Original Article

Prevalence and correlation of chronic atrophic gastritis, intestinal metaplasia and other precancerous lesions of stomach in Iran: a historical cohort study

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Background: Gastric cancer (GC) is known to be the second main cause of cancer deaths all over the world, despite, the incidence and mortality has been declining especially in industrialized countries. Our aim was to evaluate the correlations between chronic atrophic gastritis (CAG) and other precancerous lesions such as intestinal metaplasia (IM) and epithelial dysplasia (ED) with Helicobacter pylori infection (HPI) in one thousand and ninety eight patients who underwent upper gastrointestinal (GI) endoscopy in Iranian population.

Methods: Standard upper GI video endoscopy examinations were carried out under sedation with midazolam. The specimens were sent for pathology evaluation. Statistical analyses were performed using IBM SPSS statistics 19. The P values of less than 0.05 were considered statistically significant.

Results: HPI prevalence increased in the first 40 years of life and the incidence of gastric atrophy (GA) and IM steadily progress lifetime with an additive rate of increase in the adulthood. A notable increase in IM and dysplasia associated with more sever grade of GA.

Conclusions: In this study unlike previous studies who supported the evident role of HPI in the development of gastric precancerous lesions, our study showed HPI does not own a significant direct effect on the incidence of mentioned lesions but CAG alone, was an independent factor for development of IM and ED.

Keywords: Atrophic gastritis (CAG); gastritis; *Helicobacter pylori* (*H. pylori*); intestinal metaplasia (IM)

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Introduction

Gastric cancer (GC) is the second main cause of cancer deaths worldwide (1,2); however its incidence and mortality has been declined in industrialized countries in the last few years (3). GC post-operative 5-year survival is highly dependent on the time of detection which indicated the higher survivability in early GC stages compared with advanced GC (4,5). In a randomized controlled trail *Helicobacter pylori* (*H. pylori*) eradication therapy accompanied with dietary supplements has been recommended as an effective strategy to prevent GC raised from regression of gastric precancerous lesions including chronic atrophic

gastritis (CAG), intestinal metaplasia (IM) and epithelial dysplasia (ED) (6). CAG is a histopathologic entity characterized by chronic inflammatory processes of gastric mucosa that finally results in loss of gastric glandular cells and reduction of gastric secretory function. In addition, atrophy is known as a precursor factor for GC that develops as a result of autoimmune gastritis and it may be due to *H. pylori* (4,7). Several GC cases reported to begins with non-atrophic gastritis which results in CAG, IM, ED and finally adenocarcinoma (8,9). It usually takes decades for this process to be completed and the role of gastric *Helicobacter pylori* infection (HPI) is known as an initiation factor (10-12). *H. pylori* induce CAG, IM and ED with a low risk to develop stomach cancer. As the atrophy develops, the *H. pylori* density in stomach mucosa may adversely decrease and finally disappear in the late stages of atrophy (8). In a systematic review by Adamu and colleagues, reported the association between HPI and CAG incidence. They revealed that the occurrence of CAG is very low in lack of HPI (13). On the other hand, there are some regions with a high rate of HPI where the incidence of precancerous lesions and GC are low (14,15). In the current study, we evaluated the correlations between CAG and other precancerous lesions such as IM and ED and the HPI in Iranian population.

