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Analysis of gastric and duodenal biopsy results in patients presenting with dyspepsia: a cross-sectional study in a middle eastern population

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ABSTRACT

Objective Correa's cascade is a 'Model for Gastric Cancer Development' described by Peleyo Correa. The reversibility of Correa's cascade remains debatable. The literature contains insufficient data on the specific stage of the cascade during which *Helicobacter pylori* is detected, treated, and the effect on prognosis. Herein, we aim to determine the prevalence of various precancerous and cancerous gastric lesions in patients presenting with dyspepsia, the prevalence of gastritis and *H. pylori* infection, the prevalence of duodenal pathology in patients presenting with dyspepsia, identify the stage of *H. pylori* detection in relation to Correa's cascade, and investigate a possible relationship between *H. pylori* and celiac disease.

Design Retrospective cross-sectional study conducted on a middle eastern population at a Lebanese tertiary hospital centre. 1428 patients presenting with dyspepsia underwent gastroscopy with gastric and duodenal biopsies. Variables include age, sex, presence/absence of *H. pylori* infection, and histopathological analysis of gastric and duodenal biopsies.

Results Being above 40 years of age was associated with increased likelihood of exhibiting abnormal gastric biopsy result. Gastritis and metaplasia were detected more frequently than glandular atrophy ($p<0.001$) with gastritis being present the most ($p<0.001$). The presence of *H. pylori* and the gastric biopsy results were not associated with any of the duodenal biopsy results.

Conclusion The burden of *H. pylori* infection in patients with dyspepsia was high. *H. pylori* was detected at various precancerous lesions with varying significance. The prevalence of duodenal adenocarcinoma in dyspeptic patients is unexpectedly high. No association between gastric and duodenal pathologies was found.

Summary box

What is already known about this subject?

- Correa's cascade represents a stepwise transformation process that takes 30–50 years beginning with gastritis, progressing to atrophic gastritis, followed by intestinal metaplasia, intestinal dysplasia, and ending with intestinal carcinoma.
- Minimal epidemiological data is present regarding the prevalence of *Helicobacter pylori*, precancerous, and cancerous gastric lesions upon diagnosis in a middle eastern population.

What are the new findings?

- The prevalence of *H. pylori* in the studied middle eastern sample population was found to be around 37%. Abnormal gastric biopsy results were found in 56% of the studied population out of which 66% were found to have *H. pylori*.
- Increasing age and being *H. pylori* positive were associated with an increased likelihood of exhibiting abnormal gastric biopsy results.
- Comparing *H. pylori* and each of the components of Correa's cascade showed a significant relationship between *H. pylori* and each of gastritis, glandular atrophy, and intestinal metaplasia.
- Both gastritis and metaplasia were being detected more frequently than glandular atrophy upon diagnosis.

How might it impact on clinical practice in the foreseeable future?

- This manuscript provides new insight regarding the epidemiology of *H. pylori* infection among middle eastern population and the expected stage of precancerous lesion upon diagnosis.
- This manuscript stands as the initial step in the understanding of the possible reversibility of the pathological changes seen in the carcinogenesis of gastrointestinal (GI) malignancies. A complete picture could be achieved with future studies on follow up endoscopies after treatment.

INTRODUCTION

Helicobacter pylori is a microaerophilic, gram-negative bacterium that infects around half of the world's population. Although the exact mode of transmission remains unclear, multiple mechanisms may be operative, with person-to-person transmission seems the

most probable mode of acquisition.[1] The virulence of *H. pylori* comes from the bacterium characteristics that allow it to adapt to the gastric environment and invade the gastric mucosa while precipitating an immune response that contributes to the pathological changes in the host.

