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Evaluation of Duodenal Biopsies in Patients Clinically Suspected to Have Celiac Disease in Rural Rajasthan.

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ABSTRACT

Background: Celiac disease is an autoimmune disorder where the ingestion of gluten leads to damage in the small intestine. The gold standard of diagnosis of celiac disease is intestinal biopsy changes and clinical response to a gluten-free diet is sufficient to make the diagnosis of celiac disease. **Aim and objectives:** To describe the importance of duodenal biopsy performed in patients clinically suspected to have celiac disease. Secondly, to study the Prevalence of celiac disease in different sex and age groups along with the spectrum of histopathological diagnosis in suspected patients of celiac disease in rural Rajasthan. **Methods:** The prospective study was conducted in the Department of Pathology, N.I.M.S medical college, rural Jaipur. The study was carried out in 196 cases of duodenal biopsies received to rule out celiac disease from the period of 2017 to 2019. **Results:** Duodenal biopsy was performed in 196 patients clinically suspected to have celiac disease, including 101(50.5%) males and 95 (48.5$) females. Four (2.04%) samples were excluded because of a small sample, 82(42.7%) exhibited changes of celiac disease, including 36 males (43.95), 46 females (56.1%), 42 children (51.2%) and 40 adults (48.8%). **Conclusion:** Duodenal biopsy performed in patients clinically suspected to have the celiac disease has been gradually incorporated into clinical practice, and it is a useful tool for the diagnosis of celiac disease in different age and sex groups.

Keywords: Celiac Disease, Duodenal Biopsy, Rural, Anti TTG.

INTRODUCTION

Celiac disease (also known as gluten-sensitive enteropathy) is an autoimmune disorder that can occur in genetically predisposed people where the ingestion of gluten leads to damage in the small intestine.[1] It is estimated to affect 1 in 100 people worldwide.[2]

Celiac disease has numerous symptoms, according to some experts, there are about 30 possible symptoms of the disease, different people will experience the condition in different ways because the symptoms vary significantly from one person to next, often symptoms of celiac disease are confused with other disorders such as irritable bowel syndrome and lactose intolerance.

Celiac disease is induced by the ingestion of gluten which is derived from wheat, barley and rye. The gluten protein is enriched in glutamine and proline and is poorly digested in the upper gastrointestinal tract. The term "gluten"' refers to the entire protein component of wheat; Gliadin is an alcohol-soluble fraction of gluten that contains the bulk of the toxic elements. Undigested molecules of Giladin, such as a peptide from a Giladin fraction made up of 33 amino acids are resistant to degradation by gastric, pancreatic and intestinal brush borders membrane proteases in the human intestine and thus remains in the intestinal lumen after gluten ingestion. These peptides pass through the epithelial barrier of the gut, possibly during intestinal infections, or then there is intestinal permeability and interact with antigen-presenting cells in the lamina propria.

The risk of developing celiac disease is increased by specific variants of the H.L.A. –DQA1 and HLA-DQB1 genes. These genes provide instructions for making proteins that play a critical role in the immune system. The H.L.A. –DQA1 and H.L.A. –DQB1 genes belong to a family of genes called the human leukocyte antigen (H.L.A.) complex. The H.L.A. complex helps the immune system distinguish the body's own proteins from proteins made by foreign invaders, such as bacteria and viruses.

The protein produced from the HLA-DQA1 and H.L.A. –DQB1 genes, which seem to increase the risk of an inappropriate immune response to gliadin. However these variants are also found in 30 percent of the general population, and only 3 percent of individuals with the gene variant develop celiac disease.

The environmental factors that have an essential role in the development of the celiac disease have been suggested by epidemiologic studies. These include a protective effect of breastfeeding and the introduction of gluten in relation to weaning. The initial administration of gluten before 4 months of age is associated with an increased risk of disease

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development, and the introduction of gluten after 7 months is associated with marginal risk. However, the overlap of gluten introduction with breastfeeding may be a more critical protective factor in minimizing the risk of celiac disease. The occurrence of certain gastrointestinal infections, such as the rotavirus, also increases the risk of celiac disease in infancy.

The dcekiac disease is suspected in people who have signs or symptoms of recurrent diarrhea, abdominal bloating and malabsorption or malnutrition. It is crucial, therefore, to confirm suspected celiac disease with appropriate testing.

