Association of Celiac Disease with *H.pylori* Chronic Gastritis in a Sample of Iraqi Patient

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ABSTRACT:

BACKGROUND:

Celiac disease is one of the commonest autoimmune, systemic diseases, occurs at any age in genetically predisposed individuals. It occurs in female more than male. *H .pylori* chronic gastritis occurs in association with celiac disease, the relations are poorly understood, many studies showed that *H.pylori* chronic gastritis trigger autoimmune response in celiac disease, other suggest that *H.pylori* reduces immune response.

OBJECTIVE:

To evaluate the association of *Helicobacter pylori* chronic gastritis with celiac disease in terms of clinical presentation, histological features (including Marsh grading of celiac disease and Sydney system classification of chronic gastritis), celiac serology and endoscopic findings.

MATERIAL AND METHOD:

A cross-sectional retrospective study conducted in the Department of Pathology/ Collage of Medicine /Al-Nahrain University for a period from January 2020 to March 2021. A study included analysis of 164 cases of celiac disease as control group and 164 cases had celiac with *H.Pylori* associated gastritis as a case group collected sample of Iraqi patients from January 2017 to December 2019.

RESULTS:

In this study, 374 cases were included; out of this numbers, 210 cases (56.1%) had associated *H. Pylori* chronic gastritis, whereas 164 cases (43%) were endoscopically negative for changes of *H.pylori* chronic gastritis (as mentioned by gastrointestinal specialist), this relation was statistically significant (P value < 0.05). In case group (Celiac disease and *H. Pylori* gastritis), the mean age was 34.6±15.3 years; the age range was 9 -85 years. In control group (Celiac disease only), the mean age was 30.8±13.9 years; the range was 3.5 - 83 years. The commonest symptom was epigastric pain which was significantly higher in 66 patients (40.7%) in cases versus 38 patients (23.3%) in control group (p value < 0.05). The endoscopic findings were significantly different between case and control groups (p value < 0.05), normal finding was found in 5 patients (3.1%) of the cases in comparison to 81patients (49.4%) of the control .Pangastropathy was significantly higher in case group (112 patients, 69.1%) than control group (6 patients, 3.7%). Classification of duodenal histopathological changes of cases groups according to Marsh Oberhuber classification (1999) showed that Marsh 3b was more in both case and control groups. In (marsh 3a), 11patients (42.3%) had mild atrophy, 3patients (20.00%) had moderate atrophy. In (marsh 3b), 12 patients (46.20%) had mild atrophy, 12 patients (80%) had moderate atrophy, 1patient (100.00%) had severe atrophy. In (marsh 3c) 3 patients (11.50%) had mild atrophy; this relation was statistically significant (P value=0.02). In (marsh 3a), 14 patients (20.9%) had gastric atrophy. In (marsh3b), 25 patients (26%) had gastric atrophy. In (marsh 3c), 3patients had gastric atrophy, this relation was statistically significant (P value <0.05).

CONCLUSION:

There is statistically significant association between *H.pylori* chronic gastritis and celiac disease (p value=0.017). No significant difference in classification of celiac disease according to March Oberhuber (1999) between case and control groups; however, Marsh3b was in 79(48.2%) of control group and in 93(56.7%) of case group. There was a significant association between presence and grade of atrophy of gastric mucosa in chronic gastritis in and Marsh grading of celiac disease in case group.

KEYWORDS: Celiac disease, H.pylori Chronic gastritis.

INTRODUCTION:

Celiac disease (CD) is a chronic, systemic, autoimmune condition related to the presence of a permanent gluten intolerance that affects genetically predisposed individuals, producing a chronic inflammation process that usually occurs in the small bowel. It is accompanied by a relatively high frequency of simultaneous or successive involvement of various extra-digestive organs over time.[1]

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Helicobacter pylori now accepted as a very common cause of gastritis in adults and children, is the foremost infectious etiology of gastric inflammation. *H. pylori* has a predilection for gastric surface (foveolar) epithelium whether that is in the stomach or the metaplastic gastric epithelium of duodenum and Barrett's esophagus. *H.Pylori* chronic gastritis increased risk of developing peptic ulcer increased risk of developing gastric cancer Maltoma develops from acquirement of mucosal lymphoid tissue following infection.[2]