Infection with *H. pylori* can lead to a constellation of dyspeptic symptoms and to an increased risk of gastric adenocarcinoma which makes the diagnosis and treatment of *H. pylori* infection crucial.[2] Based on the Lebanese Cancer Registry, stomach cancer is one of the 10 most common cancers among the Lebanese population.[3]

Due to the debilitating consequences of chronic *H. pylori* infection, worldwide efforts are being made for gastric adenocarcinoma prevention and *H. pylori* treatment. Results from animal models and recent epidemiological studies showed that gastric carcinogenesis can be prevented with the eradication of *H. pylori* in infected subjects.[4] In addition, data from a randomised clinical trial, found that the incidence of gastric cancer was reduced with short-term treatment for the eradication of *H. pylori*.[5] Moreover, meta-analysis of primary prevention studies showed around 40% decrease in gastric cancer progression with *H. pylori* eradication.[6]

Published guidelines regarding stomach cancer prevention strategies stress on the need to find subgroups at high risk of developing stomach cancer to apply specific strategies.[7 8] The WHO and the International Agency for Research on Cancer recommend that all countries should assess the potential value of gastric cancer prevention strategies in relation to present and future economic and human impacts.[9]

The Lebanese population's increased risk of developing stomach cancer is linked to many factors such as a high sodium diet, obesity, smoking, and relatively high alcohol use.[10 11]

The literature does not contain systematic reviews on the prevalence and epidemiology of *H. pylori* in Lebanon.

Furthermore, in order to appreciate the role of *H. pylori* in the carcinogenesis of gastric carcinoma, one should take a look at Correa's cascade, which represents a stepwise transformation process that takes 30–50 years beginning with gastritis, progressing to atrophic gastritis, followed by intestinal metaplasia, intestinal dysplasia, and ending with intestinal carcinoma.[6]

Interestingly, it is unknown whether Correa's pathway is reversible, yet at the same time, studies show that treating *H. pylori* is associated with a reduction in gastric carcinoma incidences.[6] In order to investigate the possible reversibility of Correa's cascade, the first step is to identify what type of gastric lesions are being significantly detected more frequently in patients infected with *H. pylori*. These patients should be subsequently followed for progression of the transformation process after eradication of *H. pylori*.

In this study, we aim to perform an epidemiological analysis of *H. pylori* infection, stomach cancer and precancerous lesions of the stomach in symptomatic middle eastern patients in a tertiary hospital centre in Lebanon over a period of 12 months (from mid-2017 to mid-2018) while trying to identify the timing of *H. pylori* infection detection in relation to Correa's cascade. Furthermore, we aim to identify possible duodenal pathology focusing specifically on duodenal adenocarcinoma and celiac disease (CD) while investigating a possible relationship between abnormal duodenal findings and *H. pylori* infection. The findings are also compared with national and international data.

POPULATION AND METHODS

Sampling

This retrospective cross-sectional study was conducted on a middle eastern population at a tertiary hospital centre in Lebanon on a total of 1428 patients who underwent gastroscopy and duodenoscopy with biopsies by qualified physicians over a period of 12 months. Documented demographic data consisted of the age and sex of the patients.

The sample size (1428) was not reached based on the general population but rather on the number of patients presenting to St. George Hospital University Medical Center with respect to the inclusion and exclusion criteria.

Inclusion criteria

The inclusion criteria for this study were met if the patient was previously undiagnosed and is presenting with one or more dyspeptic symptoms (ie, postprandial fullness, early satiation, or postprandial epigastric pain).

The number of patients who presented for endoscopic evaluation was 1734. A total of 1574 patients met the inclusion criteria.

Exclusion criteria

Any patient that presented with one or more of the following alarm symptoms: weight loss, haematemesis, or persistent vomiting, was excluded from the study. Moreover, any patient who did not have both a gastric and duodenal biopsy submitted, was excluded as well. Additionally, patients with a recent proton pump inhibitor (PPI), histamine receptor blockers, or/and antibiotic intake were excluded from the study.

A total of 146 patients were excluded thus reducing the sample size to 1428 patients.

Endoscopy preparation and procedure

All endoscopies were performed after 6 hours of fasting. In non-sedated patients, xylocaine 5% was used as a topical anaesthetic for the oropharynx. Sedation with IV midazolam 0.1 mg/kg was used at the discretion of the physician. Patients were placed in the left lateral decubitus position, with constant monitoring of vital signs by an anaesthetist.

Endoscopies were performed using a fibre optic Olympus gastro-duodenoscope, adhering to standard procedures. Endoscopic evaluation was carried out as far as the second part of the duodenum. As per institutional

standards, punch mucosal biopsies were taken for histopathological diagnosis of *H. pylori* and CD from the antrum (two), stomach body (two), second portion of the duodenum (two), and from any suspicious area along the evaluated gastrointestinal tract. The analysis was based on the most advanced lesion found in the stomach and duodenum, respectively.