At present, the gold standard of diagnosing celiac disease is the modified European Society of Pediatric Gastroenterology, hepatology and Nutrition (ESPGHAN) criteria.[4]

According to these criteria, only intestinal biopsy changes and clinical response to a gluten-free diet are sufficient to make a diagnosis of celiac disease.

Duodenal biopsies are commonly procured as a part of the upper endoscopy procedure since the duodenum is easily accessed. Often, pathology in the duodenum reflects the state of the distal small intestine, which is not as easily accessible using current endoscopic techniques.[5]

The duodenum begins with the duodenal bulb and ends at the suspensory muscle of duodenum.[6]

People who test positive for celiac disease antibodies or who have a high probability of celiac disease regardless of the results of the blood tests should have a small intestinal biopsy to confirm the diagnosis. Immunoglobulin A (IgA) anti-tissue transglutaminase antibody is the single preferred test for the detection of celiac disease. Abnormally elevated levels of Ig a endomysia and anti-tissue transglutaminase antibodies are found, a high chance of having celiac disease.

The marsh classification is used to evaluates the duodenal biopsy for loss of villi and other characteristics of celiac disease, such as an increased number of lymphocytes according to marsh classification.

The duodenal damage that is suggested to be induced by gluten starts in the duodenal bulb and progressively extends to affect the descending duodenum and the proximal jejunum. Consequently, the size and number of fragments are essential to make a correct diagnosis of celiac disease.

In celiac disease, duodenal lesions may have a patchy distribution, especially in children, and villous atrophy may be contiguous with or coexist with mild atrophy or normal mucosa. The bulb mucosa may be the only duodenal area affected, both at diagnosis and after gluten challenge, and total or moderate villous atrophy may touch the duodenal bulb exclusively, with a normal distal duodenum. Thus, multiple endoscopic biopsy specimens are always taken, both in the distal duodenum and bulb.

Complete normalization of the intestinal villi may take months. In many adult patients, the improvement in symptoms is followed by only partial regeneration of intestinal villi.

MATERIALS AND METHODS

The duodenal biopsy received in the Department of Pathology, NIMS medical college from the period of 2017 to 2019were evaluated for loss of villi and other characteristics of celiac disease, such as an increased number of lymphocytes according to modified marsh classification.

In this study, the most inclusion criteria were all age groups with exclusion criteria were all data of duodenal biopsy in which it was not possible to reach a histological diagnosis due to technical problems and all data which were performed in already known celiac disease.

The study comprised endoscopic duodenal biopsies obtained from 200 patients who clinically suspected for celiac disease.

Table 1: Modified Marsh Classification of histologic findings in celiac disease (Oberhuber)

Marsh Type	IEL/100 enterocytes-jejunum	IEL/100 entercytes-duodenum	Crypt Hyperplasia	Villi
0	< 40	< 30	Normal	Normal
1	>40	>30	Normal	Normal
2	>40	>30	Increased	Normal
3a	>40	>30	Increased	Mild atrophy
3b	>40	>30	Increased	Marked atrophy
3c	>40	>30	Increased	Complete Atrophy

The duodenal biopsies were taken from suspicious lesions, flattened on a piece of filter paper and fixed in 10% buffered formalin. They were processed for routine paraffin embedding and trimming. Serial sections were examined in; light microscope with the help of H &E and P.A.S. stain.

Endoscopy duodenal biopsy sections of study subjects were evaluated for villous atrophy, crypt hyperplasia, increased intraepithelial lymphocytes and infiltration of the lamina propria, and graded using modified Marsh Classification.

RESULTS

A total of 196 duodenal biopsies taken from patients suspected to have celiac disease, including 101(50.5%) males and 95 (48.5%) females, the patients underwent for an endoscopic technique for duodenal biopsy. Four (2.04%) samples were excluded because of the inadequate sample.

The remaining 192 duodenal biopsies, 82(42.7%) exhibited changes of celiac disease including 36 males (43.9%) and 46 females (56.1%) and

80(41.67%) showed conditions other than celiac diseases such as duodenitis 76 (95.0%) and another tubulovillous adenoma, 4(5.0%) and 30 (15.7%) were standard samples. After excluding four cases in which it was not possible to reach a histological diagnosis, the total samples analysed were 192;93 (48%) females and 99(52%) males with an average age of 25.3 years in the age range of 1 to 76 years.

