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TISSUE INFLAMMATORY RESPONSE IN CELIAC PATIENTS OF BASRAH PROVINCE

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ABSTRACT : From 300 patients diagnosed with celiac disease, only 65 samples were positive and the rest are negative, (24) samples from healthy control was taken with age ranged from 1 -70 years (200 males and 100 females), who were admitted to Al-Basra General Hospital, Al-Sadder Educational Hospital and from two private clinical laboratories included (170 samples from inpatients and 130 samples from outpatients) during the period of October 2017 to May 2018. For diagnosis celiac patients biopsy from small intestine related to each patient was collected and processed for light microscopic examination.

Pathologist will assign a modified Marsh type to the biopsy findings, Type 3 indicates symptomatic celiac disease, however, Types 1 and 2 may also indicate celiac disease, after diagnosing the patients with celiac disease.Moreover, duodenal biopsy samples showing increased intraepithelial lymphocytes, crypts hyperplasia, villous atrophy (Marsh type 3), partial villous atrophied, sever inflammation extend to sub mucosa,some area showed completely loss of vili and the surface layer appeared flatten.The characteristic findings were absent villi with abnormalities of the lining mucosa and highly infiltration of lymphocytes.

Key words : Tissue inflammatory response, Celiac disease, Basrah province.

INTRODUCTION

Celiac disease (CD) is a chronic inflammatory disease, which develops in genetically predisposed individuals definition also as T cell-mediated inflammatory disorder with autoimmune features and it has environmental and immunologic components (Trynka *et al*, 2010). It is characterized by an immune response to ingested wheat gluten and related proteins of rye and barley that leads to inflammation, villous atrophy and crypt hyperplasia in the proximal symptoms and signs of CD include diarrhea, abdominal distention, abdominal pain, weight loss, fatigue and malnutrition (Alaedini and Green, 2005).

When people with CD eat gluten (a protein found in wheat, rye and barley), their body mounts an immune response that attacks the small intestine,these attacks lead to villi damage, small fingerlike projections that line the small intestine, that promote nutrient absorption, when the villi get damaged, nutrients cannot be absorbed properly into the body (Gonzalez *et al*, 2010). According to the World Gastroenterology Organization, Celiac disease may be divided into two types : classical and non-classical. In classical Celiac disease, patients have signs and symptoms of malabsorption, including diarrhea, steatorrhea (pale, foul-smelling, fatty stools) and weight loss or growth failure in children (Cheng *et al*, 2010).

In non-classical Celiac disease, patients may have mild gastrointestinalsymptoms without clear signs of malabsorption or may have seeminglyunrelated symptoms (Smith *et al*, 2017). Clinical and experimental studies have indicated that the permeability of the epithelial cell layer is increased in celiac disease and IELs are considered to be highly sensitive and specific for CD (Groschwitz and Hogan, 2009).

The disease develops gradually from early infiltration of intraepithelial lymphocytes (IEL) to shortening of the villous structure together with enlargement of crypts, reaching to villous atrophy and crypt hyperplasia (Marsh, 1992).

MATERIALS AND METHODS

Sample collection

A total of 300 samples from suspected patients, whose age was range between 1 and 70 years (100 males and 200 females) from Al–Basra General Hospital, AL-Sader Educational Hospital in Basrah province during the period of September 2017 to May 2018 were collected. For data collection, special questionnaire were made

including: name, age, gender, address, family history, presence and duration of gluten free diet and symptoms. Patients and control were chosen according to the results of tissue biopsy. Only biopsy-proven patients that mean those who fulfilled strict criteria of small intestine biopsy with total or partial villous atrophy (which indicated by a special pathologist), the results compared with normal structure of small intestine. All samples were processed for light microscopy examinations.

Histopathological study

Tissue samples of all the celiac specimen biopsies were collected andprepared for tissue inflammatory study according to Luna (1968) method.

RESULTS

Inflammatory tissue response

Histological studies supporting the diagnosis of celiac disease by using a modified Marsh classification to determine the changes of the small intestine mucosal layer, an increase in intraepithelial lymphocytes (IEL) counts and increase in lamina propria cells density.