Materials and methods

In this historical cohort study a total number of 1,098 subjects who underwent diagnostic upper gastrointestinal (GI) endoscopy due to different medical complaints from 2009 to 2013 in Milad hospital were respectively enrolled in our study. The pathological report files of the subjects with gastritis diagnoses, who provided informed consent, were evaluated. Standard upper GI video endoscopy examinations were carried out and assessed by endoscopy experts under sedation with midazolam, under monitoring and local pharyngeal mucosa anaesthesia with 10% lidocaein spray. Then all suspicious findings in the esophagus, stomach and duodenum were captured. A specially designed coding system to record different lesions in the pathology reports was used. One or two biopsies were taken from antrum and then flattened and placed by the muscularis mucosa side on small pieces of filter paper and were immersed immediately in neutral buffer formalin containers and labeled. A coding system was designed to register biopsies information including their numbers, sites and tissue sufficiency. All the process of biopsy preparation, fixation, labeling and recording was supervised by the pathologist in charge. The patients were kept under close observation in the recovery room according to the standard post endoscopy cautions. The biopsies were embedded in paraffin wax blocks then stained by the haematoxylin and eosin method and sectioned, all based on standard pathologic protocols. The prepared histological sections were observed by three pathologists who own special interest and experience in GI pathology. They were not aware of endoscopic and clinical presentations of study patients but were informed of the sites of biopsies. Around 10% of the samples were randomly rechecked by all pathologist to evaluate and minimize inter observer variation bias. Gastric biopsies were fixed in 10% formalin and embedded in paraffin wax by routine methods. An expert pathologist evaluated the 5-micron thick sections under haematoxylin and eosin and Giemsa staining for histopathological analysis and the intensity of the colonizing *H. pylori*, respectively. The diagnosis of HPI was done by direct light microscopy observation of the organism with Giemsa staining. We used the worldwide accepted grading scales for histopathological features, and for formulation of diagnosis as a comprehensive standardized one according to the updated Sydney System (16). All statistical analyses were performed using IBM SPSS statistics 19 for windows. Categorical variables were analyzed using Chi-square test or Fisher's exact test and binary logistic regression. The P values of less than 0.05 were considered statistically significant.

Results

One thousand and ninety eight patients including: 625 (56.9%) men, 473 (43.0%) women were enrolled in this study. The youngest participant was 2 and the oldest 91 (mean age, 49.39; SD, 20.36) years old. The age of 953 cases were recorded and 145 ones' were missing so we had to limit our population to 953 in order to find out how age might affect the other variables of our study. In the *Table 1*, the distribution of inflammatory activity (IA), HPI, CAG, IM and ED of stomach according to age is shown. In this table, the patients were classified into age groups that range 20 years; juvenile (≤19 y), early adulthood (20-39 y), middle adulthood (40-59 y) and late adulthood (≥60 y). The presence of all IA (53.58-64.32%), HPI (59.34-72.77%), CAG (2.20-6.10%) and IM (1.10-4.69%) increases between juvenile and early adulthood. Between adulthood age spans CAG (6.10 to 19.14 to 24.00), IM (4.69 to 17.28 to 29.54) and ED (0.00 to 1.85 to 3.08) increase steadily but no remarkable enhancement was seen in IA

Table 1 The distribution of inflammatory (neutrophil) activity, *H. pylori* infection, gastric atrophy, intestinal metaplasia, and dysplasia according to age spans

Characteristics	Age spans (%)				Total	P value
	Juvenile (≤19 y)	Early adulthood	Middle adulthood	Late adulthood		
Gender						0.690
Male	50 (54.95)	114 (53.52)	186 (57.41)	190 (58.64)	540	
Female	41 (45.05)	99 (46.48)	138 (42.59)	135 (41.54)	413	
Inflammatory activity						0.132
Inactive	42 (46.15)	76 (35.68)	110 (33.95)	129 (39.69)	357	
Active	49 (53.85)	137 (64.32)	214 (66.05)	196 (60.31)	596	
H. pylori infection						0.000
None	37 (40.66)	58 (27.23)	99 (30.56)	146 (44.92)	340	
Positive	54 (59.34)	155 (72.77)	225 (69.44)	179 (55.08)	613	
Gastric atrophy						0.000
None	89 (97.80)	200 (93.90)	262 (80.86)	247 (76.00)	798	
Positive	2 (2.20)	13 (6.10)	62 (19.14)	78 (24.00)	155	
Intestinal metaplasia						0.000
None	90 (98.90)	203 (95.31)	268 (82.72)	229 (70.46)	790	
Positive	1 (1.10)	10 (4.69)	56 (17.28)	96 (29.54)	163	
Dysplasia						0.028
None	91 (100.00)	213 (100.00)	318 (98.15)	315 (96.92)	937	
Positive	0 (0.00)	0 (0.00)	6 (1.85)	10 (3.08)	16	

