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A STUDY OF CELIAC DISEASE IN DUODENAL BIOPSIES AT A TERTIARY CARE HOSPITAL IN AHMEDABAD

Pathology

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ABSTRACT

Introduction: Celiac disease (CD) is the manifestation of an immune hypersensitivity reaction towards gluten in genetically predisposed people(carriers of HLA-DQ2 and DQ8 haplotypes).It is characterized by inflammation of the small intestinal mucosa and progressive loss of absorptive function. Clinical manifestations include gestrointestinal and systemic menifestations.

Aims & Objectives: The aim of the present study was to evaluation of histological diagnostic criteria for CD using two different grading methods in duodenal biopsy .

Material &Method: Study was conducted at GCSMCH & RC by reviewing the records of 50 patients ,clinically suspected for CD, whose duodenal biopsies received in pathology. Patients already treated for the same were excluded. 3 sections from each tissue block were stained with H&E stain, diagnosis & staging was done according to Modified Marsh Oberhuber & Corrazza staging systems.

Results: Out of 50 patients, 28 were female and 22 were male(F:M Ratio1.27:1).Patients ranged in age group from 3-57 years. According to Modified Marsh Oberhuber staging system & Corrazza staging system majority of patients staged as 3a [26 (52%)] & B1 [37 (74%)] respectively.

Conclusion: CD is commonly seen in female patients, though the reason for this is uncertain. According to both staging systems, presence of IEL is the key feature. As duodenal biopsy is an important and safe means to identify underlying celiac disease, it should be routinely considered in all patients undergoing endoscopic evaluation for clinical symptoms suggestive of CD.

KEYWORDS

Celiac Disease, Intra Epithelial Lymphocytes(iel),duodenal Biopsy

INTRODUCTION

At the core of Celiac disease (CD) manifestations lies immune hypersensitivity reaction towards gluten in genetically predisposed people (carriers of HLA-DQ2 and DQ8 haplotypes).[1]

The characteristic pathology is seen in proximal intestinal mucosa. The hall mark is inflammation of mucosa wchich varies according to stage of disease. Clinically a large no of gastrointestinal and systemic manifestations like diarrhea, abdominal discomfort, fatigue, bloating, weight loss, iron deficiency anemia etc can be seen.[2]

CD has a worldwide distribution. In USA it is estimated that 1 in 113 people suffer from CD and there has been a constant rise in incidence of CD over past 50 years. Apart from typical CD associated with malabsorption; atypical CD presenting with anemia, osteopenia, infertility and neurological symptoms is also known. Also there is a substantial population identified with silent CD who do not have any symptoms despite having histopathological and serlogical evidence of CD.[3]

Serological tests for the diagnosis of CD are IgA antigliadin, Anti endomysial and Anti tTG antibodies.[4]

Characteristic histologic findings are restricted to the mucosa and include:

Increase in Intraepithelial lymphocytes(IEL).
Absence or reduced height of villi which causes flat appearance with increased crypt cell proliferation resulting in crypt hyperplasia and loss of villous architecture.

Cuboidal appearance of cells and nuclei that are no longer oriented in surface epithelium.

Increased number of lymphocytes and plasma cells in lamina propria.[5]

In practice, a combination of clinical suspicion, morphologic abnormality, and positive serologic findings is used for the initial diagnosis of most patients with celiac disease.[6]

MATERIALAND METHODS :

This study was conducted at GCSMCH & RC by reviewing the records 123 duodenal biopsies received referred to histopathology department from Jan - 2016 to Apr - 2018 and 50 biopsies were selected for the study based on following criteria

Patients who were clinically suspected for CD with one or more symptoms like abdominal pain, heartburn, nausea, vomiting, diarrhea and/or weight loss & whose upper endoscopic biopsies were taken and sent to histopathology department were included.

Patients already treated for the CD were excluded.
For evaluation, 3 sections from each tissue block were routinely stained with H&E stain & the diagnosis was made.

Duodenal biopsies which were reported as 'consistent with celiac disease' were included in the study.

Data were collected for following morphology:
Intraepithelial lymphocytosis
Crypt hyperplasia

Shortening ,blunting or flattening of villi
Mild, moderate or severe lymphoplasmacytic infiltrate.

