Clinical and Morphological Aspects of Celiac Disease

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A B S T R A C T

Objective: To assess the clinical and morphological aspects of celiac disease.

Patients and Methods: This cross sectional study was conducted at Department of Pathology, Al Nafees Medical College & Hospital for a period of 8 months. After taking approval from Institutional review board, a written informed consent was taken from all the enrolled patients depending upon inclusion and exclusion criteria. Clinical data including the symptoms and signs and their severity was collected and entered on a specially designed proforma. Morphological data was collected with the help of patient's endoscopic biopsy. Histopathological biopsies were graded according to modified Marsch grading system. For qualitative variables frequencies and percentages were calculated. Quantitative variables were measured in terms of mean and standard deviation.

Results: There were 77 patients with suspicion of celiac disease whose endoscopic biopsy was done. Among these 42% were males and 58 % were females. Maximum number of patients were in the age group of 13-30 years. Among symptoms, diarrhea was present in 83.11% (n=64) patients, abdominal distention and pain was present in 53% and 63.6% patients respectively. Lesser frequent symptoms including vomiting and weight loss was significant in only 16.9% patients and constipation in 14.3% patients. According to modified Marsch grades, maximum celiac patients were graded in Marsch-3a (15.6%) and Marsch-3b (19.5%).

Conclusion: Majority of patients with Celiac disease presented with typical gastrointestinal signs and symptoms in which diarrhea was the commonest complaint. The disease is more common in adults with female predominance. Majority of patients belong to the 3a and 3b type lesion of the modified Marsch grading system.

Key words: Celiac disease, Malabsorption, Morphology, Modified Marsch grades.

Introduction

Celiac disease (CD) is a chronic disease of the small intestine in which intake of gluten found in rye, wheat and barley determines the injury of the intestinal mucosa in genetically susceptible individuals.[1] It is an inflammatory process which mainly involves the mucosa of small intestine resulting in atrophy of intestinal villi along with clinical manifestations. Gluten proteins are resistant to digestive enzymes resulting in peptide derivatives leading to immunogenic response in CD patients.[2] Celiac disease affects 0.6-1.0% people worldwide and different studies showed the prevalence of 0.3% in Germany and 2.4% in Finland.[3-5] Celiac disease affects around 1% of the general population with increasing prevalence over time as reported in the United States and Europe.[6-8] Diagnosis of Celiac disease is based on clinical manifestations, laboratory tests, histological aspects of small intestine

mucosa and serological markers.[9-10] Patients suffering from celiac disease usually present with features of malabsorption represented by diarrhea, steatorrhea, weight loss or failure to thrive. CD patients can also present with variety of extraintestinal symptoms and signs including anemia, vague abdominal symptoms, ataxia, neuropathy, depression, short stature, osteoporosis, osteomalacia, liver diseases and lymphoma.[11-15]

Characteristic histopathological changes in the mucosa of small intestine are taken as the standard criteria for diagnosis of celiac disease. According to the modified Marsch grading system, histopathological changes are categorized as 0-4.[16] The severity of mucosal changes in celiac disease is variable ranging from almost normal to total atrophic villi.[17] Marsh proposed histopathological classification system which was later modified by Oberhuber. Marsh-Oberhuber grading system includes five grades of lesions as type 0 with normal histology, type 1 with increased Intraepithelial lymphocytes (IEL) only; type 2 with increased IEL and crypt hyperplasia, type 3 with increased IEL, crypt hyperplasia and villous atrophy which is further classified as 3a, 3b and 3c for mild, marked and total villous atrophy and type 4 lesion with flat atrophic villi.[18]

The current study is aimed at determining how patients with celiac disease present to the physicians and what are the morphological attributes in these patients. This study will help identify the current trends of presentation of celiac disease patients in our settings.

Patients and Methods

This cross sectional study was conducted over a period of eight months from May 2015 to December 2015 in department of Pathology, Al Nafees Medical College and Hospital. Both males and females from all age groups, having symptoms of malabsorption and later labeled as celiac disease patients on intestinal biopsy were included in the study. Patients diagnosed with other causes of malabsorption, improperly processed samples and improperly stained slides were not included in the study.

Written and informed consent was taken from all patients. Data regarding procedure performed and history of patient was collected along with each specimen. Proforma was filled. Surgically removed endoscopic duodenal biopsy specimens, placed immediately in 10% buffered

formalin, were received in the pathology lab. After fixation the gross examination of biopsy was carried out. These gross specimens were sent for processing and Hematoxylin & Eosin staining. The stained sections of the specimen were examined microscopically at low power (4x, 10x objective), medium power (20x objective) and high power (40x objective). The microscopic details were analyzed by using modified Marsch grading system. Data was computed using SPSS version 20. Qualitative variables were analyzed in terms of frequencies and percentages. For quantitative variables mean and standard deviation was calculated.

