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RESEARCH ARTICLE

Histological spectrum of celiac disease in 63 newly diagnosed patients at a tertiary care hospital.

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Abstract

INTRODUCTION: Celiac disease (CD) is characterized by malabsorption, altered small bowel histology induced by dietary exposure to gluten in genetically predisposed individuals. In spite of the tremendous increase in our knowledge regarding the clinical, pathological and genetic aspects of CD, the histological examination still remains the gold standard for its diagnosis. Recently, Corazza and Villanacci introduced a classification that reduces the number of categories and the interobsrver variation. This study was undertaken to evaluate the various morphological spectrums of duodenal pathology in CD according to the new classification system proposed by Corazza and Villanacci.

MATERIALS AND METHODS: The present study comprises of 63 patients who tested positive for anti TTG antibodies at Sri Guru Ramdass Institute of Medical Sciences and research, Amritsar, Punjab. Anti TTG levels were documented at initial presentation to the hospital. The detailed history of the patient i.e. age, sex and duration of symptoms and other investigations performed, were recorded.

OBSERVATIONS & RESULTS: The age group ranged from 07-64 years. The mean age was 29.4 years. There were 39 females and 24 males in the study group with a M:F ratio of 1:1.6. The mean serum anti TTG level at presentation was 142.4 U/ml, ranging from 14 to 456. Anti TTG levels of > 100 were found in 27 patients. There was significant positive correlation between anti TTG levels and histological changes as per Corazza staging. The histology was classified according to Corazza staging into Type A, B1 and B2. 3 patients were classified into type A, 25 into type B1 and 35 into type B2.

CONCLUSION: Although histopathology is considered as the gold standard in its diagnosis, a single test cannot diagnose this entity and thus it requires a combination of clinical features, serology and histopathological features to give a presumptive diagnosis of CD. The final diagnosis rests on the improvement of the symptoms/serological values/biopsy findings after gluten free diet.

INTRODUCTION

Celiac disease (CD), also known as gluten induced enteropathy is an immune mediated disorder characterized by malabsorption, altered small bowel histology induced by dietary exposure to gluten (a protein found in wheat) in genetically predisposed individuals. There is prompt improvement in the clinical features after a gluten free diet. [1,2,3,4] The major site of the disease is duodenum followed by jejunum.[1]

In spite of the tremendous increase in our knowledge regarding the clinical, pathological and genetic aspects of CD, the histological examination still remains the gold standard for its diagnosis. [1,3,4] Histological abnormalities characteristic of CD were described in 1954 by Paulley. Marsh in 1990 classified the various histologic patterns seen in CD which were further modified by Oberhuber in 1999.[3] Recently, Corazza and Villanacci introduced a modification of the above classification that reduces the number of categories. Type 1 and 2 have been clubbed into Grade A, 3a and 3b into Grade B1, 3c into grade B2. Type 4 category of Marsh Oberhuber has been deleted. This classification system further simplifies the criteria and reduces the number of categories and hence the interobserver variation. [4,5,6,7]

The mucosal changes on histology can be subtle in cases of intact duodenal villous architecture and villous atrophy is also seen in a variety of other conditions. Also, these changes can be variable and may range from just an increase in the intraepithelial lymphocytes to complete atrophy of the small bowel mucosa. [1,2,5] Serological testing for anti tissue transglutaminase (TTG) is a useful adjunct although it is not fully sensitive or specific for the disease. Also, serological findings may be normal in patients with minimal biopsy findings. Thus, a combination of clinical features, biopsy findings, and serological values should be used for a presumptive diagnosis of CD. The improvement of clinical features, serological values or biopsy findings renders the initial diagnosis of CD definitive. [1,3,4,5,6]

This study was undertaken to evaluate the various morphological spectrums of duodenal pathology in CD according to the new classification system proposed by Corazza and Villanacci.

MATERIALS AND METHODS:

The aim of the study was to study the histopathological profiles in patients of CD.

