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Case Report

Preneoplastic Gastric Lesions and Helicobacter Pylori in Endoscopic Detection and Early Diagnosis of Gastric Cancer in Lebanese Population. A Retrospective Study from 2019-2020

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Abstract

Background: Gastric cancer (GC) ranks as the fifth leading cause of cancer worldwide and is the fourth leading cause of cancer mortality. Premalignant gastric lesions (PGL) are considered as the most significant risk factor for GC. The purpose of this study was to determine the prevalence, characteristics, and risk factors of premalignant gastric lesions among Lebanese patients.

Methods: This was a retrospective study conducted among patients admitted to the endoscopy units of the Rafic Hariri University Hospital (RHUH) and Bahman Hospital in Lebanon between Jan 2019 and Dec 2020. Medical information including gastric pathology, type of PGL, indication of endoscopy, endoscopic findings and H. pylori infection were obtained from the medical records of all patients. A total of 2400 patients were initially identified and used to calculate the prevalence of PGL. Patients were then contacted by phone to obtain demographic data, smoking status, alcohol consumption, family history of GC, and lifestyle characteristics. We managed to collect 1062 responses. A binary logistic regression was done to determine the risk factors of PGL.

Results: Out of 2,400 patients having undergone gastric endoscopy **with gastric biopsies**, 218 were identified with PGL giving it a prevalence of 9.8%. Atrophic gastritis was the most frequently identified PGL (68%), followed by intestinal metaplasia (30%). The mean age of our final population (1064 patients) was 53.03 (±18.01) years. H. pylori infection was found among 44% of them. The most common indication for gastric endoscopy was abdominal pain (28%), followed by dyspepsia (25%). Erythema was the most common finding (51%), followed by erosions (19%). Binary regression analysis showed that older age (≥ 40 years) (ORa = 3.06), family history of GC (ORa = 10.79), alcohol consumption (ORa = 9.21), and H. pylori (ORa = 4.95)

were associated with increased risk of PGL). Being active and having a healthy diet were protective factors for PGL. Finally, no association was found between gender and PGL.

Conclusion: In comparison to neighboring countries, our findings revealed that the prevalence of PGL and H. pylori infection was low, but still need attention. The risk factors for developing premalignant gastric lesion were older age (40 years), a family history of gastric cancer, alcohol consumption, and H. pylori infection.

Keywords: Gastric Cancer; Premalignant Gastric Lesion; H. Pylori; Risk Factors

Introduction

Gastric cancer (also known as stomach cancer) ranks as the fifth leading cause of cancer in the world. It is estimated that over one million patients are diagnosed with gastric cancer each year, accounting for nearly 6% of all cancer cases [1]. According to worldwide estimations, gastric cancers occur more frequently in developing nations [2]. In addition, reports from different countries revealed a significant variation in the incidence of gastric cancer among all geographic regions and cultures, and showed high incidence rates in Eastern Asia, and Eastern Europe, whereas rates are lowest in Northern America, Northern Europe, and African regions [1].

Worldwide, cancer of the stomach is the fourth leading cause of cancer mortality with 769,000 deaths in 2020 [1], making it responsible for 8.3% of all cancer deaths. Furthermore, since the majority of patients were diagnosed at advanced stages, the mortality rates of gastric cancer remain high. The majority of gastric cancers are adenocarcinomas, which are classified into two histological types: diffuse (undifferentiated) and intestinal (well-differentiated). Intestinal type gastric cancer accounts for 60% of all cancers and is typically preceded by a series of precursor lesions [3]. These precursor lesions are involved in the Correa Cascade, a multistep process that is initiated by the development of chronic gastritis [4]. However, H. pylori has been shown to be the most common infectious etiology associated with chronic gastritis, making it the initiator of this carcinogenic pathway [5]. After an acute H. pylori infection, acute gastritis can progresses to chronic gastritis, which eventually leads to metaplasia, dysplasia, and gastric adenocarcinoma [4]. According to several studies, patients infected with H. pylori have a tenfold increased risk of developing GC [6].

Premalignant gastric lesions are considered a major risk factor for the development of GC. However, because symptoms are often absent in PGL patients, data on the prevalence of these lesions are rare [7]. Several factors have been identified as risk factors for the development of PGL such as H. pylori infection, older age, gender (male), and smoking. Other factors include obesity and diabetes mellitus [8].