Modified Marsh - Oberhuber & new Corrazza staging system were used for staging of CD.[1,2]

TABLE NO 1: Criteria for Modified Marsh-Oberhuber Stages of Celiac Disease[3]

Criteria	Type 0	Type1	Type 2	Type 3a	Type 3b	Type 3c	Type 4
IEL / 100 Epitheial Cells	< 30/ 100	>30/ 100	>30/ 100	>30 /100	>30/ 100	>30/ 100	< 30/ 100
Crypt Hyperplasia	absent	absent	present	present	present	present	absent
Villous Atrophy	Pre Infiltrative	Infiltrative	Infiltrative - Hyperplastic	Mild Flat Destructive	Moderate	Total	Total Atrophic Hypoplastic

Highest IEL density was counted on H&E-stained sections of biopsy fragment, at ×400 magnification, along the luminal border, avoiding the crypts & reported as number of IELs per 100 epithelial cells.

TABLE 2: Criteria for New Corazza Stages of Celiac Disease[11]

Criteria	Nonatrophic - A	Atrophic B1	Atrophic B2
Intraepithelial lymphocytosis	Present	Present	Present
Villi	Normal	Still detectable	Undetectable
Marsh-Oberhuber equivalent	Types 1 and 2	Types 3a and 3b	Type 3c

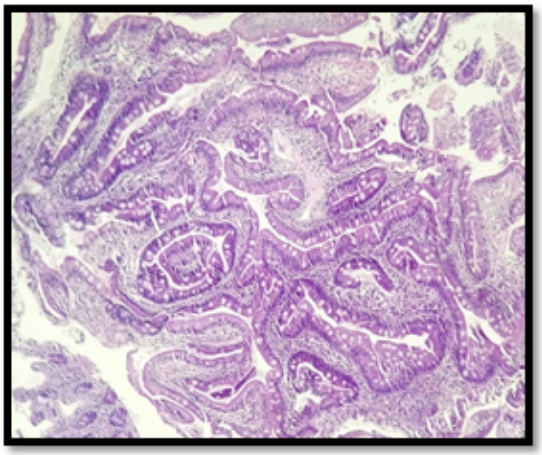

FIGURE 1 - Crypt Hyperplasia (10x H & E)

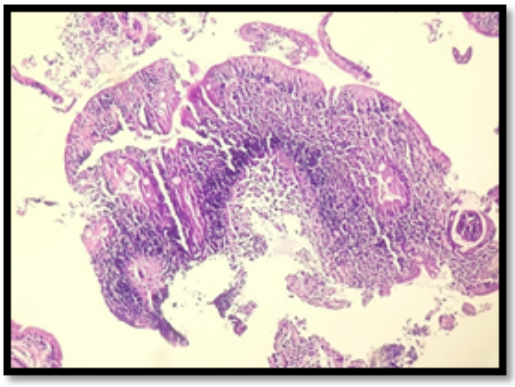

FIGURE 2: Lymphoplasmacytic Infiltration (10x H & E)

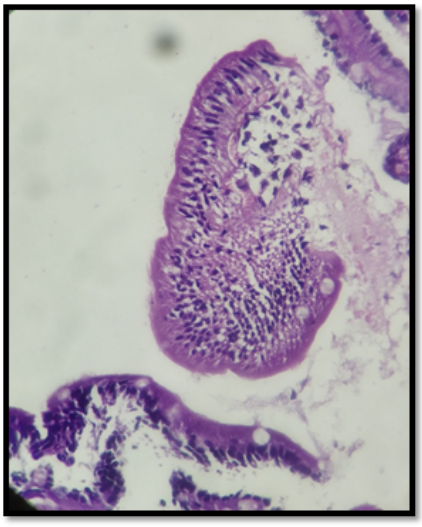

FIGURE 3: Intra Epithelial Lymphocytes (40x H & E)

RESULTS :

The number of biopsy fragments received per case ranged from 1 to 6, with a median of 3.

The study group of 50 patients consisted of 28 female and 22 male patients (female-male ratio, 1.27:1).

Patients ranged in age from 3 to 57 years (mean age 34.9 years),

11 patients (22%) were below 20 years of age, 18 patients (36%) were between 21 - 40 years of age while 21 patients (42%) were above 40 years of age.

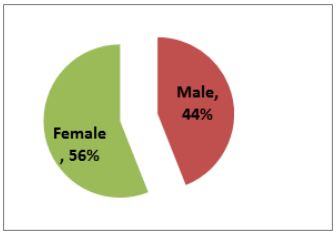

FIGURE 4: Sex Distribution -

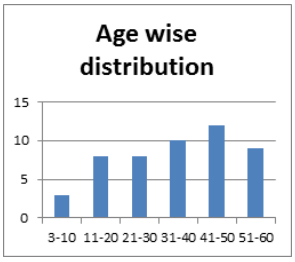

FIGURE 5 : Age vise distribution of celiac disease.