The present study comprises of 63 patients who tested positive for anti TTG antibodies at Sri Guru Ramdass Institute of Medical Sciences and research, Amritsar, Punjab

The duodenal biopsies were retrieved by an endoscope. The biopsies were carefully oriented on a filter paper and fixed in 10% formalin. They were then embedded in paraffin wax, processed and stained with hematoxylin and eosin. The slides were then examined according to the new classification system proposed by Corazza and Villanacci.

Anti TTG levels were documented at initial presentation to the hospital. The detailed history of the patient i.e. age, sex and duration of symptoms and other investigations performed, were recorded.

The following features were assessed on histopathological examination.

1) Intraepithelial lymphocytes (IELs).
2) Crypt hyperplasia.
3) Villous architecture (normal, mild flattening, marked flattening)
4) Degree of lymphoplasmacytic inflammation within the lamina Propria.

- Criteria for increased IELs was > 25 IELs/100 enterocytes.
- The villous architecture was graded according to Corazza and Villanacci classification. (Table 1)
- Degree of lymphoplasmacytic inflammation was graded as under:
    a) Grade 0- Infllamatory cells in < $1/3^{rd}$ of lamina Propria surface
    b) Grade 1- Infllamatory cells in up to $2/3^{rd}$ of lamina Propria surface
    c) Grade 2- Infllamatory cells in full thickness of lamina Propria surface

RESULTS:

63 patients were included in this study group.

Age distribution: The age group ranged from 07-64 years. The mean age was 29.4 years. The age wise distribution of the patients is as follows.

Age group	Number of patients	Percentage
< 10 years	19	30.15%
10-20 years	24	38.09%
20-30 years	07	11.11%
40-50 years	09	14.28%
> 50 years	04	6.34%

Range: 07-64 years
Mean Age: 29.4 years

Sex Distribution: There were 39 females and 24 males in the study group with a M:F ratio of 1:1.6.
Urban and Rural distribution: The urban population constituted 54% of the study group whereas rural population formed 46% of the group with urban:rural ratio of 1.17.
Presenting complaints: The chief presenting complaints were diarrhea (51.5%), abdominal pain (32.1%) and vomiting in 10.7% of the cases. The other symptoms were failure to thrive, abdominal distension and constipation. Family history of the CD was observed in 3 cases.
Investigations: The mean Hb at presentation was 9.42±1.5 g/dl. The serum anti TTG levels at presentation was also recorded. The normal values of the antibody are as under

- <4.0 U/ml: Negative
- 4.0-10.0 U/ml: Weak positive
- >10.0 U/ml: Positive

The mean serum anti TTG level at presentation was 142.4 U/ml, ranging from 14 to 456. Anti TTG levels of > 100 were found in 27 patients. There was significant positive correlation between anti TTG levels and histological changes as per Corazza staging (Table 2).

Histological Examination: The histology was classified according to Corazza staging into Type A, B1 and B2. 3 patients were classified into type A, 25 into type B1 and 35 into type B2 (Table 2), (Fig 1,2,3).

Lymphoplasmacytic infiltrate within the lamina Propria was also graded into grade 0, 1 and 2.

Grade 0: 04
Grade 1: 29
Grade 2: 30

The grade of the infiltrate was also correlated with Corazza stage (Table 3).

1. . TABLE 1

Criteria	**Type A (Non Atrophic)**	**Type B1 (Atrophic)**	**Type B2 (Atrophic)**
Intraepithelial Lymphocytosis	Present	Present	Present
Villi	Normal	Still detectable	Undetectable
Marsh Oberhuber Equivalent	Type 1 and 2	Type 3a and 3b	Type 3c

TABLE 2

Anti TTG Ab	**Type A (Non Atrophic)**	**Type B1 (Atrophic)**	**Type B2 (Atrophic)**