In Lebanon, many factors have been found to be associated with increased risk of stomach cancer including a high sodium diet, obesity, smoking, and moderate alcohol consumption [9]. However, to the best of our knowledge, epidemiological data of PGL in the Lebanese population has never been reported. Therefore, in this retrospective study we aimed to determine the prevalence and characteristics of premalignant gastric lesions and their relationship with Helicobacter Pylori infection. We also aimed to investigate if there is a possible relationship between premalignant gastric lesions and different demographic and lifestyle factors.

Subjects and Methods

This study is a retrospective study conducted in Lebanon among patients admitted to the endoscopy unit of RHUH and Bahman Hospital during a period of 2 years from January1, 2019 to December 31, 2020. We included patients over 18 years of age in this study. However, patients were excluded if they are younger than 18 years old, and if they were diagnosed with advanced neoplastic disease. This study was reviewed and approved by the research ethics committee of the included hospitals.

First, we reviewed the medical records of all patients admitted to the endoscopy units of the RHUH and Bahman hospital and recorded the following information: demographic data (gender and age), indication of gastric endoscopic findings, type of premalignant gastric lesion, histology, and presence of H. Pylori infection. We then proceeded to contact all the patients via phone calls to confirm oral informed consent. Those who approved our request were asked about their substance use (smoking status, alcohol consumption), and their lifestyle characteristics (diet and physical activity).

