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Clinical, Serological and Histopathological Aspect of Celiac Disease at AL-Ramadi Province West of Iraq

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ABSTRACT

Background: Celiac disease (CD) is a public hereditary, autoimmune &multifactorial gastro-intestinal disorder in children and adults defined as a permanent gluten-sensitive Enteropathy. There is no previous study on Socio-demographic, clinical, endoscopic, and histological features of celiac disease in the AL-Ramadi district (west of Iraq) patients.

Objective: To identify the clinical, endoscopic, and histological features of celiac disease at Al-Ramadi district (west of Iraq) to reach the accurate CD diagnosis.

Patients and Methods:161 consecutive new CD cases diagnosed in the Gastroenterology Clinic of AL-Ramadi teaching hospital between August 2017 and March 2020 were included in a retrospective cross-sectional study, of them, 85 females were females76 males. The clinical features and endoscopic findings were recorded for each CD patient. In all cases, gastro-intestinal biopsies with serum ''anti-tissue transglutaminase' (Anti¬tTG) had been determined & tested for the CD diagnosis. Histopathology results had been divided using modified Marsh taxonomy.

Results: The mean age of celiac disease patients was 24.16 ± 14.751. There was a non- statistically significant differences between the genders in studied countries (p = 0.478). Abdominal pain, Bloating, Diarrhea, vomiting, altered bowel habit, Pallor, short stature and Constipation were the most common finding of CD patients with the following percent (23.6%), (23.0%), (14.3%),7.5%,6.2%,5.0%,5.0% respectively. The CD investigations shows were: (a) IDA in 105 (65.2%) patients; (b) low ferritin in 17 (10.6%) patients; (c) elevated SGPT 3 (1.9%) patients; (d) pancytopenia and 1 (0. 6%) patients. IgA anti-tTG <10iu/ml 6.2%, IgA between 10.1-20 iu /ml 82.0% while IgA anti tTG>20iu/ml in 11.8%. A statistical correlation was found between endoscopical and histopathological findings of celiac disease (p = 0.0001), and this correlation was more prominent in the scalloping aspect of duodenal mucosa. A statistical correlation was found between Anti- tTG IgA iu /ml levels and histopathological findings of celiac disease (p = 0.0002).

Conclusion: Histopathological findings correlate both with the endoscopic finding and the IgA TTGA levels of celiac disease patients. Furthermore, half of the CD patients with Iron deficiency anemia.

Keywords: Endoscopy, Celiac disease, IgA ant -tTG, histopathology, descriptive cross-sectional study, Ramadi district (Iraq).

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INTRODUCTION

Coeliac disease (CD) a communal family, autoimmune¬multifactorial gastro¬intestinal syndrome defined as a long¬lasting gluten¬sensitive enteropathy that progresses in hereditarily susceptible persons during their lifetime. Usually, CD happens in age group 6 - 18 months of age, after the introduction of gluten containing diet [1] lead to malabsorption & small bowel mucosal damage, however, it can present at any age and the peak of onset of an adult CD is during the 4th and 5th decades in females and 5th and 6th decades in males [2]. The prevalence of CD differs from country to country, in general effects 1% of the world's population [3].

There is a variation in the clinical manifestations of CD, but the majority of patients are suffering from problems with the gastrointestinal tract such as abdominal pain, Bloating, Diarrhea, Vomiting, altered bowel habit, short stature, and Constipation. The CD is predominant in childhood within the age group 6 -18 months of age diagnosed within the first two years of life [4-5].

Numerous CD patients of current with commonly non¬GI symptoms with manifestations such as anemia, "short¬**stature**", "Aphthous¬stomatitis", repeated gastrointestinal¬ pain with pica, late of puberty, "osteopenia", & "dental¬enamel¬hypoplasia", with ("atypicalCD"). Ferritin -deficiency anemia are the predominant atypical CD presentations that lack response to iron treatment & iron therapy[6-7].

Duodenal biopsies are recommended for CD diagnosis when the results of serological tests are positive, and also for CD patients who show normal serological results accompanied by appearances and symptoms extremely suspicious for CD, those patients must undertake an endoscopic assessment as nearly 10 % CD cases might be sero¬negative [8]. Serological testing includes. Endomysial (EMA) and tissue transglutaminase (TG IgA) autoantibodies are the most sensitive and specific for the diagnosis of CD[9]. Duodenal biopsies consider the common standard methods for CD identification, despite the specificity of serological procedures such as anti¬gluten & anti¬tissue transglutaminase (anti-tTG) antibodies. Correlation of clinical, serological, & histopathological findings is necessary for conclusive CD diagnosis[10]. The current study aimed to identify the clinical, endoscopic, and histological features of celiac disease at the Al-Ramadi district (west of Iraq) to reach the accurate CD diagnosis.