Pathology analysis

In order to stratify the different abnormal gastric and duodenal biopsy results, micro-cuts were taken from each biopsy sample, and were stained with H&E.

The histopathological findings of the gastric biopsy were stratified into normal finding, chronic gastritis, atrophic gastritis, intestinal metaplasia, dysplasia and intestinal type-gastric cancer. All other results were considered negative. Abnormal duodenal biopsies results were stratified into normal, villous atrophy, intra-epithelial lymphocytes infiltrates and adenocarcinoma. CD was defined as duodenal histology featuring villous atrophy and/or intraepithelial lymphocytes.

Modified Giemsa stain was used to diagnose *H. pylori* infection from the different biopsy specimens.

Statistical analysis

Data analysis consists of χ^2 tests testing the relationships between *H. pylori* and each gastric biopsy result, comparing the detection significance of the various gastric biopsies, testing the relationships between the presence of *H. pylori* and each duodenal biopsy result along with the relationships between each of the gastric biopsies with each of the duodenal biopsy results.

Additionally, the analysis consists of the regression analysis. The data consists of three independent categorical variables including (age stratified into two groups: 'less than 40 years old' and '40 years and above'; gender stratified into two groups: 'males' and 'females'; and *H. pylori* stratified into two groups: '*H. pylori*' and 'non-*H. pylori*') that are presented as frequencies and percentages. A p value of less than 0.05 was chosen as the cut-off for significance. SPSS V.24 was used for data entry, data cleaning, and analysis. Binomial logistic regression tests were run to assess the predictors of exhibiting abnormal gastric and duodenal biopsy results. The dependent variables are 'Gastric Biopsy Result' and 'Duodenal Biopsy Result', treated as categorical variables (abnormal or normal). A third binomial regression was run to test the effects of gender and age on the presence of *H. pylori*. Adjusted ORs and a 95% CI are reported.

The results are presented as epidemiological data, analysis of gastric biopsy results and analysis of the duodenal biopsy results in relation to the various variables previously mentioned.

RESULTS

Epidemiological data

A summary of the epidemiological presentation of the patient sample and biopsy results is shown in table 1. The prevalence of *H. pylori* in the studied sample was found to be 37%. Abnormal gastric biopsy results were found in 56% of the studied population out of which 66% were found to have *H. pylori*. Gastric intestinal carcinoma was found in 0.4% of the patients. With regards to the duodenal biopsy results, 4% were abnormal with celiac being present in 3.8% of the patients and duodenal carcinoma being present in 0.2%.

Table 1 Epidemiological representation of the patients sample and biopsy results

Variables	N	%
Patient gender		
Female	756	53
Male	672	47
Patient age		
Less than 40 years	432	30
Greater than 40 years	996	70
H. pylori		
H. pylori	524	37
Non-*H. pylori*	904	63
Gastric biopsy result		
Normal	764	54
Gastritis	487	34
Glandular atrophy	35	2
Intestinal metaplasia	134	9
Intestinal dysplasia	2	0.1
Carcinoma	6	0.4
Normal gastric biopsy result		
Normal	764	54
Abnormal	664	46
Duodenal biopsy result		
Normal	1371	96
Villous atrophy	6	0.4
Intraepithelial lymphocytes	23	2
Villous atrophy and intraepithelial lymphocytes	25	2
Duodenal carcinoma	3	0.2
Normal duodenal biopsy result		
Normal	1371	96
Abnormal	57	4

Analysis of gastric biopsies results

Binary logistic regression: age, *H. pylori*, gender versus gastric biopsy result

A binomial logistic regression was performed to ascertain the effects of age, *H. pylori*, and gender on the likelihood that patients have an abnormal gastric biopsy result (table 2).