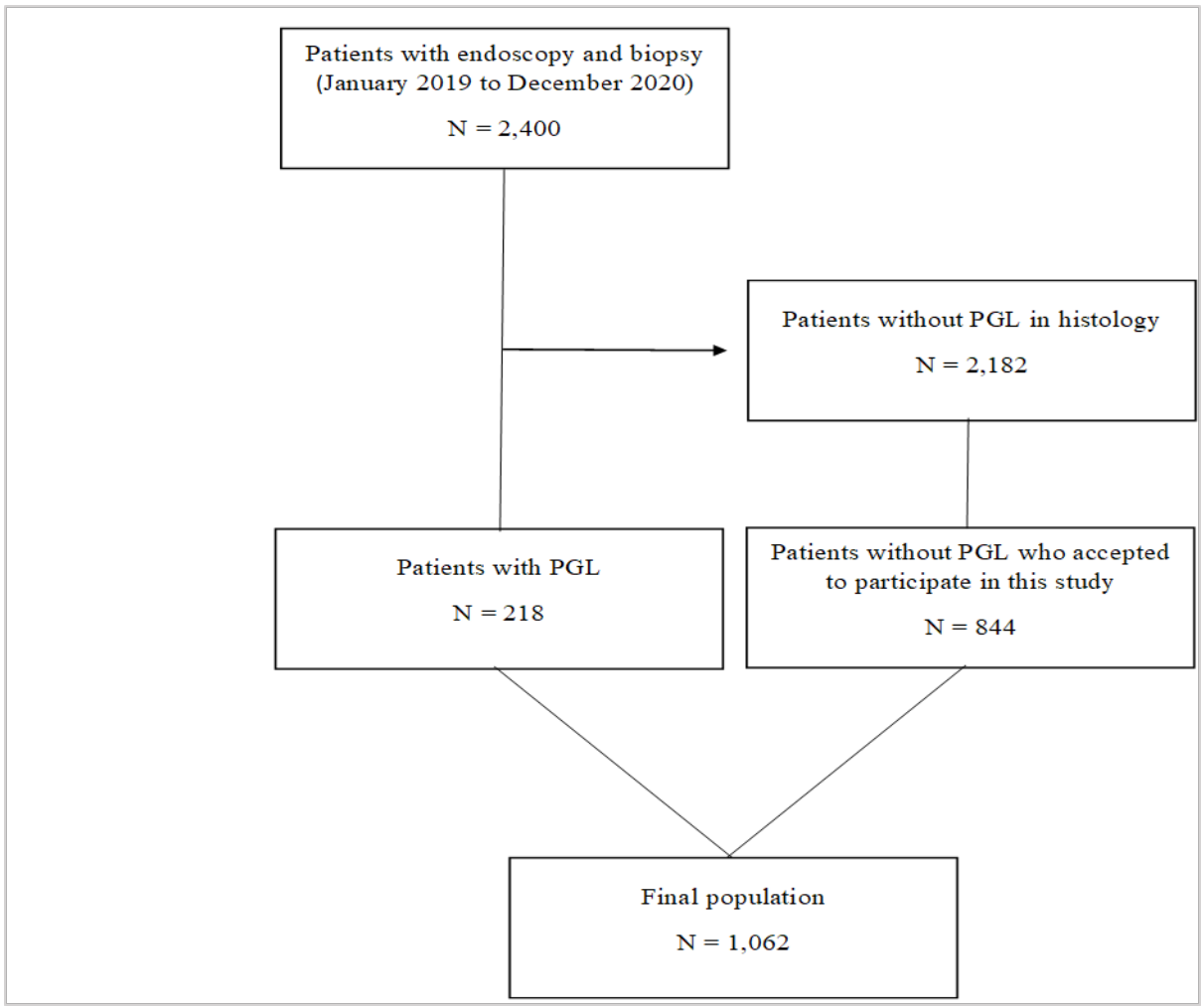

Figure 1: Flow chart of the study. PGL: premalignant gastric lesions.

Statistical Analysis

Data was analyzed using the Statistical Package for Social Sciences (SPSS), version 24. Descriptive statistics, mainly means, were used for continuous variables and proportions were used for categorical variables. A Chi square test was conducted to assess the individual relationship between each PGL and the studied variables including age, gender, family history of GC, smoking status, alcohol intake, diet, physical activity, and H. pylori infection. A p-value of <0.05 was considered statistically significant.

Binary logistic regression was performed to identify the risk factors associated with the development of PGL. All variables with a p-value < 0.2 in the bivariate analysis were included in the logistic regression model. Results were expressed as adjusted odds (ORa) ratio and their 95% confidence intervals.

Results

Prevalence of Premalignant Gastric Cancer

During the study period, from January 2019 to December 2020, a total of 2400 Lebanese patients underwent endoscopies and gastric biopsies at the endoscopy unit of RHUH and Bahman Hospital. Out of these patients, 218 were identified as having PGL, giving it a prevalence of 9.8%. The most frequently identified PGL was atrophic gastritis (148 of 218, 68%), followed by intestinal metaplasia (65 of 218, 30%). Only 5 patients (2%) were diagnosed with superficial neoplastic infiltration (Figure 2).

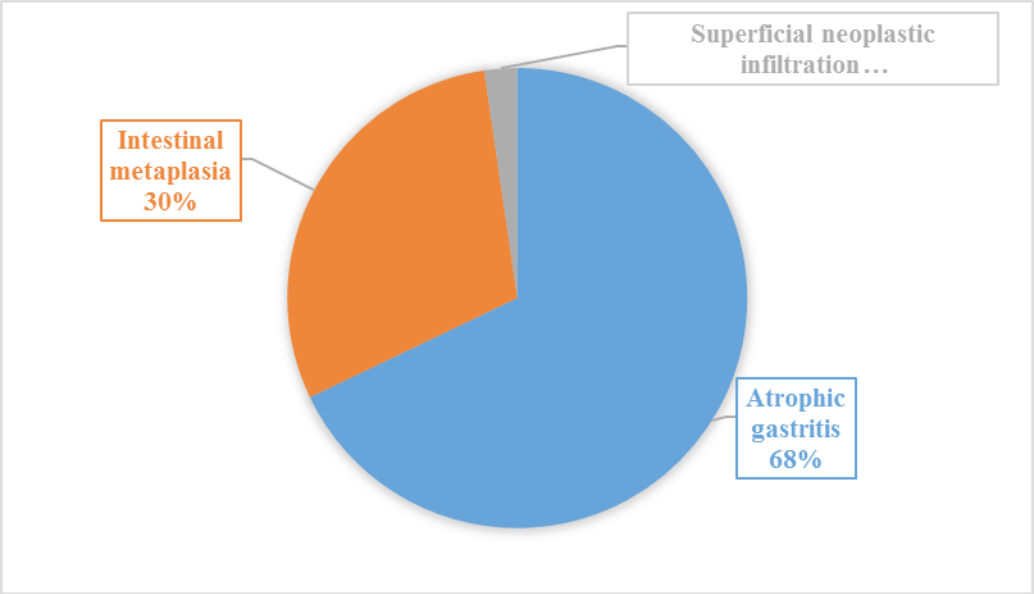

Figure 2: Prevalence of histopathologic findings. n= 2400 patients.