Table 2 Results of binary logistic regression analysis age spans by inflammatory (neutrophil) activity, gastric atrophy, intestinal metaplasia, and dysplasia

Variable	≤19 to 20-39 y			≤19 to 40-59 y			≤19 to ≥60 y		
	P value	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI
Gender	0.820	1.059	0.647-1.734	0.675	0.905	0.567-1.445	0.549	0.866	0.543-1.384
Inflammatory activity	0.087	1.545	0.939-2.543	0.034	1.668	1.040-2.673	0.269	1.302	0.815-2.080
H. pylori infection	0.022	1.831	1.093-3.067	0.071	1.557	0.963-2.518	0.469	0.840	0.524-1.347
Gastric atrophy	0.168	2.892	0.639-13.087	0.001	10.531	2.524-43.936	0.000	14.053	3.382-58.389
Intestinal metaplasia	0.159	4.433	0.559-35.154	0.004	18.806	2.566-137.817	0.000	37.729	5.182-274.682
Dysplasia	N	–	–	0.997	30480657.391	0.000	0.997	51284915.640	0.000

N, the dependent variable has less than two non-missing values. For logistic regression, the dependent value must assume exactly two values on the cases being processed. Execution of this command stops; OR, odds ratio; CI, confidence interval.

(64.32 to 66.05 to 60.31) HPI (72.77 to 69.44 to 55.08) between the mentioned age spans. By means of Chi-square analysis, prevalence of HPI, CAG, IM and ED revealed no significant (P=0.05) correlation by increase in age. Binary logistic regression analysis was employed to predict the probability of change in the rate of IA, HPI, CAG, IM and ED by means of an alteration in the age spans. *Table 2* shows the results applying a 0.05 criterion of statistical significance. Alteration from juvenile to early adulthood just adds to the probability of enhancement in HPI by an odds ratio (OR) of 1.831 and confidence interval (CI) of 1.093 to 3.067. Similarly, alteration of age spans from early to middle adulthood significantly predicts an increase in the rates of IA (OR =1.668, 95% CI: 1.040-2.673), CAG (OR =10.531, 95% CI: 2.524-43.936) and IM (OR =18.806, 95% CI: 2.566-137.817). Finally, alteration from middle

Table 3 The distribution of inflammatory severity, inflammatory (neutrophil) activity, gastric atrophy, intestinal metaplasia, and dysplasia according to the severity of *H. pylori* infection

Characteristics	*H. pylori* infection (%)				Total	P value
	None	Mild	Moderate	Sever		
Cases (N)	397	519	110	72	1,098	
Gender						0.147
Male	236 (59.45)	282 (54.34)	70 (63.64)	37 (51.39)	625	
Female	161 (40.55)	237 (45.66)	40 (36.36)	35 (48.61)	473	
Inflammatory activity						0.000
Inactive	290 (73.05)	100 (19.27)	16 (14.55)	6 (8.33)	412	
Active	107 (26.95)	419 (80.73)	94 (85.45)	66 (91.67)	686	
Inflammatory severity						0.000
None	261 (65.74)	383 (73.80)	68 (61.82)	28 (38.89)	740	
Mild	101 (25.44)	46 (8.86)	9 (8.18)	1 (1.39)	157	
Moderate	17 (4.28)	13 (2.50)	14 (12.73)	4 (5.56)	48	
Sever	18 (4.53)	77 (14.84)	19 (17.27)	39 (54.17)	153	
Gastric atrophy						0.000
None	305 (76.83)	462 (89.02)	99 (90.00)	63 (87.50)	929	
Mild	68 (17.13)	46 (8.86)	7 (6.36)	5 (6.94)	126	
Moderate	19 (4.79)	10 (1.93)	3 (2.73)	3 (4.17)	35	
Sever	5 (1.26)	1 (0.19)	1 (0.91)	1 (1.39)	8	
Intestinal metaplasia						0.000
None	293 (73.80)	465 (89.60)	97 (88.18)	65 (90.28)	920	
Mild	79 (19.90)	49 (9.44)	11 (10.00)	5 (6.94)	144	
Moderate	13 (3.27)	0 (0.00)	2 (1.82)	2 (2.78)	17	
Sever	12 (3.02)	5 (0.96)	0 (0.00)	0 (0.00)	17	
Dysplasia						0.056
None	385 (96.98)	512 (98.65)	110 (100.00)	72 (100.00)	1,079	
Positive	12 (3.02)	7 (1.35)	0 (0.00)	0 (0.00)	19	