From these results, one can see that age (p<0.001) and *H. pylori* (p<0.001) added significantly to the model/

Table 2 Binary logistic regression: age, *H. pylori*, gender versus gastric biopsy result. The table shows significant association between age and *H. pylori* with abnormal gastric biopsy results p<0.001. Gender was not associated with abnormal gastric biopsy results with p=0.090

								95% CI for EXP(B)	
		B	SE	Wald	df	Sig.	Exp(B)	Lower	Upper
Step 1*	Age (1)	0.984	0.230	18.265	1	0.000	2.675	1.703	4.200
	H. pylori (1)	8.048	1.008	63.790	1	0.000	3127.488	433.992	22537.707
	Gender (1)	−0.319	0.188	2.870	1	0.090	0.727	0.503	1.051
	Constant	−2.271	0.219	107.399	1	0.000	0.103		

*Variable(s) entered on step 1: age, *H. pylori*, gender.

prediction, but gender (p=0.090) did not significantly add to the model.

It was found that increasing age (namely the 40 years and above category) was associated with an increased likelihood of exhibiting abnormal gastric biopsy results (β=2.68, 95% CI 1.703 to 4.20). Patients who were *H. pylori* positive were more likely to have an abnormal gastric biopsy result than patients who were *H. pylori* negative (β=3127, 95% CI 433.9 to 22537.7).

Binary logistic regression: age, gender versus *H. pylori*

A binomial logistic regression was performed to ascertain the effects of age and gender on the likelihood that patients have an *H. pylori* positive result (table 3).

From these results, one can see that only age (p<0.001) added significantly to the model/prediction.

It was found that increasing age (namely the 40 years and above category) was associated with an increased likelihood of exhibiting a positive *H. pylori* result (β=1.67, 95% CI 1.306 to 2.128).

χ^2 analyses: *H. pylori* versus gastric biopsy histopathology result

χ^2 analyses for *H. pylori* and each of the components of Correa's cascade showed a significant relationship between *H. pylori* and each of gastritis, glandular atrophy, and intestinal metaplasia (table 4). However, no significant relationship was found between *H. pylori* and each of Intestinal Dysplasia and Gastric Carcinoma groups.

χ^2 analysis for the difference in the prevalence of the various gastric biopsy histopathology result regardless of the presence of *H. pylori*

The aim of these tests was to identify which tissue biopsy lesion is being significantly detected more frequently in our sample regardless of the presence of *H. pylori* (including the normal results). Using the χ^2 test, the percentage of patients that had glandular atrophy differed by those that had gastritis, X2(1, n=1428)=18.569, p<0.001. The percentage of patients that had intestinal metaplasia did not differ by those that had glandular atrophy, p=0.070. The percentage of patients that had intestinal metaplasia differed by those that had gastritis, X2(1, n=1428)=76.531, p<0.001. These results show that gastritis is significantly being detected more frequently than glandular atrophy and intestinal metaplasia. Figure 1 shows a representation of the various gastric biopsy results with age.

χ^2 analysis for the difference in the prevalence of the various gastric biopsy histopathology results in patients with *H. pylori*

The aim of this test was to identify which tissue biopsy lesion is being significantly detected more frequently in our sample, among patients infected with *H. pylori*. The results show that only one case had both positive *H. pylori* and a normal gastric biopsy result. In *H. pylori* positive patients, the prevalence of gastritis, glandular atrophy, and intestinal metaplasia was 81%, 5%, and 13%, respectively. More cases of gastritis are being detected in comparison to cases of metaplasia (p<0.001). Moreover, both gastritis and metaplasia are being detected more frequently than glandular atrophy (p<0.001). A detailed analysis is presented in table 5.

Analysis of duodenal biopsies results

The three cases of duodenal carcinoma were all well differentiated adenocarcinoma, ulcerating, located at the second portion of the duodenum (periampullary), had a

Table 3 Binary logistic regression: age, gender versus *H. pylori*. This table shows that there is no difference in genders regarding the presence of *H. pylori* with p=0.256. However, being above 40 years of age was associated with an increase likelihood of having positive *H. pylori* results with p<0.0001

								95% CI for EXP(B)	
		B	SE	Wald	df	Sig.	Exp(B)	Lower	Upper
Step 1*	Gender (1)	0.126	0.111	1.289	1	0.256	1.134	0.913	1.408
	Age (1)	0.511	0.125	16.841	1	0.000	1.667	1.306	2.128
	Constant	−0.969	0.119	66.410	1	0.000	0.379		

*Variable(s) entered on step 1: gender, age.