Patient's Characteristics

As mentioned previously, participants of this study were recruited from the list of patients admitted to the endoscopy unit of the RHUH and Bahman Hospital between Jan 2019 and Dec 2020. A total of 2400 patients were initially identified and used to calculate the prevalence of PGL. However, demographic and lifestyle data were collected from 1062 patients, which consisted our final study population.

The mean age of patients was 53.03 ± 18.01 years. Of the total sample, 45.3% were male and 54.7% were female. A few percent of patients (2.6%) had family history of CRC. Regarding substance use, 31.3 % of the patients were cigarette smokers, and only 1.4% consumed alcohol. The dominant percentage of patients was physically active (65.1%). Finally, when patients were asked about their eating habits, most of them reported consuming healthy food (74.5%). Description of the study population is shown in Table 1.

SOCIO-DENOGRAPHIC CHARACTERISTICS	
Age (mean, SD)	53.03 (18.01)
Gender, N (%)	
Male	481 (45.3)
Female	581 (54.7)
Family history, N (%)	
No	1034 (97.4)
Yes	28 (2.6)
SUBSTANCE USE	
Smoking status, N (%)	
No	730 (68.7)
Yes	332 (31.3)
Alcohol consumption, N (%)	
No	1047 (98.6)
Yes	15 (1.9)
LIFESTYLE CHARACTERISTICS	
Physical activity	
Sportive	244 (23.0)
Active	691 (65.1)
sedentary	127 (12.0)
Diet	
Unhealthy	271 (25.5)
Healthy	791 (74.5)

SD: Standard deviation.

Table 1: Baseline characteristics of study participants (N = 1062).

Indications

In the present study, 11% of participants were asymptomatic. The main indication for gastric endoscopy was abdominal pain (28%), followed by dyspepsia (25%). Patients undergoing endoscopy due to anemia or epigastric pain represented 16% of the population. The smallest percentage of patients underwent endoscopy for weight loss (5%).

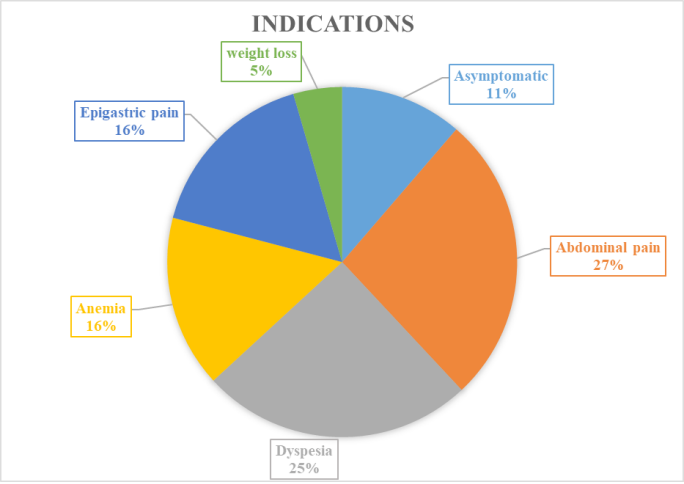

Figure 3: Indications for upper endoscopy.

Endoscopic findings.

931 patients of 1062 patients (88%) demonstrated macroscopic findings of gastric pathology, with Erythema representing the most common endoscopic findings (51%), followed by erosions (19%). Ulcers are seen in 15% of patients, and masses in 1% of subjects. However, in 1% of cases, the GI mucosa appeared normal.