PATIENT AND METHODS

161 consecutive new CD cases diagnosed in the Gastroenterology Clinic of AL-Ramadi teaching hospital between August 2017 and March 2020 were included in a retrospective cross-sectional study, of them, 85 females were females76 males. The clinical features and endoscopic findings were recorded for each CD patients. In all cases, Intestinal biopsy & serum anti-tissue

transglutaminase (anti-tTG) had been detected & used for the CD identification. Histopathology results had been categorized rendering to the modified Marsh ordering[11] [12]. Chronic blood loss was ruled out. complete blood count, blood film, s ferritin, s iron, TIBC, SGPT. lgA Anti-tTG levels had been done using ELISA. Patients with IgA anti-tTG<10 IU/ml had been considered as a negative case and IgA anti- tTG 10.1-20 IU/ml suspicious even in the absence of clinical symptoms. IgA anti-tTG>20 IU/ml were considered positive as per manufacturer recommendation and it had a calibration range of 3 to 100 IU/ml. Upper gastrointestinal endoscopy was carried out in patients with the suspicion of celiac disease after obtaining written informed consent.4 duodenum biopsies from D2 were taken, with the assessment of duodenal endoscopic markers including scalloping of folds, reduction in duodenal folds, vascularity and nodularity of the mucosa. the specimen was examined by an experienced pathologist. Both sexes who were diagnosed as a CD depending on the 'Gastroenterology' World Organization' criteria [13] were appropriate. CD diagnosis usually depending on positivity of the serological EMA IgA antibodies[14],&/or anti-tTG antibodies[15] in addition to anti-tTG histopathological features intestinal mucosa[16].

Inadequate medical records of CD patients had been excluded. Family consent was obtained from all patients. Ethical approval had been obtained from the Anbar medical college Ethics approval Committee, Iraq.

Statistical Analysis

Data were analyzed using IBM SPSS software version 22. The results were presented in tables as frequencies and percentages. The chi-Square test used to compare the variables through cross-tabulations and P-Value under than 0.05 measured a statistically significant difference

RESULT

Overall, 85 (52.8%) females & 76 (47.2%) males (mean of age (± standard deviation) SD) were 24.16 ± 14.751 years old, age range 3-66 years old) with a CD confirmed diagnosis had been included. Patients ranged 1-18-year-old were considered as children and older as adults. There was a non- statistically significant differences between the genders in studied countries (p = 0.478).

Table 1 showed Socio-epidemiological clinical, Investigations, Endoscopic, and Histopathology features with IgA anti- tTG IU/ml levels of celiac disease patients in the study population.

Abdominal pain, Bloating, Diarrhea, Vomiting, Altered bowel habit, short stature, and Constipation were the most common finding of CD patients with the following percent (23.6%), (23.0%),(14.3%),7.5%,6.2%,5.0%,5.0% respectively whereas the other clinical findings of CD patients were less frequent.

The CD investigations shows were: (a) IDA in 105 (65.2%) patients; (b) low ferritin in 17 (10.6%) patients; (c) elevated SGPT 3 (1.9%) patients; (d) pancytopenia and 1 (0. 6%) patients. IgA anti-tTG <10iu/ml 6.2%, IgA between 10.1-20 iu /ml 82.0% while IgA anti tTG>20iu/ml in 11.8%.

The endoscopic aspects were: (a) normal in 55 (34.2%); (b) scalloping in 77 (47.8%); (c) reduction in duodenal folds in 26 (16.1%); (d) nodularity in 2 (1.2%); and (e) paucity of duodenal folds in 1 (0.6%) (Table 1).

The histopathological of CD patients were: (a) normal in 55 (34.2%).

(b) scalloping in 77 (47.8%); (c) reduction in duodenal folds in 26 (16.1%).

(d) nodularity in 2 (1.2%); and (e) paucity of duodenal folds in 1 (0.6%) (Table 1). histopathological aspect was G3A 58 (36.0%), G3B (36.0%), G3C 29 (18.0%), G2 11 (6.8%) and G1 (0.6%). All these finding presented in Table 1, Figure 1, Figure 2.