Table 4 χ^2 analyses for *H. pylori* and each gastric biopsy result. This table presents the association of *H. pylori* with each of the components of Correa's cascade. The data showed a significant relationship between *H. pylori* and each of gastritis, glandular atrophy, and intestinal metaplasia with p<0.001. However, no significant relationship was found between *H. pylori* and each of intestinal dysplasia and gastric carcinoma groups with p values of 0.134 and 0.675, respectively

Gastric biopsy result	Pearson χ^2 value	df	Asymptotic significance (2-sided)	Comment
Gastritis	800.576	1	0.000	The percentage of patients that had gastritis differed by *H. pylori* result X2(1, n=1428)=800.58, p<0.001.
Glandular atrophy	25.270	1	0.000	The percentage of patients that had glandular atrophy differed by *H. pylori* result X2(1, n=1428)=25.27, p<0.001.
Intestinal metaplasia	12.569	1	0.000	The percentage of patients that had intestinal metaplasia differed by *H. pylori* result X2(1, n=1428)=12.57 p<0.001.
Intestinal dysplasia	–	–	0.134 (Fisher's exact test)	The percentage of patients that had intestinal dysplasia and gastric carcinoma did not differ by *H. pylori* results.
Gastric carcinoma	–	–	0.675 (Fisher's exact test)	
Valid cases (N)	1428			

diameter of 3.1 cm, 3.6 cm and 4.3 cm (mean 3.7 cm) and the histological examination of margins was negative.

Based on table 6, there is no significant relationship between *H. pylori* and each of the four duodenal biopsy results.

χ^2 analysis for gastric biopsy result and duodenal biopsy result

The χ^2 analysis for '

' and 'duodenal biopsy result' showed that the percentage of patients that had an abnormal duodenal biopsy result did not differ by gastric biopsy result, X2(1, n=1428)=0.902, p=0.342.

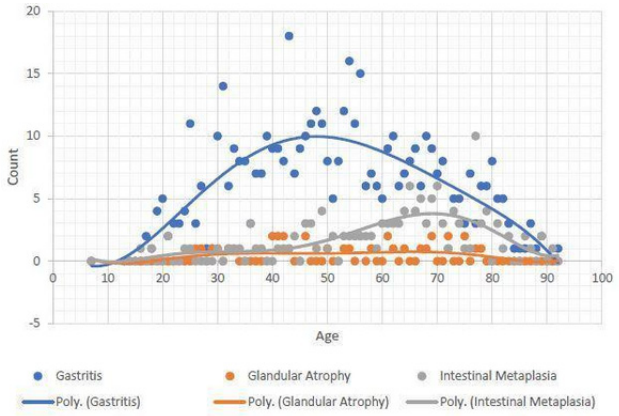

Figure 1 Frequency of gastritis, glandular atrophy and intestinal metaplasia with increasing age. This is a scatter (XY) chart with trend lines representing the change in the frequency of each type of precancerous gastric lesions with increasing age. The chart represents the higher prevalence of gastritis relative to intestinal metaplasia and glandular atrophy.

Binomial logistic regression: age, *H. pylori*, and gender versus abnormal duodenal biopsy result

A binomial logistic regression was performed to ascertain the effects of age, *H. pylori*, and gender on the likelihood that patients have an abnormal duodenal biopsy result.

From these results, one can see that none of the predictors added significantly to the model/prediction, since the p values for gender, age and *H. pylori* were greater than 0.05 (0.949; 0.869 and 0.605, respectively). Furthermore, the 95% CIs for all three predictor variables include the null value of 1.00, which further supports that the respective ORs are not statistically significant. This may be due to the fact that our sample size may be small to have enough power to detect a statistically significant result if one truly does exist.

DISCUSSION

The epidemiological data showed that the prevalence of *H. pylori*, as detected by histology, was 37%, regardless of the presence of any gastric lesion. This is consistent with some studies in the European literature which reports a 30% detection rate by histology.[12] Moreover, a study conducted in a setting similar to ours, shows similar results with *H. pylori* being detected in 36% of the patients on histology.[13] A systemic review presented a prevalence varying between 22% and 87.6% in the Eastern Mediterranean region.[14] Regarding the investigations done in Lebanon, one study found the prevalence to be 52.4% on histology at a peripheral hospital in north Lebanon.[15] The variation of results between our study and the aforementioned study could be due to the fact that it was conducted in a relatively peripheral hospital whereas our study was conducted in a central hospital (north Lebanon vs Beirut).