Light microscopic observations on small intestine specimen from celiac disease patients showed alterations in small intestine architecture characteristic by abnormal mucosal layer with irregular villi, degenerated absorptive cells (enterocytes), loss of basilar alignment layer of enterocytes nuclei and the epithelial layer became flat stratified columnar epithelium, at the base of some villi the leiburkuhn crypts showed hyperplasia with inflamed lamina propria and highly infiltration of inflammatory cells (Figs. 1, 2) compared with normal small intestine sections, which showed normal villi extend to the lumen lining with simple columnar epithelium ,basal oval nuclei without any signs of inflammation and intestinal glands opened at the villous base (Fig. 3).

Recent findings revealed to mucosal changes, focal

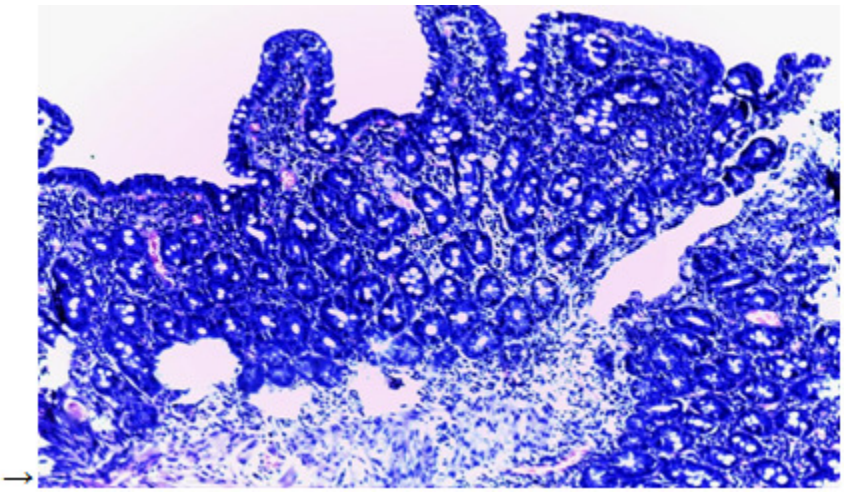

Fig. 1 : Section of the small intestine from celiac disease patient showed shortening villi flat surface, crypts hyperplasia, sever inflammation in the lamina propriaand within the intervillus spaces (H&E) stain (X40%).

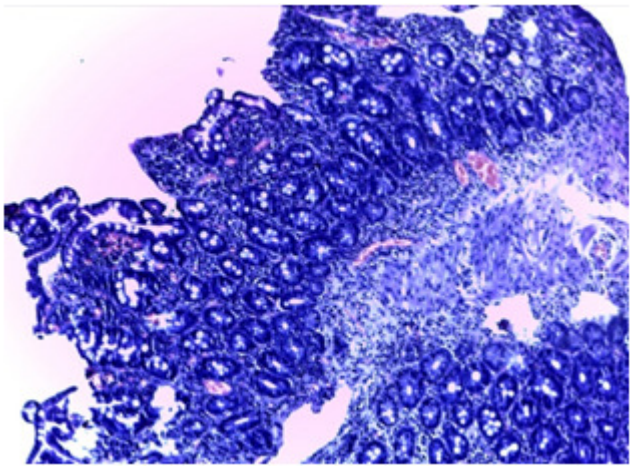

Fig. 2 : Section of small intestine from celiac disease patients showed complete destruction of mucosa layer, crypts hyperplasia, congested capillaries and severe inflammation. (H &E) stain (X 40).

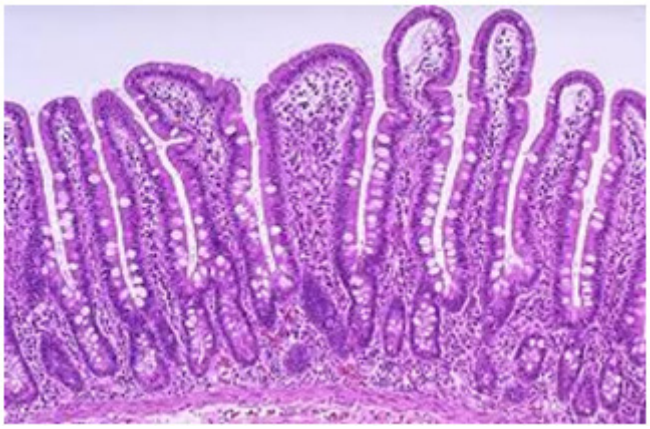

Fig. 3 : Section in normal intestine showed normal villi lining with columnar epithelium, goblet cells at the base of villi there was normal crypts (H &E) stain (X 10).