The relationship between *H.pylori* infection and CD is not clear; the literature contains many opposing results.[3]

Prior investigations found a positive association between *H. pylori* and duodenal intra-epithelial lymphocytes (IELs), a finding consistent with the early intestinal mucosa damage in CD.[4]

Helicobacter pylori infection seems to be less frequent in celiac patients among those celiac subjects with concomitant Helicobacter pylori infection, histological damage degree and presence of endoscopic markers suggesting villous atrophy seem to be similar to those without *Helicobacter pylori* infection.[5]

Some studies suggest that the gastric mucosal lymphocyte infiltration could be secondary to the combination of Helicobacter *pylori* infection and chronic gluten ingestion in gluten-sensitive subjects. On the other hand, an inverse relationship between *HP* and CD has also been proposed, with HP even conferring protection against CD.[6]

AIM OF THE STUDY:

To evaluate the association of Helicobacter pylori chronic gastritis with celiac disease in relations to clinical presentation, histological features (including Marsh grading of celiac disease and Sydney system classification of chronic gastritis), celiac serology and endoscopic findings

RESULTS:

Age distribution

In case groups, those with Celiac disease and *H. Pylori* gastritis, the mean age was 34.6±15.3 years ; the age range was 9 -85 years. In control group (only Celiac disease), the mean age was 30.8±13.9 years; the range was 3.5 - 83 years.

The age distribution of case group (celiac disease with *H.pylori*) showed that the highest age group was 20-29 years with 39 cases (23.8%). In control group, the highest age group was also 20-29 years with 44 cases (26.8%). The age distribution showed non-significant statistical difference (p value > 0.05**).**

The endoscopic examination findings

The endoscopic findings were significantly different between case and control groups (p value < 0.05), including the following: normal finding of duodenal was found in 5 patients (3.1%) of the cases in comparison to 81 patients (49.4%) of the control. Pangastropathy was significantly higher in case group (112 patients, 69.1%) than control group (6 patients, 3.7%).as shown in table (1)

Table 1:The endoscopic examination findings.

OGD finding	Celiac only (Control)		Celiac with *H.pylori* gastritis (cases)		Total		P value
	Freq.	%	Freq.	%	Freq.	%	
Normal duodenal mucosa	81	49.40%	5	3.10%	86	26.40%	0.01 S
Pangastropathy	6	3.70%	112	69.10%	118	36.20%	0.001 S
Serrated d2 fold	39	23.80%	60	37.00%	99	30.40%	0.009 S
Scalloping of D2	13	8.00%	2	1.20%	15	4.60%	0.04 S

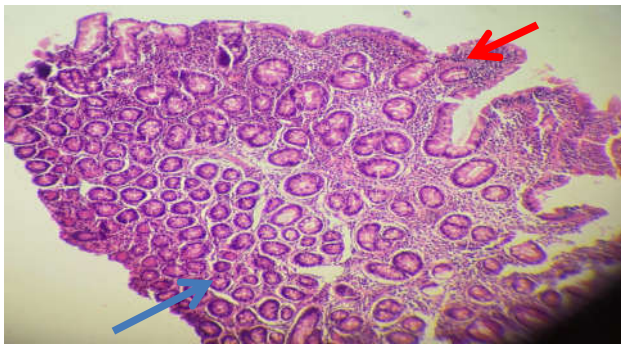
The relation between severity of gastric atrophy and duodenal histopathological changes of celiac disease

Out of 67 cases of celiac disease (marsh 3a), 53 patients (43.4%) had no atrophy (43.4%), 11 patients (42.3%) had mild atrophy, 3patients (20.00%) had moderate atrophy, and no case of severe atrophy in this relation was statistically significant (P value=0.02), as shown in table (2)

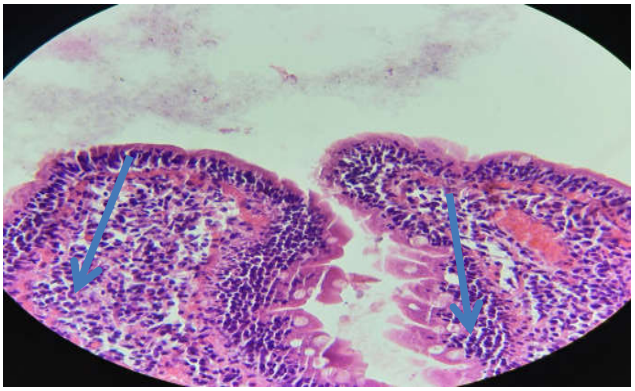
Table 2: **The relation between severity of gastric atrophy and duodenal histopathological changes of celiac disease.**