Table 5 χ^2 analysis for the difference in the prevalence of the various gastric biopsy histopathology results in patients with *H. pylori*. The table shows that in patient with *H. pylori*, gastritis is being detected more frequently than metaplasia and glandular atrophy (p<0.001) and that intestinal metaplasia is being detected more frequently than glandular atrophy (p<0.001)

	Gastritis (G)	Glandular atrophy (A)	Intestinal metaplasia (M)	G versus A	G versus M	M versus A
Positive biopsy results of each of the lesions	427	27	68	The χ^2 statistic is 622.6932. The p value is <0.001	The χ^2 statistic is 494.2695. The p value is <0.001	The χ^2 statistic is 19.4623. The p value is 0.001
Negative biopsy results of each of the lesions	97	497	456			
% of Positive biopsy results for each of the lesions	81	5	13			

Gastric intestinal carcinoma was found in 0.4% of the patients. Around 4% of the duodenal biopsy results were abnormal, with villous atrophy being present in 2.2% of the cases. Our results are numerically close to the study done in a primary health centre in Beirut which showed a prevalence of 1.8%.[16] Moreover, the results in Lebanon are similar to the results of other studies done worldwide.[17] Unfortunately, the prevalence of CD is difficult to assess in the absence of well-defined criteria. However, many different studies, with some variations in the diagnostic criteria, showed similar results with a prevalence of CD varying between 1% and 5%.[16–21]

Duodenal carcinoma was present in 0.2% of our cases. To our knowledge, the prevalence of duodenal carcinoma in patients presenting with gastrointestinal symptoms in general or dyspepsia in specific has never been investigated. The 0.2% prevalence found in our sample of patients presenting with dyspepsia, is 180 times higher than the prevalence of all small intestine carcinomas in the US general population, which was around 0.002% in 2004. Also, this study results are 780 times higher than the prevalence of small intestine adenocarcinoma in France, which was found to be 0.0002% in a study conducted between 1976 and 2001.[22] However, it is important to note that this study deals with the prevalence of duodenal carcinoma in symptomatic patients in contrast to the USA and France's studies which deal with the general population, thus emphasising the need to further investigate the likelihood of duodenal carcinoma in this specific subset of individuals.

Moreover, the results show that being above 40 years of age is associated with an increased likelihood of exhibiting a positive *H. pylori* result. The increased risk of infection with age is still controversial, with conflicting reports in the literature. Studies done in Iran,[23] Morocco,[24] Ethiopia,[25] and many European epidemiological studies show a positive correlation between age and increased risk of *H. pylori* infection. However, a number of other studies, including one conducted in Lebanon, found no such association, attributing the other positive findings to a birth cohort effect. Our results showed no association between gender and *H. pylori* detection rates, which

Table 6 χ^2 analyses for *H. pylori* and each duodenal biopsy result. The table shows no association between *H. pylori* and any of the duodenal biopsy results

Duodenal biopsy result	Pearson χ^2 value	df	Asymptotic significance (two-sided)	Comment
Villous atrophy	0.978	1	0.323	The percentage of patients that had villous atrophy did not differ by *H. pylori* result X2(1, n=1428)=0.978, p=0.323.
Intraepithelial lymphocytes	0.357	1	0.550	The percentage of patients that had Intraepithelial lymphocytes did not differ by *H. pylori* result X2(1, n=1428)=0.357, p=0.550.
Villous atrophy and intraepithelial lymphocytes	0.585	1	0.445	The percentage of patients that had both villous atrophy and Intraepithelial lymphocytes did not differ by *H. pylori* result X2(1, n=1428)=0.585, p=0.445.
Duodenal carcinoma	–	–	0.303 (Fisher's exact test)	The percentage of patients that had Duodenal Carcinoma did not differ by *H. pylori* result (p=0.303).
Valid cases (N)	1428			

is consistent with most of the literature, including local data.[15 26–28]

Correa's cascade is an established pathway for the carcinogenesis of gastric carcinoma. This transformation process involves the following stages in chronological order: gastritis, atrophic gastritis, intestinal metaplasia, intestinal dysplasia, intestinal carcinoma. *H. pylori* plays an important role in this cascade, which usually spans 30–50 years.

