grade III B.(figure 1)

Figure-1: Patients classification by Marsh grading

We found that frequency of crypt hyperplasia, influx of immune cells in lamina propria and enterocytes change in both duodenal bulb and distal part biopsies were equal while only frequency of villous atrophy and intraepithelial lymphocytes were different in both biopsies.(table 2)

Table-2: Distal portion and duodenal biopsy distribution

Variables	Distal portion	Duodenal Bulb
Results of Biopsies		
crypt hyperplasia	86 (100%)	86 (100%)
influx of immune cells in lamina propria	83 (96.5%)	83 (96.5%)
enterocytes change	82 (95.3%)	82 (95.3%)
villous atrophy	84 (97.7%)	86 (100%)
intraepithelial lymphocytes	85 (98.8%)	83 (96.5%)

We found that 96.5% patients reported a high level of correlation, while only 3.5% reported no correlation.(table 3)

Table-3: Association of correlation between distal portion and duodenal biopsy

Variables	Frequency	Percentage
Correlation		
Yes	83	96.5
No	3	3.5

DISCUSSION

Affecting a large percentage of the population, celiac disease is a global health problem. It's a chronic intestinal condition that affects around half a percent of the people in the United States and a percent or two more in Europe. The true rate of celiac disease incidence in Pakistan is unknown. While there has been significant progress in raising awareness of the illness among medical professionals, it is still frequently ignored by even the most skilled practitioners.[13,14]

In current study 86 children with CD symptoms were presented. Forty nine (56.97%) patients were females and 37 (43.03%) cases were males. Children's mean age was 6.4±3.27 years with mean weight 15.9±6.19 kg. Mean height of the cases was 94.7±10.42 cm. There were 51 (59.3%) children had urban residency. Results were comparable to the studies conducted in past.[15,16] According to marsh grading, majority of the cases 50 (58.1%) had grade IIIC, 2 (2.3%) cases had grade I, 4 (4.7%) cases had grade II, 6 (6.97%) cases had grade IIIA and 24 (27.1%) cases had grade III B. Results were comparable to the past study.[17] In spite of major advancements in CD identification brought about by the discovery of serologic and endoscopic markers, the essential approach for conclusive diagnosis continues to be the intestinal biopsy. The golden rule stipulates the presence of villous atrophy in at least three or four biopsy samples.[18]

We found that frequency of crypt hyperplasia, influx of immune cells in lamina propria and enterocytes change in both duodenal bulb and distal part biopsies were equal while only frequency of villous atrophy and intraepithelial lymphocytes were different in both biopsies. As a result, 96.5% patients reported a high level of correlation, while only 3.5% reported no correlation. The authors (Ravelli et al.) reported on two adult individuals for whom a diagnosis of CD required a duodenal bulb biopsy. Results from biopsies of the distal duodenum in these individuals were negative[19]. The patchy pattern of villous atrophy and the utility of duodenal bulb biopsies to boost the diagnostic yield of CD have both been verified by studies in children and adults with elevated endomysial antibody or tissue transglutaminase antibody titers. [20] From their research, Prasad et al. drew the conclusion that the duodenal bulb was likewise associated with the terminal ileum. Biopsies from the bulb and the distal duodenum region showed alterations in his sample of 52 youngsters suspected of having CD. We can get a high histopathological diagnostic yield, he said, if we merely collect samples from the duodenal bulb region. [20]

Bonamico et al. also showed that freshly diagnosed instances of celiac disease and previously diagnosed patients on a gluten-free diet both had lesions of a patchy form. Villous atrophy and other alterations characteristic of celiac disease were observed in the duodenal bulbar mucosa of all research subjects (total 95 in number). Researchers also discovered that in 4.2% of cases, the duodenal bulbar mucosa was the only place where

alterations consistent with celiac disease were present, while the remainder of the duodenal mucosa was normal. [21]

Researches has shown that haemoglobin levels and Marsh grading are inversely related. Hemoglobin and anti-tTG antibody titers were shown to have a statistically negative relationship, suggesting that mucosal epithelium loss and anaemia severity go hand in hand.[22,23] Hopper et al. also studied how many samples should be taken and from what locations to confirm a CD diagnosis. He obtained nine biopsies total; four from the upper gastrointestinal tract, four from the lower gastrointestinal tract, and one from the duodenal bulb. From these findings, they deduce that duodenal bulbar mucosal involvement is common in CD. By combining and including duodenal bulb samples, we were able to increase the diagnostic yield from our first set of biopsies. [24]

CONCLUSION

Both biopsy sites agree strongly. We may now suggest duodenal bulb biopsy alone. Since the endoscopic method of distal duodenum is laborious and requires more knowledge and time, obtaining biopsies from the proximal section is easier and requires less experience, therefore this strategy may be used even at facilities with junior paediatric gastroenterologists.

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