< 15	01	02	01
15-100	02	08	22
101-300	00	08	04
>300	00	07	08
	03	**25**	**35**

TABLE 3

Lymphoplasmacytic infiltrate	**Type A (Non Atrophic)**	**Type B1 (Atrophic)**	**Type B2 (Atrophic)**
Grade 0	01	02	01
Grade 1	02	21	06
Grade 2	00	02	28

Fig 1: Type A CD: Normal villi with increase in intraepithelial lymphocytes (H&E x 400)

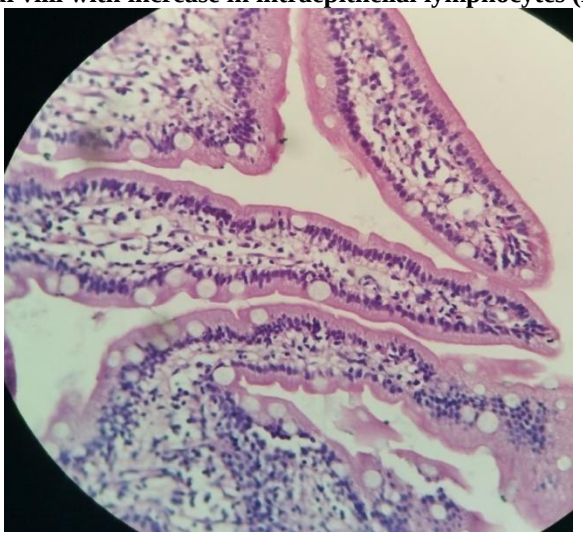


Fig 2: Type B1 CD: Partial atrophy of villi with increase in intraepithelial lymphocytes (H&E x 100)

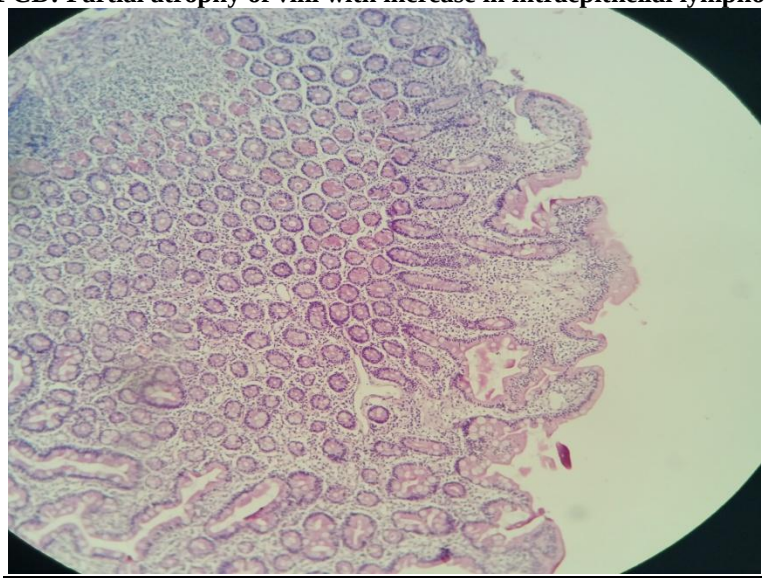
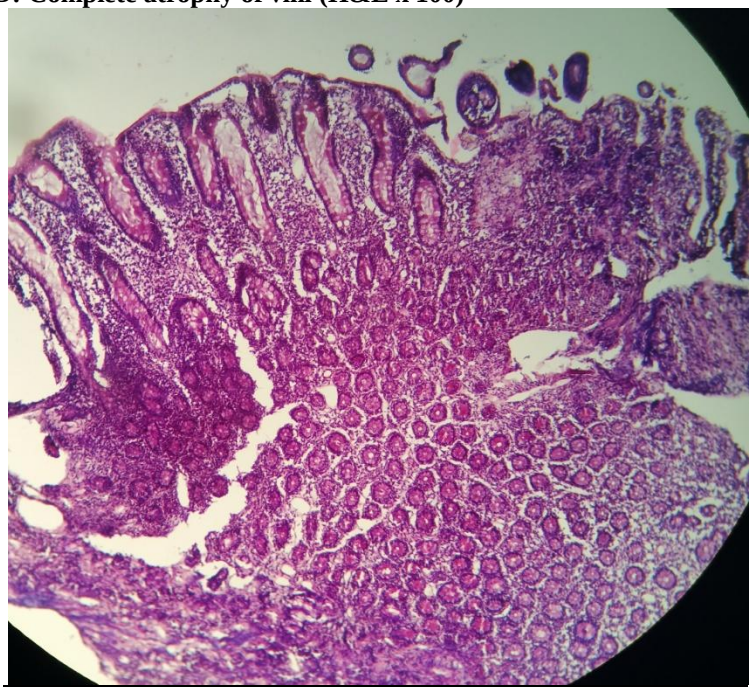