Table1: Socio-epidemiological, clinical, investigations, endoscopic and histopathology features with IgA anti- tTG IU/ml levels of celiac disease patients

Parameters	Frequency (%)	Parameters	Frequency (%)
Age	24.16 ±14.751	**lgA anti- tTG iu/ml**	
Presentation Abdominal pain	38 (23.6%)	< 10	10 (6.2%)
Altered bowel habit	12 (7.5%)	10.1----20	132 (82.0%)
Bloating	33 (23.0%)	>20	19 (11.8%)
Diarrhea	23 (14.3%)	**Endoscopical finding**	
Vomiting	14 (8.7%)	Normal	55 (34.2%)
Pallor	10 (6.2%)	Scalloping	77 (47.8%)
Constipation	8 (5.0%)	Reduction in duodenal folds	26 (16.1%)
Short stature	8 (5.0%)	Paucity of duodenal fold	1 (0.6%)
Dysphagia	3 (1.9%)	Nodularity	2 (1.2%)
Nausea	3 (1.9%)	**Histopathology**	
Bone pain	3 (1.9%)	G1	1 (0.6%)
Migraine	3 (1.9%)	G2	11 (6.8%)
GERD	2 (1.2%)	G3A	58 (36.0%)
Weight loss	1 (0.6%)	G3B	58 (36.0%)
Investigations		G3C	29 (18.0%)
IDA	105 (65.2%)	Normal	4 (2.5%)
Low ferritin	17 (10.6%)		
Pancytopenia	1 (0.6%)		
SGPT >50 IU	3 (1.9%)		

Correlation of endoscopic with histopathological findings of CD

Endoscopic & histopathological findings correlation of CD patients

The correlation between endoscopic and histological findings for CD patients revealed: (a) Amongst 55 normal endoscopic findings 4 with normal histology,33 with the G3A type & 7 with G3B, 6 with G2 & 1 with G1; (b) Among 77 scalloping. endoscopic results 16 with the G3A type and 38 had G3B, 22 had the G3C type 1 had G2: (c) Among 26 Reduction in Duodenal Folds endoscopic results none of them had normal histology,8 had the G3A type and 11 had G3B, 3 had the G3C type, none of them had had G2 and G1. Depending on the histopathological inconsistency demonstrated below, a statistical association had been registered between CD endoscopic & histopathological findings (p = 0.0001), and this correlation was more prominent in the scalloping aspect of duodenal mucosa these are presented in Table 2, Figure 1, Figure 2.