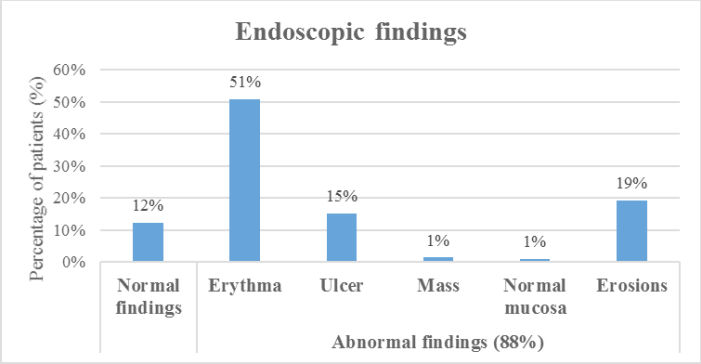

Figure 4: Findings of gastric endoscopy.

Prevalence of H. pylori infection

In the present study, H. Pylori infections were found in 44% of patients (Figure 5).

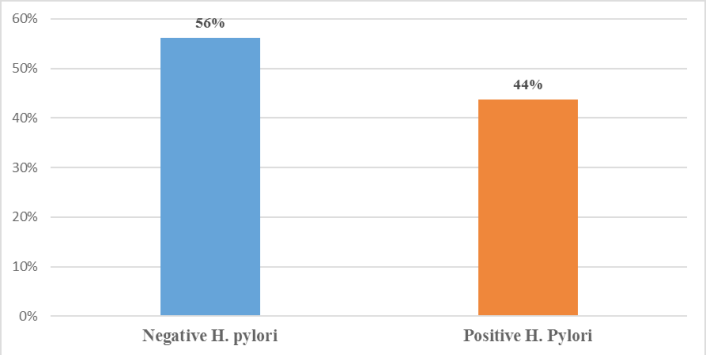

Figure 5: Prevalence of H. pylori infection.

Factors associated with premalignant gastric lesions

The results of the Chi-square test showed that age, family history of gastric cancer, smoking, alcohol consumption, physical activity, diet, and H. pylori infection were significantly associated with premalignant gastric lesions. We found that 71.4% of patients with family history of GC developed gastric premalignant lesions. Furthermore, premalignant gastric lesions were seen in 53.5% of patients with a smoking history, in 51.2% of patients who reported having a sedentary lifestyle, and in 35.3% of patients with H. pylori infection (Table 2).

	Gastric premalignant lesion		p-value*
	No	Yes	
Age (years)			0
< 40	237 (91.9)	21 (8.1)	
≥ 40	607 (75.5)	197 (24.5)	
Gender			0.422
Male	377 (78.4)	104 (21.6)	
Female	467 (80.4)	114 (19.6)	
Family history			0
No	836 (80.9)	198 (19.1)	
Yes	8 (28.6)	20 (71.4)	
Smoking status			0
No	603 (82.6)	127 (20.1)	
Yes	79 (46.5)	91 (53.5)	
Alcohol consumption			0
No	838 (80.0)	209 (20.0)	
Yes	6 (40.0)	9 (60.0)	
Physical activity			0
Sportive	234 (95.9)	10 (4.1)	
Active	548 (79.3)	143 (20.7)	
sedentary	62 (48.8)	65 (51.2)	

Diet			0
Unhealthy	155 (87.1)	102 (12.9)	
Healthy	689 (57.2)	116 (42.8)	
H. pylori			0
Negative	547 (90.7)	56 (9.3)	
Positive	297 (64.7)	162 (35.3)	

*p-value was calculated using chi square test. A p-value of < 0.05 was considered significant.

Table 2: Association between socio-demographic variables, substance use, lifestyle characteristics, H. pylori infection with premalignant gastric lesions.

Multivariate analysis

The results of logistic regression of predictors of premalignant gastric lesions are shown in Table 3, where, age was found associated with development of PGL: patients aged 40 years and more were 3 times more likely to develop PGC (ORa = 3.06, p-value = 0.000), family history: patients with family history of gastric cancer were at higher risk of developing PGL (ORa = 10.79, p-value = 0.002), alcohol consumption was associated with greater odds of developing premalignant gastric (ORa = 9.21, p-value = 0.001), and H. pylori infection: patients infected with H. pylori were about 5 times more likely to develop PGL compared to non-infected patients (ORa = 4.95, p-value = 0.000).

Additionally, this analysis demonstrated that being active (OR = 0.07, p-value = 0.000), being sportive (ORa = 0.37, p-value = 0.000) and consuming healthy food (ORa = 0.32, p-value = 0.000) were protective against PGL.

