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Diagnostic accuracy of endoscopic findings in patients with celiac disease

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ABSTRACT

Objective: To determine the diagnostic accuracy of endoscopic findings in patients with celiac disease, keeping histopathology as the gold standard at Isra University Hospital Hyderabad.

Methodology: This descriptive study was conducted at the Gastroenterology department of Isra University Hospital, from June 2017 to December 2017. All the patients with age between 20-50 years as suspected cases of celiac disease and either of gender were included. Patients underwent upper gastrointestinal endoscopy and if their duodenal folds showed any finding related to celiac disease, and then specimens for biopsies were taken. The entire specimens immediately were sent to the diagnostic laboratory for histopathology. All the data was recorded in the predesigned Proforma and analyzed by SPSS version 20.

Results: A total of 112 patients of celiac disease were studied, most of the patients 73.2% were found in age group of 20-30 years. Abdominal distension was most common among 80.4%. Out of all 49.1% of patients had disease duration 11-15 weeks. All patients had endoscopic findings suggestive of celiac disease. According to the histological findings regarding celiac disease, 78.6% had positive histological findings and 21.4% had negative histological findings. Diagnostic accuracy endoscopic sensitivity was 100% and specificity was 24%. The negative predictive value was 0% and the positive predictive value was 78%.

Conclusion: It was concluded that endoscopy showed 100% sensitivity in the diagnosis of celiac disease by taking histopathology as gold standard. It is a reliable safe and less complicated diagnostic tool for celiac disease.

Keywords: Celiac disease, Endoscopy, Histology.

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Introduction

Celiac disease is a common disorder that affects genetically predisposed individuals on the ingestion of gluten.[1,2] The frequency of celiac disease in the United States is relatively low, about 1 case in 3000 persons. Estimates suggest that approximately 1% of the Western population is affected, but celiac disease is underdiagnosed in most affected people. [3,4]Approximately 3 million people in Europe and another 3 million people in the United States are estimated to be affected by celiac disease. Celiac disease is prevalent in European countries with temperate climates. The highest prevalence of celiac disease is in Ireland and Finland and in places to which Europeans emigrated, notably North America and Australia. In these populations, celiac disease affects approximately 1 in 100 individuals. The incidence of celiac disease is increasing among certain populations in Africa (Saharawui population), Asia (India),[5] and the Middle East. CD prevalence in Latin American countries is comparable to the prevalence from North American or European countries. Females are affected slightly more

than males. Approximately 20% of patients with celiac disease are older than 60 years.[6] It has been widely accepted that typical clinical features include chronic diarrhea with malabsorption of nutrients.[7] It is underdiagnosed due to lack of specificity of clinical symptoms, and the diagnosis is often made after considerable delay.[8-10] Dyspepsia, abdominal pain, bloating, and gastro-esophageal reflux symptoms are more common in patients with celiac disease than in the general population.[11-13] These symptoms are common indications for upper gastrointestinal endoscopy and celiac disease is common in patients undergoing duodenal biopsy for various indications, with a prevalence of 1.0% –5.2%.[14] Thus, a protocol for detecting celiac disease in patients presenting for EGD would be of value because the best screening strategy in this population is not known. Its diagnosis is based on the presence of histological signs of villous atrophy with increased intraepithelial lymphocytes on duodenal biopsies and positive antibodies against specific targets, mainly tissue transglutaminase, gliadin or endomysium.[15]

In adults with diarrhea or suspected malabsorption, a diagnosis of celiac disease requires that two criteria be fulfilled: first, a demonstration of typical pathological changes of untreated disease in biopsies from the proximal small bowel; and second, evidence should exist that clinical (and/or pathological) changes are gluten-dependent, most often as an unequivocal response to a gluten-free diet. Pathological abnormalities of celiac disease may include severe or variably severe (mild or moderate) small bowel mucosal architectural abnormalities that are associated with both epithelial cell and lymphoid cell changes, including intraepithelial lymphocytosis. Architectural changes tend to be most severe in the duodenum and proximal jejunum and less severe, or absent, in the ileum. These findings, while characteristic of celiac disease, are not specific because several other conditions can produce similar changes.

Some serological assays (eg, tissue transglutaminase antibody assays) are very useful screening tools in clinical practice because of their high specificity and sensitivity, but these do not provide a definitive diagnosis. However, current guidelines indicate histological analysis as the gold standard for the diagnosis of CD: specific pathological features are infiltration of the lamina propria, crypt hyperplasia, and villous atrophy, classified according to the Marsh classification and its modifications.[16] To perform a correct diagnosis, biopsy specimens have to be well oriented, and of good quality. The purpose of this study is to determine the correlation between serological findings with endoscopic findings in patients with celiac disease keeping histopathology at gold standard.