TABLE 3: Pathologic characteristics of 50 patients with Celiac Disease.

Corazza Stage	No (%)	Marsh Oberhuber Stage	No (%)
A	07 (14%)	1	05 (10)%
		2	02 (04%)
B1	37 (74%)	3a	26 (52%)
		3b	11 (22%)
B2	6 (12%)	3c	05 (10%)
		4	01 (2%)
Total	50 (100%)		50 (100%)

Out of 7 patients with Corazza stage A1 lesions,5 were corresponding with Marsh oberhuber stage 1 while 2 were with stage 2 lesions.

Out of 37 patients with Corazza stage B1 lesions, 26 were corresponded with Marsh stage 3a and 11 with stage 3b lesions.

Out of 06 patients with Corazza stage B2 lesions, 05 were corresponded with Marsh stage 3c and 01 with stage 4.

Characteristics	Value
Mean ± SD IEL count/100 epithelial cells (range)	42-100 (mean =71)
Lymphoplasmacytic cells infiltrate	**(n=50)**
Mild (1/3rd lamina propria infiltration)	15
Moderate (2/3rd lamina propria infiltration)	30
Severe (Full thickness lamina propria infiltration)	05
Villi	**(n=50)**
Shortening	30
Blunting	13
Flattening	07

DISCUSSION

No of biopsy fragments received were 1 to 6 with a median of 3 which is comparable to study carried out by Ian.S.Brown et al.[1]

Females are more affected in our study, as has been observed in similar study carried out by Walker Smith et al. [1,8] although gender was not found to be asignificant risk factor for CD.

Larger age group involved was 41-60 years, that may be due to change in the food habits or environmental factors.

In our study maximum number of patients had Corazza stage B1(74%) and Marsh-oberhuber stage 3a (52%) lesion, while in study of Ian.S.Brown and et al [1] maximum number of patients had Corazza stage B2 (56.6%) and Marsh-oberhuber stage 3c lesion. Geographic Factors or Genetic predisposition might be able tho explain the variation

No of Positive biopsies (50 / 123) might be due to high prevalence, high sensitivity of physicians towards CD, availability of high resolution endoscopy or simply more cases due to ours being a tertiary car

Other recent studies have also suggested and added hypothesis that a true change in appearance of celiac disease may have occurred, possibly due to other confounding environmental factors.[9,10]

Lymphoplasmacytic infiltration and mild shortening of villi can be attributed to other sprue like intestinal disorders- tropical sprue ,infections, patients taking NSAIDS and other enteropathies like bacterial overgrowth, blind loop syndrome and immunity mediated diseases like dermatitis herpetiformis etc. [10,11] . This makes it imperative that all care be taken to avoid false diagnosis of CD. Use of IgA antibodies as supportive tools can help reduce number of false positives

To avoid interobserver variation and to standardize staging , histopathology report should include following findings:

- Presence of IEL, crypt hyperplasia, change in villi height like shortening , minor villous blunting, intermediate villous atrophy or flat mucosa .[12]

Only moderate (intermediate)villous atrophy(Marsh type3b) and total villous atrophy(flat mucosa ,Marsh type 3c) should be reported as "suggestive of celiac disease".[13]

CONCLUSION:

CD is more commonly seen in female patients, though the reason for this is uncertain.

According to both staging system (Modified Marsh Oberhuber & Corrazza) presence of intraepithelial lymphocytes (IEL) is the key feature.

As Corrazza staging system is based on presence or absence of IEL not on the number of IEL, interobserver variation can be minimised suggesting that it is a simplified & more reproducible system .

Duodenal biopsy with moderate lympho-plasmacytic infiltrate should be reviewed by an experienced pathologist for changes in villi and glands.

With availability of high resolution fiber-optic endoscopes a duodenal biopsy from highly suspected lesion is easy to procure and should be a mainstay of diagnosis and management

Even though serological tests are pretty specific regarding diagnosis of CD; biopsy can reveal the true nature and severity of disease and should be considered to have a baseline from which to monitor progress of disease.

A large no of diseases that than masquerade as CD makes the diagnosis of CD a challenging one. Detailed history, properly considered investigations and good communication between clinician & pathologist can considerably eliminate false contenders.

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