	Adjusted OR	95% CI	P-value
Age (years)			0
< 40 (ref)			
≥ 40	3.067	1.80-5.21	
Family history			0.002
No (ref)			
Yes	10.79	2.23-31.26	
Alcohol consumption			0.001
No (ref)			
Yes	9.21	2.35-35.97	
Physical activity			0
sedentary (ref)			
Active	0.07	0.03-0.16	0
Sportive	0.37	0.23-0.59	0
Diet			0
Unhealthy (ref)			
Healthy	0.32	0.22-0.47	
H. pylori			0
Negative (ref)			
Positive	4.95	3.38-7.23	

Logistic regression. Adjusted odds ratio and 95% confidence intervals (CI) were adjusted for all these variables

Table 3: Multivariate analysis of factors associated with gastric premalignant lesion.

Discussion

GC represents one of the most common cancers worldwide, and is associated with poor prognosis (25-30%) (10). PGL are well-known risk factors for the development of GC. Therefore, Identification of patients with PGL and the risk factors associated with these lesions appears to be the best strategy for reducing GC mortality [11]. We organized this study to investigate the prevalence of PGL and its risk factors in Lebanon, **a topic that has not received any attention previously.**

Accurate assessment of the prevalence of GPL is still difficult, and significant differences have been reported, depending on the geographical regions, and the design of the study. In our study, the prevalence of PGL was 9.8%, and this finding was lower than that reported in several previous studies where rates ranged from 13 to more than 90 percent [12-14]. in an Indonesian prospective study, the prevalence rate of PGL was 29.2% [12]. In Netherland, De Veries et al (2007) [13] found a PGL prevalence of 14%. The prevalence of PGL was very low (3.2%) in a large retrospective study conducted in France, among 16,764 patients who underwent an upper endoscopy with gastric biopsies between 2000 and 2015 [14].

A multistep process from chronic gastritis to AG, IM, and dysplasia to cancer can be used to explain the pathogenesis of intestinal type gastric cancer [15]. Our study showed that AG developed in 68%, IM in 30%, and superficial neoplastic infiltration in 2% of patients with PGL. A multicenter study conducted in Korea in 2006, among 25,536 asymptomatic participants found that the prevalence of endoscopic AG and IM was 27.1% and 7.1% respectively [16]. In the aforementioned French study, the most frequent lesions were intestinal metaplasia (78.9%), followed by LGD (17%), HGD (2%), and AG (2%) [14]. In patients with H. pylori infection in Tunisia, the prevalence of GI and IM was 35% and 11%, respectively. This variation in the reported detection rates of AG and IM depends upon several factors including ethnic differences, rates of H. pylori infection, diets, the method of screening, and study design [12,14,15].

According to our study, age, family history of GC, alcohol consumption, and H. pylori were associated with increased risk of PGL with OR of 3.06, 10.79, 9.21, and 4.95 respectively. In contrast, we found that healthy diet and physical activity were protective factors against PGL. However, no association was noted between gender and PLG.

H. pylori infection is the most important risk factor for AG and IM among the many risk factors identified for PGL [17]. The prevalence of *H. pylori* infection varies by countries; In general, the prevalence ranges from 30% to 50% in developed countries and more than 80% in developing countries [17,18], In the present study the prevalence of H. pylori was 44%, which is similar to what was found in a previous study conducted in Lebanon between 2011 and 2015 and among 271 healthy Lebanese population (42.1%) [19]. Furthermore, the prevalence of H. pylori infection in this study was considerably lower than that reported in neighboring Arab countries including Egypt (86%) [20], Kuwait (84%) [21], Bahrain (79%) [22], Saudi Arabia (78%) [23], and Jordan (77.5%) [22]. However, much lower percentages were found in many developed countries such as Netherland (22%) [24], and Switzerland (18.9%) [25].

In addition, we found that patients with H. pylori infection were significantly associated with precancerous conditions, with infected patients having a greater than 4-fold increased risk of developing PGL, which is consistent with other studies' results. These findings were consistent with those of et GA Siregar et al, who discovered that patients with H. pylori infection had a 4.63-fold increased risk of gastric premalignant lesion (12). Previous research in Korea by Joo et al. (2013) found that H. pylori are a major risk factor for both AG and IM [26].