Methodology

This descriptive study was conducted in the department of gastroenterology and medicine at Isra University Hospital, Hyderabad. Six months after the approval of the synopsis. Patients with age between 20-50 years as suspected cases of celiac disease and either of gender were included. Patients already known with celiac disease and those were not agreed to participate in the study were excluded. Sample size calculation was done **b**y using the sample size calculator for diagnostic accuracy, taking statistics for (sensitivity as 60.4% and specificity 88.2%, and prevalence of celiac disease 57.5%).[17] Margin error for sensitivity has 12% and specificity 9.2%, the calculated sample size came out n= 112. Complete medical history and clinical examination were done. All the selected patients underwent upper gastrointestinal endoscopy and if their duodenal folds showed any finding related to celiac disease, underwent biopsy for histopathology from that part. Endoscopies were taken by senior gastroenterologists having experience of more than 5 years. During endoscopy specimens were taken for biopsies. The entire specimens immediately were sent to the diagnostic laboratory for histopathology. All the demographic information of the patients including endoscopic findings and histopathological findings were noted on the Performa.

The data was entered and analyzed in statistical program SPSS version 16.0. Mean and standard deviation were estimated for quantitative variables like age. Simple frequency and percentage were calculated for categorical variables. 2X2 table will be used to calculate the Sensitivity (SE), specificity (SP) “positive predictive value (PPV), negative predictive value (NPV) and accuracy of “Endoscopic findings” will be calculated by taking histopathology as gold standard.

Results

A total of 112 patients of celiac disease were studied, most of the patients 73.2% were found with the age group of 20-30 years, followed by 23.2% had age group of 31-40 years and only 3.6% of patients had age group of 41-50 years. Out of all study participants, females were 53.6% and males were 46.4%. Abdominal distension was

most common among 80.45 of the patients, while 19.65 had no abdominal distension. Anemia was most common among 99.1% of the patients, while 0.9% had no anemia. Most of the patients 49.1% had a disease duration was 11-15 weeks and 37.5% of patients had a disease duration of 5-10 weeks, followed by 8.0% of patients who had disease duration >15 weeks and only 5.4% of patients presented with disease duration of <5 weeks. (Table no. 1)

All patients had endoscopic findings positive regarding the celiac disease. According to the histological findings regarding celiac disease, 78.6% had positive histological findings and 21.4% had negative histological findings. (Table II)

Table I: Demographic characteristics of patients (n=112)

Variables	Statistics
Age	
20-30 years	82(73.2%)
31-40 years	26(23.2%)
41-50 years	4(3.6%)
Gender	
Male	52(46.4%)
Female	60(53.6%)
Abdominal distension	
Yes	90(80.4%)
No	22(19.6%)
Disease duration	
<5 weeks	6(5.4%)
5-10 weeks	42(37.5%)
11-15 weeks	55(49.1%)
>15 weeks	9(8.0%)
Total	112(100.0%)
Age (mean±SD) 27.41±6.84 years	

Table II: Patients distribution according to endoscopic and Histopathological findings (n=64)

Variables	Frequency	Percentage
Endoscopic findings		
Positive	112	100.0%
Negative	00	00%
Histopathological findings		
Positive	88	78.6%
Negative	24	21.4%

According to the diagnostic accuracy endoscopic sensitivity was 100% and specificity was 24%. Negative predictive value was 0% and positive predictive value was 78%. (Table III)

Table III: Diagnostic accuracy of endoscopic findings by taking histopathology as gold standard (n=64)

Endoscopic findings	Histopathological findings		Total
	Positive	Negative	
Positive	88	24	112
Negative	00	00	00
Total	88	24	112

Sensitivity: TP/TP+FNx100 = 100%
Specificity: TN/FP+TNx100 = 100%
PPV: TP/TP+FPx100 = 100%
NPV: TN/FN+TNx100 =0%

Discussion

Celiac disease is a permanent intolerance to gluten (a protein present in wheat, rye, and barley), which causes damage to the small intestinal mucosa by an autoimmune mechanism in genetically susceptible individuals. In our study, most of the patients 73.2% were found in age group of 20-30 years, and females were 53.6% as compared to males who were 46.4%. In comparison to our results, a study conducted by Masood N et al [18] reported that the most common age group was 18-30 years; (mean, 23.5±5.6) comprised 56.6%. Females were dominated and the male to female ratio was 3:1(63 % vs. 22%). This ratio is matched with many national and international studies.