Severity of gastric atrophy	Duodenal Histopathological results according to Marsh oberhuber classification(1999)			Total
	3a	3b	3c	
No atrophy	53	68	1	122
	43.4%	55.7%	0.80%	100.00%
Mild atrophy	11	12	3	26
	42.30%	46.20%	11.50%	100.00%
Moderate atrophy	3	12	0	15
	20.00%	80.00%	0.00%	100.00%
Severe atrophy	0	1	0	1
	0.00%	100.00%	0.00%	100.00%
Total	67	93	4	164
	40.90%	56.70%	2.40%	100.00%

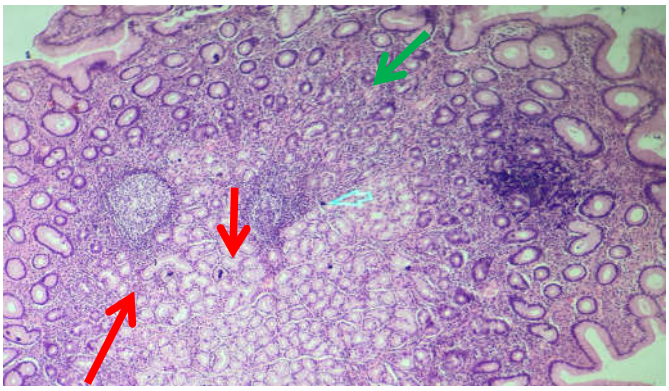
Likelihood ratio test =15.04, df=6, p- value 0.02 significant



Section of duodenum from patient with celiac disease Marsh 3c increased intraepithelial lymphocyte (>30 per 100 enterocytes), crypt hyperplasia (blue arrow) and near total flattening of villi (red arrow).(10X , H&E)



Section of duodenum from patient with celiac disease showing increased intraepithelial lymphocyte (>30 per 100 enterocytes)(blue arrows). (40X,H&E)



Section of chronic active gastritis showing diffuse lymphoplasmacytic infiltrate of lamina propria,lymphoid follicles(red arrows) with mild atrophy of gastric glands(green arrow).(10X,H&E)

DISCUSSION:

Age

In the present study, the control group (only celiac disease), the mean age was 30.8±13.9 years, which is parallel to Iraqi study done on celiac disease by Younis *et al* in 2014 which found that mean age was 30.67± 9.72 years, and parallel to study in America by Riddle *et al* in 2012 showed that celiac disease increases after 38 years.[7] [8]

The gender distribution

In case group, number of female patients was 106 (64.6%), whereas the number of male patients was 58(35.4%). Male to female ratio was 1:1.83. In control group female patients represent 122 (74.4%) while male patients were 42 (25.6%), the male to female ratio is 1:2.9.In control group this agrees with study done in Dohuk in 2019 by Mohammad *et al* , showed 44 were females (62.9%) and 26 were males (37.1%), also in agreement with a study done in America by Jansson Knodell *et al* 2017, showed that (females 65%, median age 39 years), the female to male ratio was 1.85:1.[9,10]

The relation between activity of *H.pylori* chronic gastritis and duodenal histopathological changes according to Marsh Oberhuber classification (1999) of case group

Out of 67 cases of celiac disease (marsh 3a),16 patients (23.9%) had chronic active gastritis, out of 93 cases of celiac disease (marsh 3b), 22 patients (23.7%) had chronic active gastritis, out of 4 cases of celiac disease (marsh 3c), 0 patient had chronic active gastritis. These results disagree with study done in Argentin by Diamanti *et al* 1999 in which activity in chronic gastritis reported in 9%.[11]

These results disagree also with study on celiac disease and *H.pylori* infection in Iran done by Rostami-Nejad *et al* 2009 in which activity of *H.pylori* chronic gastritis reported in Marsh 3a (1%) Marsh3b (1%) Marsh 3c (2%).[12]

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