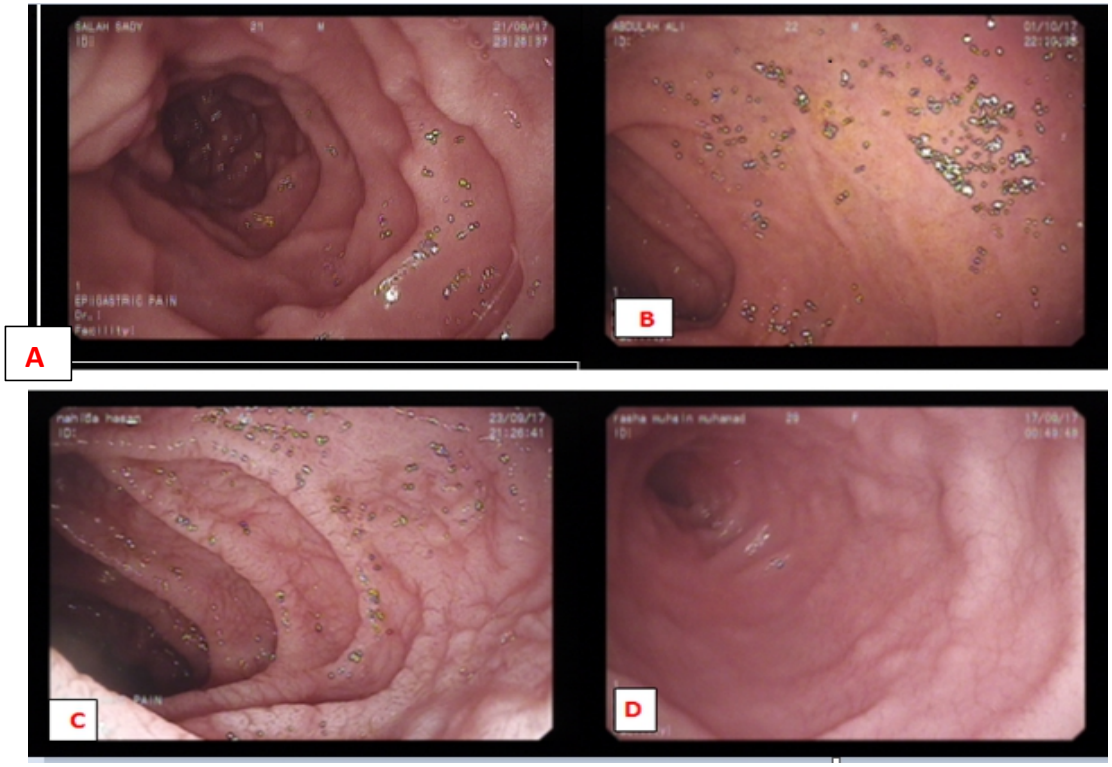

Figure 1. Endoscopic findings of CD patients: A. Nodularity; B: Reduction in duodenal folds; C: Scalloping; D. Paucity of duodenal folds

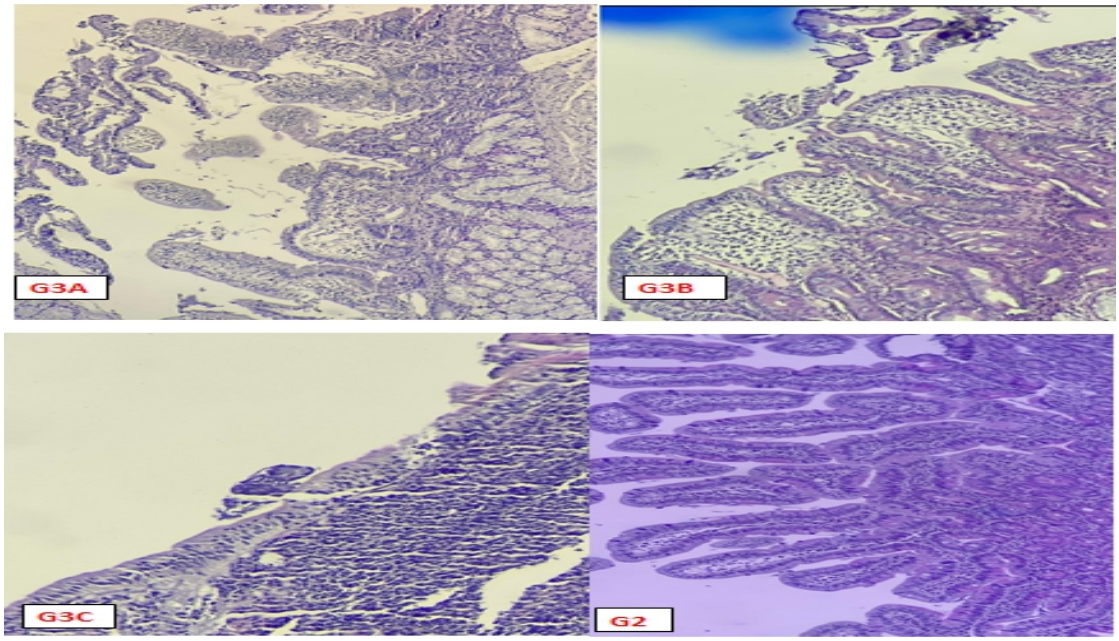

Figure 2. Histopathological findings of CD patients that represent G3A, G3B, G3C, and G2

Table2: Association between endoscopic & histopathological features of CD patients (n = 161)

Endoscopic finding	Histopathology frequency (%)						Total	P-Value
	G1	G2	G3A	G3B	G3C	Normal		
NODULARITY	0 (0.0%)	0(0.0%)	1(50.0%)	1(50.0%)	0(0.0%)	0(0.0%)	2(100.0%)	0.000
NORMAL	1(1.8%)	6(10.9%)	33(60.0%)	7(12.7%)	4(7.3%)	4(7.3%)	55(100.0%)	
POUCITY OF DUODENAL FOLDS	0(0.0%)	0(0.0%)	0(0.0%)	1(100.0%)	0(0.0%)	0(0.0%)	1(100.0%)	
REDUCTION IN DUODENAL FOLDS	0 (0.0%)	4(15.4%)	8(30.8%)	11(42.3%)	3(11.5%)	0(0.0%)	26(100.0%)	
SCALLOPING	0 (0.0%)	1(1.3%)	16(20.8%)	38(49.4%)	22(28. %)	0(0.0%)	77(100.0%)	
Total	1 (0.6%)	1 (6.8%)	58 (36.0%)	58 (36.0%)	29(18. %)	4 (2.5%)	161(100.0%)	