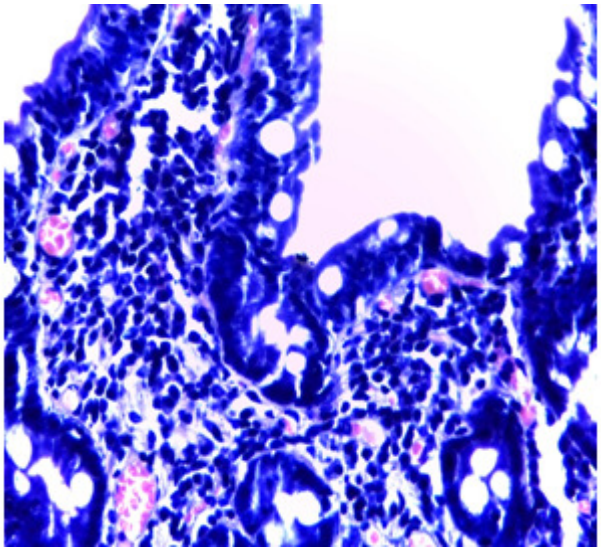

Fig. 4 : Photomicrographof small intestine from celiac disease patients illustrate structure of villous, irregular surface, stratified columnar epithelial, heavy inflammatory cells most of lymphocytes, congested capillaries and mild goblet cells (H&E) stain (X 40).

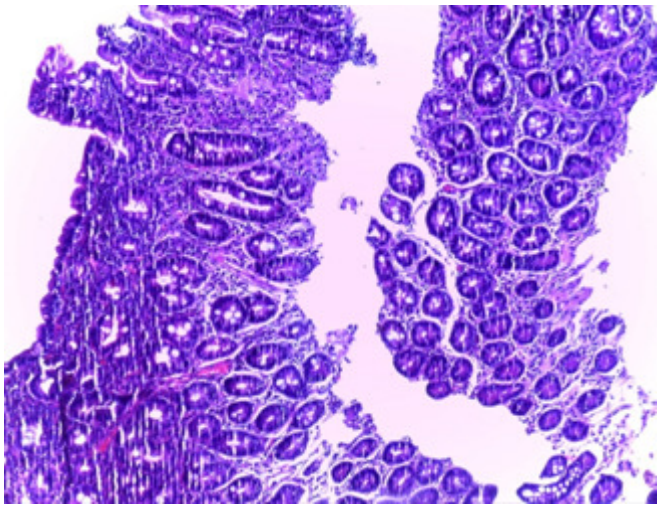

Fig. 5 : Section of small intestine biopsy from celiac disease patients showed complete flatmucosa, crypts hyperplasia mild hemorrhage, (H&E) stain (X 40).

and extensive inflammation, variable severity may be shown, or classical flat mucosa, great reduction in villi height, most villi with partial atrophy and the biopsy from duodenum and jejunum showed short, flat, spade-shape, with irregular size and all villi lined with low columnar epithelial cells and the lamina propria appeared more cellular and vascular (Figs. 4, 5).

Moreover thick bundles of collagenous fibers extend at the sub – epithelial region and strand of smooth muscle also extend upward among the crypts, total atrophied mucosal layer, lamina propriabeneath the villi showed severe inflammation ,hemorrhage and heavy inflammatory cells most of lymphocytes and plasma cells, cryptitis and

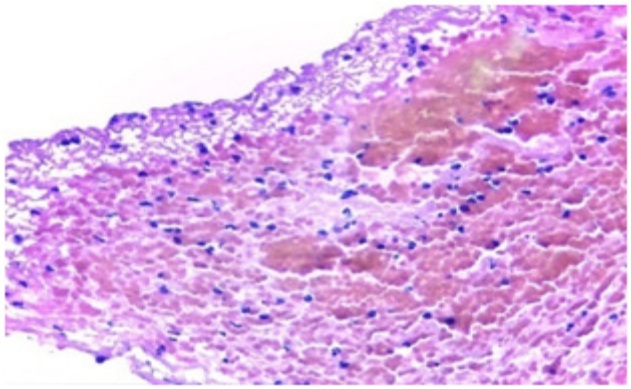

Fig. 6 : Section of small intestine biopsy from celiac disease patients showed extensive damaged of mucosa.