It is important to note that it is still unknown whether Correa's cascade is a reversible process or not, regardless of the fact that treating *H. pylori* infections results in a reduced gastric carcinoma incidence. In order to establish a reversibility in Correa's cascade, an assessment of which gastric lesions (if any) are being significantly detected more frequently needs to be carried out. Patients should be followed to assess the progression/regression of their gastric lesions after the eradication of *H. pylori*.

Here, we investigated the effects of age, *H. pylori*, and gender on the likelihood of a patient to have an abnormal gastric biopsy result. It was found that being above 40 years of age and/or having a positive *H. pylori* result, were associated with an increased likelihood of exhibiting abnormal gastric biopsy results. In relationship to Correa's cascade, we are significantly detecting more cases with gastritis in comparison to patients with metaplasia ($p<0.001$). Moreover, both gastritis and metaplasia are being detected at a higher rate than glandular atrophy ($p<0.001$) in patients infected with *H. pylori*. However, gender was not associated with any positive biopsy results.

The association of *H. pylori* and abnormal gastric biopsy results is a well-established finding.[6] For age and gender, we know that gastric cancer is more common in males and elderly.[28] However, to our knowledge, there is no study investigating the significance of having precancerous gastric lesions (PCGLs) in relationship to gender and age. Although an increase in PCGLs with age is expected, this is the first study to provide empirical evidence for this increase. On the other hand, and counterintuitively, we did not find a difference between males and females in relationship to PCGLs.

The absence of association between all the above-mentioned factors and gastric carcinoma is probably due to the low number of cases of carcinoma in our sample, which reflects a high early detection of the precursor gastric lesions and relative early eradication of the infection in the population involved.

Additionally, it was interesting to identify which tissue biopsy is being significantly detected more frequently in our sample, regardless of the presence of *H. pylori* (including the normal results). It was found that more gastritis cases are being significantly detected relative to intestinal metaplasia and glandular atrophy, with no significant difference between the last two.

Figure 1 shows the distribution of the various gastric biopsy results in relation with age. Although the graph cannot be used as a definitive tool for interpretation, it helps one to visualise a relative bimodal distribution of gastritis in the population (peaking around 55), with an increase in the frequency of intestinal metaplasia after 40 years of age. One can attribute the decrease in gastritis could be partially due to the transformation to more advanced stages (which can be explained by the rise in both intestinal metaplasia and atrophy). However, other causes such as regression of the disease, decrease population size, and treatment should be considered as well.

Moreover, and as expected, having positive *H. pylori*, positive gastric biopsy results, gender and age were not associated with positive duodenal biopsy results for CD, with no relationship found with any of the biopsy findings. In the literature, a study done by Lebwohl *et al* found that *H. pylori* infection was lower in CD positive patients than in those without CD.[17] Many other studies found similar *H. pylori* infection rates among individuals with and without CD, with one showing the presence of variations in CD's histological damage depending on the *H. pylori* strain.[18 29] No difference between gender and between ages was found in the literature.[17–25 27–30]

The patient sample number was based on the number of patients presented to St. George Hospital University Medical Center in the period between mid-2017 and mid-2018 with respect to the aforementioned inclusion and exclusion criteria. As such, the patient sample number was not based on the general population which may be considered as a limitation to this study.

Finally, our results were compatible with the abstract presented at the European Society of Gastrointestinal Endoscopy (ESGE) Days Congress 2019.[31]

CONCLUSION

In conclusion, a high rate of *H. pylori* was detected in the sample of patients presenting with dyspepsia, with *H. pylori* being found along different PCGLs with varying significance. Moreover, in this sample of patients presenting with dyspepsia, an unexpectedly high prevalence of duodenal adenocarcinoma was found. The different gastric and duodenal pathologies found were unassociated. A follow-up study is planned in the same sample to monitor the progression of the PCGLs after *H. pylori* eradication, in order to identify the possible reversibility of Correa's cascade.

Contributors YG, MHK, SF: study idea, study plan, study design, and literature review. NB-A: statistical analysis, writing, and proofreading the article. HB-A: statistical analysis. AT: writing, proofreading, reviewing, and submitting the article. NM, RY, GC, GJ, SK, KB: literature review, writing the article, study plan. MA: pathology data analysis.

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Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information.

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