Results

Total 77 patients were enrolled in the study. Among them, 39% were male and 61% were female. The stratification of patient data according to patient age group is shown in Table-1. Maximum number of patients were between ages 13 to 30 years. Among all symptoms, diarrhea was the commonest in both male and female (Figure 1), noted in 83.11% (n=64) patients. Abdominal distention and pain were present in 67.53 % (n=52) and 63.6% (n=49) patients respectively. Vomiting was noted in 16.9% (n=13) patients and constipation was present in 14.3% (n=11) patients.

Endoscopic duodenal biopsy findings of all patients were recorded and grouped into different grades as per Modified Marsch grading system. Marsch-0 included 28.6% (n=22) patients, Marsch-1 consisted of 9.1%(n=7) patients and Marsch-2 included 13%(n=10) patients. Whereas, Marsch-3a, Marsch-3b and Marsch-3c comprised of 15.6% (n=12), 19.5% (n=15) and 14.3% (n=11) patients respectively as shown in Graph-2.
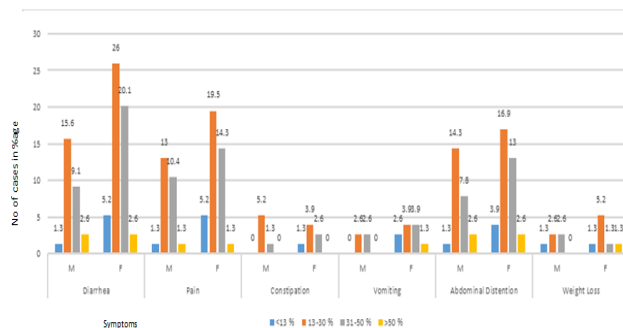

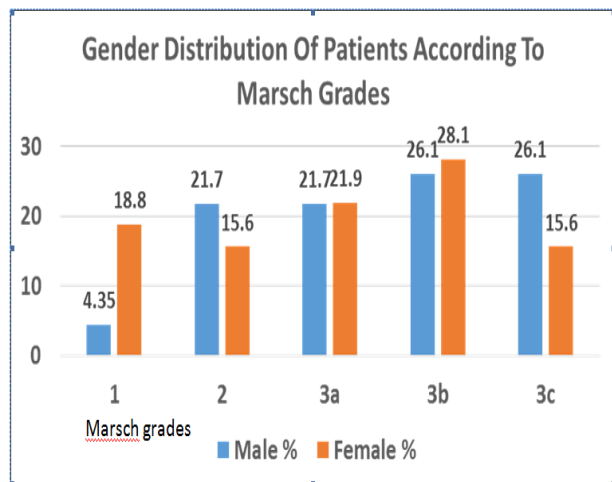**Figure1: Percentage distribution of patients according to symptoms**

Figure 2: Gender distribution according to Marsch Grades

Table-1: Distribution of Patients According To Age Groups			
Gender	Males	Females	Total
Age	n(%)	n(%)	n
<13 years	2(6.7)	4(8.5)	6
13-30 years	15(50.0)	24(51.1)	39
30-50 years	10(33.3)	17(36.2)	27
>50 years	3(10.0)	2(4.3)	5
Total	30(100)	47(100)	77

Discussion

Celiac disease is known as one of the most important gastrointestinal diseases. Diagnosis of celiac disease is difficult because of the unusual presentation of large number of patients with intestinal and extraintestinal signs and symptoms.[19] In the current study, findings about distribution of patients according to age shows that maximum number of patients lie in the age group of 13 to 30 years while pediatric (n=6) and old (n=5) age group has lesser number of patients. In contrast a study conducted by *Rashtak S et al* showed that median age of patients at the time of diagnosis was under the age of 50 while one third of patients were diagnosed above the age of 65.[20] Another study carried out by *Marine M et al* reported that the prevalence of celiac disease in the pediatric age group had increased fivefold as compared to the adult age group.[21] The current study reveals that female adults are more commonly affected by celiac disease as compared to males. These findings are in favor of other study conducted by *Makharia G* which revealed that celiac disease is more frequent in adult women than in men with a ratio of 4:1.[22] In another study done by Thomas H also showed similar results that the prevalence of celiac disease was high in women to that in men.[23] In current study, amongst all symptoms, diarrhea, abdominal pain and abdominal distention are maximally present in the patients and also in the same group of 13 to 30 years. A study conducted by *Santiago V et al* reported that diarrhea, malnutrition, bloating and vomiting

were more prevalent in children less than 2 years while dyspepsia, iron deficiency anemia and constipation were maximally present in adult age group.[24] Another study conducted by *Kivela L* revealed that the clinical presentation of celiac disease in children were minor especially in the 1990s while most of these changes had reached a peak in recent years.[25] Histopathological findings graded by modified Marsch revealed that maximum number of both male and female patients suffered from 3a and 3b type lesion of the celiac disease among all Marsch categories. Study conducted by *Parveen malothra et al in 2015* also had similar findings, which revealed that maximum number of patients belonged to grade 3a of modified Marsch grading system.[26]

Conclusion

Majority of patients with celiac disease present with typical gastrointestinal signs and symptoms in which diarrhea is the commonest finding. Majority of patients were adults with female predominance. Histopathological findings showed that 3a and 3b type lesion of the modified Marsch grading system were the commonest.

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