Correlation OF IgA anti tTG level with histopathological findings of CD patients

The correlation between Anti-tTG IgA levels and histological findings for CD patients showed: (a) Among 10 of normal <= 10.0 Anti-tTG IgA levels results, 8 had the G3A type,2 had G3B.: (b) Among 119 of 10.1 - 20.0 Anti-tTG IgA levels results, 4 had normal histology,44 had the G3A type,45 had G3B, 14 had G3C 11 had G2 and 1 had G1; (c) Among 23 of 20.1 - 60.0 Anti-tTG IgA levels results 4 had the G3A type,7 had G3B, and 12 had G3C;(d) Among 9 of 60.1+Anti-tTG IgA levels results,2 had the G3A type, 4 had G3B, 3 had G3C. Depending on the histopathological differences demonstrated below, a statistical association had been established between Anti- tTG IgA IU /ml levels and histopathological findings of celiac disease (p = 0.0002) shown in Table 3.

Table 3: Correlation of Histopathological findings with Anti - tTG IgA levels of celiac disease patients

Anti- tTG IgA iu /ml (Group)	Histopathology Frequency (%)						Total	P. Value
	G1	G2	G3A	G3B	G3C	Normal		
<= 10.0	0(0.0%)	0(0.0%)	8(80.0%)	2(20.0%)	0(0.0%)	0(0.0%)	10(100. %)	0.002
10.1 - 20.0	1(0.8%)	11(9.2%)	44(37.0%)	45(37.8%)	14(11.8%)	4(3.4%)	119(100.%)	
20.1 - 60.0	0(0.0%)	0(0.0%)	4(17.4%)	7(30.4%)	12(52.2%)	0(0.0%)	23(100.0%)	
60.1+	0(0.0%)	0(0.0%)	2(22.2%)	4(44.4%)	3(33.3%)	0(0.0%)	9(100.0%)	
Total	1(0.6%)	11(6.8%)	58(36.0%)	58(36.0%)	29(18.0%)	4(2.5%)	161(100.%)	

DISCUSSION

Our study shows that 52.8% of patients were female, this majority of female patients, on the other hand, was not statistically significant. Researches regarding the gender of the CD patients show a female predominance in certain [17],[18], & males in the others. [19]. Our research demonstrated that abdominal pain & bloating were predominant primary compliant in this cluster of CD patients which equivalent with European states [20] [21] our study shows that 5.0% of CD have constipation which was compatible with the study done by Sharma, Poddar, and Yachha [22]. which shows (4%) of CD with constipation. Our study shows that 12% of CD have diarrhea, 5.0% with short stature and 65.2% with anemia which was incomparable with the study done by Azita Ganji1, Abbas Esmaielzadeh1, et al [23] which shows (20%) (12.8%)(7.7%), diarrhea, anemia& short stature respectively may be because patients numbers are higher than our study. our study shows that 65.2% of CD have anemia which was similar to a new study in Iran[20] , and

incompatible with a study done by Pooja Semwal, et al [24] which shows anemia 54.5%. this may be nutritional.

Our study shows that 1.9% of CD patients have migraine which was incompatible with the study done by Briani et al[25] . which shows 5.6% this may be explained by those patients with headache usually consult the neurology department. our study shows Endoscopic findings had been compared with the histopathological finding & the associations gained was highly statistically significant (P<0.000). which was comparable with another study that shows endoscopic injury were found to be associated with Marsh grades increasing & the CD classical form. [26] And incompatible with another study which showed that the correlation was not significant(p=0.431) [27].

Our study showed that there was a statistically significant correlation between IgA anti- tTG level and histopathological finding which was comparable with other studies that showed a statistically significant relation was observed between the serological titer and positive pathologic results in patients with suspected CD. P < 0.001[28] .

We concluded that Histopathological findings correlate both with the endoscopic finding and the IgA ant tTG levels of celiac disease patients. Additional studies of larger sample sizes are very important for increasing the accuracy of diagnosis and management of this disease.

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