These findings confirm that H. pylori play a significant role in the development of PGL, and thus routine biopsies can help with H. pylori eradication and PGL treatment. In patients with extensive AG and IM, European guidelines recommend a 3-year screening interval [27]. Finally, it should be mentioned that the risk of premalignant lesions for each individual following H. pylori infection is most likely determined by a combination of demographic and lifestyle factors [28].

Another important factor that has been discovered to play an important role in the development of PGL is age. Our results showed that being above 40 years is associated with an increased likelihood of developing PGL, which is consistent with other studies' results. Several studies confirmed that the risk of developing PGL is higher in older patients. A multicenter prospective study in Korea found that being over the age of 61 was a risk factor for atrophic gastritis and intestinal metaplasia [29]. According to Benberin et al., the prevalence of gastric premalignant lesion increased with age. This condition was rare in individuals under the age of 40 [30].

Family history of gastric cancer is considered an important predisposing factor for the development of PGL. Results from several research showed that the risk of developing PGL is higher among patients with a family history of gastric. In our study, 71.4% of patients with family history of GC developed PGL, and were at higher risk of developing PGL (0Ra = 10.79, p-value = 0.002), these results were congruent with those present in the literature. According to a meta-analysis study, first-degree relatives of patients with gastric cancer may be at an increased risk of developing gastric cancer [31]. Similar results were found by El Omar et al.. in this study, PGL are more common in relatives of patients with gastric cancer, and patients with a family history of

gastric cancer had a significantly higher risk of developing a PGL [32]. The pathophysiology is unknown, but it could be attributed to genetic factors, the same carcinogen exposure (nitrogen, cigarette smoke, alcohol) among family members, the same diet (high salt, smoked), hygiene level, and H. pylori infection. Results from several research showed that the risk of developing PGL is higher among patients with a family history of gastric [12].

The effects of alcohol on PGL are still debatable. This study discovered that drinking alcohol significantly increased the risk of developing a gastric premalignant lesion. The effects of alcohol on PGL may be explained by the fact that alcohol can damage the gastric mucosa and cause chronic gastritis. Furthermore, alcohol may promote carcinogen absorption while decreasing liver detoxification activity [33].

Previous research has found that men are more likely than women to develop gastric cancer, most likely due to smoking and alcohol consumption [3]. Furthermore, and according to Zhou et al. [34] estrogen hormones protect against gastric cancer. By inhibiting cell growth and malignant progression, estrogen receptor overexpression can reduce cancer cell motility and invasion [34].

In the present study, no significant associations between gender and gastric premalignant lesion were found ($p>0.05$). Previous research support this finding, and discovered no significant link between gender and gastric premalignant lesion [24,30,35]. For instance, Malik et al. organized a retrospective study among 518 patients with endoscopic diagnosis of AG, and found that males had more gastric premalignant lesions than females, but the difference was not statistically significant [36].

There were several limitations in this study. First, the study was retrospective and we were unable to collect lifestyle factors from all admitted patients. Second, we did not include information about the location, severity and extent of PGL, which are considered important indicators of PGL regression or progression. Third, lifestyle risk factors, substance abuse and family history were obtained from patients, leading that information open to patient interpretation. Moreover, we did not include specific information about the ingested food, which may improve the content of the study. **Finally, because the PGL are patchy lesions, there is always the possibility of false negative results.**

Conclusion

In conclusion, despite the fact that the prevalence of PGL in this study was 9.3% and the prevalence of H. pylori infection was 44%, the results draw attention to the significance of their correlation. In addition, this study found that H. pylori infection, a family history of gastric cancer, alcohol consumption, and an age $\geq$ 40 years were the most important factors in predicting an individual's risk of developing PGL. We believe that the assessment of risk factors associated with PGL could be more useful in the prevention of gastric cancer than an assessment of risk factors associated with gastric cancer. Therefore, further studies on larger groups of patients, and covering all medical centers from different geographical areas across Lebanon are required to have a holistic view on the matter. Other strategies to identify individuals with an increased risk of PGL, such as screening methods based on risk factors analysis are also needed.

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