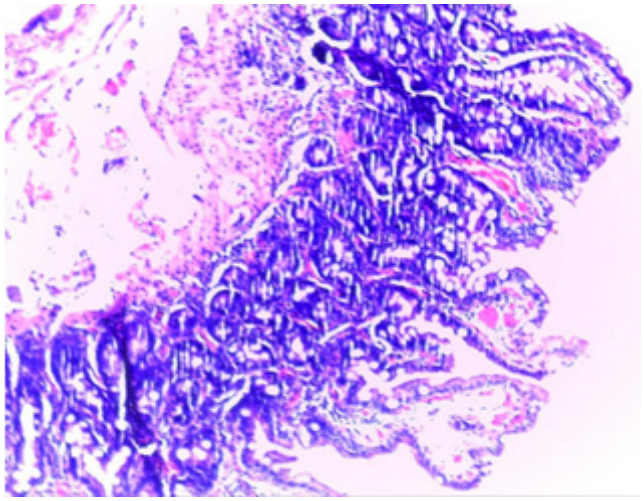

Fig. 7 : Section of jejunum biopsy from celiac disease patients showed variable destruction of mucosa.

great depth of intestinal crypt glands was obvious (Fig. 6).

Histological observations showed that celiac disease associated with increased of intraepithelial lymphocytes among absorptive cells, goblet cells hyperplasia with cryptitis, more degenerated or elongated crypts and capillariasis, congested blood vessels and hemorrhage within intervillus spaces (Fig. 7).

DISCUSSION

Tissue inflammatory response

In the present study, duodenal biopsy samples showing increased intraepithelial lymphocytes, crypt hyperplasia, and villous atrophy (Marsh type 3) with positive celiac serology in patients, since data show a similarly high positive predictive value of tTG concentrations that are increased to this degree, and further data suggest that discrepancies occur in the interpretation of duodenal histopathology in the absence of formal morphometric measurements this deal with many studies (Butwicka *et al*, 2017 and Jozefczuk *et al*, 2018).

However, it is premature to conclude that this strategy should be extended to adult practice. Moreover, the risk of having CD is increased in children with specific genetic disorders while,the adults who do not have coeliac disease risk being committed to a gluten-free diet (Pastore *et al*, 2008 and Jericho *et al*, 2017).

Furthermore, any changes in patient diet can affect the accuracy of biopsy results,it is necessary for the patient to be eating gluten every day for at least 4-8 weeks before the procedure. Furthermore, it is necessary to the patient who's scheduled for a biopsy not eating gluten to get accurate results. Even if the patient have eaten gluten only a short time before the test, the patient and the physician will not know if a negative test result is accurate or due to your diet (Lionetti *et al*, 2010; Thawani *et al*, 2015 and Krigel *et al*, 2016).

The present study, showed that mucosal damage in CD occurs with both a natural and an acquired immune response by ingestion of the protein gliadin that bond with Ttg and stimulate immune system against villi of small intestine,this intestinal inflammation in celiac patients is due to different cytokines produced by CD4 T cells and that these are responsible for the pathogenesis of the disease (Kapoor *et al*, 2013; Deora *et al*, 2017). Tissue transglutaminase (TG2) is the key component that it is involved in cell apoptosis because it prevents the exit of cytoplasmic material and, when secreted outside the cell, it collaborates in the remodeling of the extracellular matrix during tissue repair (Tosco *et al*, 2013).

TG2 mostly located intracellular, but appears extracellular in response to tissue injury, in normal gut, TG2 is expressed in sub epithelial areas, in the lamina propria (LP) mucosa and in connective tissue around the cryptsIn addition, this enzyme may play a role in the retrotranscytosis mechanism and in gliadin peptide passage through the epithelium, because it has been demonstrated that TG2 can interact with CD71 and secretory IgA (sIgA) on the apical surface of enterocytes in biopsies of patients with CD (Lebreton *et al*, 2012).

Finally, this study could be benefit for researchers, who are interested with celiac diseasepathgenicity, results can be extremely valuable resources for the advancement medical knowledge.

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