Fig 3: Type B2 CD: Complete atrophy of villi (H&E x 100)



DISCUSSION:

This study was undertaken in 63 patients with positive serological test to study the histological spectrum of CD and correlate it with anti TTG levels.

The age group in our study ranged from 07 to 64 years with a mean age of 29.4 years. The most common age group affected was between 10-20 years followed by <10 years. In western countries, the classical age of presentation is 9-`18 months with diagnosis within 6 months of presentation.[1,3,5,6,8] The possible explanation for this discrepancy may be due to delayed weaning, late introduction of gluten and due to the fact that diarrhea (commonest symptom of CD) is very common in children in India and hence investigations for CD are often overlooked.

In our study, M:F ratio was 1:1.6. this is in correlation with various other studies which demonstrate that CD affects females more often than males .[1,3,6,9] The exact reason for this variation is unknown.

The major symptoms that the patients presented with were diarrhea (51.5%), abdominal pain (32.1%) and vomiting in 10.7% of the cases. The other symptoms were failure to thrive, abdominal distension and constipation. These findings were also in accordance with other studies both in India and in western countries [1,2,3,68,9,10].

The mean serum anti TTG level at presentation was 142.4 U/ml, ranging from 14 to 456. Anti TTG levels of > 100 were found in 27 patients. There was significant positive correlation between anti TTG levels and histological changes as per Corazza staging. The severity of histological changes increased from type A to B1 and B2 as the levels of anti TTG increase. Levels of >300 were found in 15 patients, 7 of which showed type B1 and 8 showed type B2 histology according to Corazza classification (Table 2). Thus higher TTG levels correlated with severe duodenal damage. [1,2,3,6,9,10.11.12]

The histological grading was done according to the Corazza classification (Table 1 and 2). 03 were classified as type A, 25 as type B1 and 35 as type B 2. 27/60 (45%) classified as type B1 and B2 showed TTG levels > 100 further establishing that increased TTG levels correlate with histological severity. These findings were in accordance with various other studies. [1,2,3,4,6,8,9,10].

Lymphoplasmacytic infiltrate within lamina Propria was also graded from 0-2 (Table 3).

a) Grade 0- Infllamatory cells in < 1/3rd of lamina Propria surface
b) Grade 1- Infllamatory cells in up to 2/3rd of lamina Propria surface
c) Grade 2- Infllamatory cells in full thickness of lamina Propria surface

Grade 2 infiltrate was found in 30 patients out of whom 28 were classified as type B2. Thus increased grade of the infiltrate was found to correlate well with increased histological severity. The findings in this study were similar to other studies that examined this fact [(1)].

The diagnosis of CD has been a challenge for the physician, gastroenterologist and the pathologist. The morphologic spectrum of CD is increasing and so is the number of tests involved in its diagnosis. Although histopathology is considered as the gold standard in its diagnosis, a single test cannot diagnose this entity and thus it requires a combination of clinical features, serology and histopathological features to give a presumptive diagnosis of CD. The final diagnosis rests on the improvement of the symptoms/serological values/biopsy findings after gluten free diet.

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