Eighty-two patients were diagnosed with celiac disease, which accounted for 42.7% of the duodenal biopsies which performed according to the clinical suspicion of celiac disease (based on the presence of chronic diarrhea, nonspecific digestive symptoms etc.) or by finding of persistent analytical changes (anemia and /or iron deficiency).

In our study, the cases were divided into two groups which were less than 18 years and more than 18 years so that the Prevalence of celiac disease in adult was (35.09%) which represent (35%) male and (65%) female and the Prevalence of celiac disease in children was (53.85%) which represent (52.3%) male and (47.7%) female.

The histopathological grading of the celiac disease, according to Marsh classification, was done. Out of 82 cases which had some findings of celiac disease microscopically were classified as type I in 4cases (4.88%); type II in 23 cases(28.05%); type IIIa in 20 cases(18.29%), type IIIb in 15 cases (18.29%) and type III c in 20 cases(24.39%).

DISCUSSION

The study evaluates the value of duodenal biopsies in patients suspected to have celiac disease to determine its value in diagnosis or excluding celiac disease and further to define cut-offs for declaring a positive or negative stat by duodenal alone.

Celiac disease was diagnosed more frequently in females than in males (49% vs 36%), although gender was not a significant risk factor for celiac disease.[12,15] The Prevalence of celiac disease was significantly higher in children compared with adults (54% vs 35%). This difference may be due to environmental factors influencing infancy or latency of celiac disease in adulthood.[13] In our study, we also observed that duodenal has very important in the diagnosis of celiac disease where there were 192 cases of patients suspected to have celiac disease, of these 82 (42.7%) cases exhibited changes of celiac disease. There are many studies that show the importance of duodenal biopsy in the diagnosis of celiac disease, which is better than serological tests such as (tTg-Ig A test).[14]

The villous atrophy of intestinal mucosa in celiac disease was classified according to Marsh classification. This classification is essential to determine the degree of villous atrophy. It is graduated from type zero (normal) to class 4 (atrophic).

In our study the most eighty-two cases of celiac disease (78) exhibited similar changes between type II and typed III with its subtype (IIIa, IIIb, IIIc).

Advancement in the knowledge of the celiac disease has led to an increase in the indications for performing a duodenal biopsy to ensure a correct diagnosis. It is currently known that mild digestive symptoms (dyspepsia, abdominal discomfort, etc.) Or analytical alterations (anemia), could be some forms of presentation of celiac disease.[11]

In the past duodenal biopsy was usually made in persons with a classical or malabsorption syndrome, while at present, this was mainly performed in subjects with anemia so that duodenal biopsy is made even in the absence of symptoms of enteropathy or without previous serological studies.

According to the modified European society of Paediatric gastroenterology, hepatology and nutrition (ESPGHAN) criteria (4), only intestinal biopsy change and response to G.F.D. are sufficient to make a diagnosis of celiac disease so that the villous atrophy is synonymous with celiac disease.

However the differential diagnosis of celiac disease may include cow's milk protein sensitive enteropathy, viral or bacterial infection, medication (especially aspirin-like arthritis medication., autoimmune enteropathy, helicobacter pylori infection, Giardiasis, A.I.D.S, common variable immunodeficiency, tropical sprue, severe intestinal bacterial overgrowth, eosinophilic enteritis, lactose intolerance and lymphoma of the intestine are all possible causes of small intestine changes that may mimic celiac.

CONCLUSION

Celiac disease is an autoimmune disorder where the ingestion of gluten leads to damage in the small intestine. The gold standard of diagnosing celiac disease is the modified European society of pediatric gastroenterology, hepatology and nutrition criteria.

According to these criteria, only intestinal biopsy changes and clinical response to gluten-free diet are sufficient to make a diagnosis of celiac disease. Duodenal biopsy is now commonly procured as a part of the upper endoscopy procedure since the duodenum is easily accessed. The villous atrophy was seen under microscopy and was classified as per Marsh staging. The maximum cases were in grade III(a+b+c), which comprise 57.5 % of the cases; 28% consist of grade II and the remaining 4% were of class I.

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