Green et al [19] enrolled 1612 patients from all United States and the women predominated (2.9:1). They also shown age of presentation in adult celiac disease could be as late as 5th decade. The majority of respondents were diagnosed in their fourth to sixth decades. This ratio was lower than a study conducted in Hyderabad by Sadique [120] et al where they found thirty patients (50/30) were female (60%) and mean age of participants was 33.25+ 9.7 years. Majority of (86%) patients presented with typical gastrointestinal symptoms. In their study, they measure four clinical presentations while in our study we have 8 clinical presentations. Another study conducted by Israeli E et al [21] reported that celiac disease was highly prevalent in the young adult population in their study. In our study, abdominal distension was most common among 80.45 of the patients, while 19.65 had no abdominal distension. Celiac disease can present with many symptoms, including typical gastrointestinal symptoms (e.g. diarrhea, steatorrhea, weight loss, bloating, flatulence, abdominal pain) and also non-gastrointestinal abnormalities (e.g. abnormal liver

function tests, iron deficiency anemia, bone disease, skin disorders, and many other protean manifestations). Indeed, many individuals with celiac disease may have no symptoms at all. Iron is an important micronutrient that may be depleted in celiac disease. Iron deficiency and anemia may complicate well-established celiac disease, but may also be the presenting clinical feature in the absence of diarrhea or weight loss. If iron deficiency anemia occurs, it should be thoroughly evaluated, even if the celiac disease has been defined since other superimposed causes of iron deficiency anemia may be present. Most often, impaired duodenal mucosal uptake of iron is evident since the surface absorptive area in the duodenum is reduced, in large part, because celiac disease is an immune-mediated disorder largely focused in the proximal small intestinal mucosa. In our study, anemia was most common among 99.1% of the patients.

In comparison to our results, a study conducted by Al lawati TT et al [22] reported in their results that anemia was noted in 3 children at the time of diagnosis but It was not clear if anemia was related to celiac disease per se or is it primarily nutritional iron deficiency anemia. Similar results were seen in a study conducted by Praygya Sharma et al [23], whose results showed that chronic diarrhea (48.5%), short stature (27.0%), and chronic anemia (9.0%) were the common modes of presentation. Elevated level of aminotransaminase was present in 50 (24.3%) patients. In our study, iron deficiency was present in both sexes. Our study matched with Sanders DS et al [24] who has provided evidence to support atypical symptoms was 2.5 times more common than the classically described gastrointestinal presentation. In particular iron deficiency anemia accounted for a majority of patients.

In this study, all patients had endoscopic findings positive regarding celiac disease. Endoscopy is a valuable tool for obtaining duodenal biopsy samples. Endoscopy may show typical duodenoscopic features that are highly predictive of mucosal damage. According to the histological findings regarding celiac disease, 78.6% had positive histological findings and 21.4% had negative histological findings. In comparison to our results, study conducted by Bonatto MW et al [25] reported in their results that that changes in the duodenal mucosa detected on EGD were significantly and positively associated with histopathologic findings; An upper endoscopy with biopsy of the duodenum (beyond the duodenal bulb) or jejunum is performed to obtain multiple samples (four to eight) from the duodenum. Not all areas may be equally affected; if biopsies are taken from healthy bowel tissue, the result would be a false negative.[26] In our study, according to the diagnostic accuracy endoscopic sensitivity was 100% and specificity was 24%. Negative predictive value was 0% and positive predictive value was 78%. No one test for CD has a perfect sensitivity or specificity. Thus, individual tests may be combined in commercially available panels. This strategy may increase the sensitivity if any positive test is regarded as an overall positive result; however, the increased sensitivity comes at the expense of a reduction of specificity.[27] Unless all patients who test positive in the panel undergo histological confirmation of CD, this practice may lead to incorrect and over diagnosis followed by unnecessary treatment with GFD. Conversely, if the threshold is set that all tests within the panel must be positive for a "positive" panel test, then the specificity and hence positive predictive value (PPV) for CD will be increased, but at the expense of sensitivity.[28] Histological abnormalities associated with CD can be patchy.[29,30] Multiple biopsies of the duodenum should be performed if the diagnosis of CD is considered.

Conclusion

It was concluded that endoscopy showed 100% sensitivity in the diagnosis of celiac disease by tacking histopathology as gold standard. It is a reliable safe and less complicated diagnostic tool for celiac disease.

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