OR, odds ratio; CI, confidence interval.

to late adulthood causes a probable increase in the rate of CAG (OR =14.053, 95% CI: 3.382-58.389) and IM (OR =37.729, 95% CI: 5.182-274.682). There were 701 subjects (63.84% of total cases) with HPI; among these patents, 579 subjects (82.60%) had simultaneous IA. In *Table 3*, the distribution of different grades of inflammatory severity (IS), IA, CAG, IM and ED of stomach according to severity of HPI is shown. According to Chi-square analysis results, there was a significant correlation between HPI severity and IS, IA, gastric atrophy (GA) and IM. For example IS was remarkably higher in the presence of sever HPI (54.17% of all 39 severely *H. pylori* infected cases had simultaneous sever inflammation comparing with 14.84%, 17.27% of all 77 mild and 19 moderate cases). The positivity of HPI was significantly higher in inflammatory active patients (84.40% of a total 686 subjects) compared with those without activity (29.61% of a total 412 subjects). The *Table 4* shows the distribution of IS, HPI, GA, IM and ED according to the presence or absence of IA. There was a significant correlation between IA and all above variables ($P<0.05$). There were 169 subjects (15.39% of total cases) with CAG; 4.73% of them had severe CAG. The percentage of IA and HPI positivity in subjects with sever CAG (12.50% and 37.50%) was remarkably lower than that of the mild (48.41% and 46.03%) and moderate (57.14% and 45.71%). The presence of IM and ED was remarkably higher in CAG positive patients than CAG negatives (55.03% and 4.73% to 9.15 % and 1.18%). In *Table 5*,

Table 4 The distribution of *H. pylori* infection, inflammation severity, gastric atrophy, intestinal metaplasia and dysplasia according to the presence or absence of inflammatory activity

Characteristics	Inflammatory activity (%)		Total	P value
	Inactive	Active		
Cases (N)	412	686	1,098	
Gender				0.570
Male	230 (55.83)	395 (57.58)	625	
Female	182 (44.17)	291 (42.42)	473	
Inflammatory severity				0.000
None	256 (62.14)	484 (70.55)	740	
Mild	123 (29.85)	34 (4.96)	157	
Moderate	22 (5.34)	26 (3.79)	48	
Sever	11 (2.67)	142 (20.70)	153	
H. pylori infection				0.000
None	290 (70.39)	107 (15.60)	397	
Mild	100 (24.27)	419 (61.08)	519	
Moderate	16 (3.88)	94 (13.70)	110	
Sever	6 (1.46)	66 (9.62)	72	
Gastric atrophy				0.000
None	326 (79.13)	603 (87.90)	929	
Mild	65 (15.78)	61 (8.89)	126	
Moderate	15 (3.64)	20 (2.92)	35	
Sever	6 (1.46)	2 (0.29)	8	
Intestinal metaplasia				0.000
None	314 (76.21)	606 (88.34)	920	
Mild	74 (17.96)	70 (10.20)	144	
Moderate	10 (2.43)	7 (1.02)	17	
Sever	14 (3.40)	3 (0.44)	17	
Dysplasia				0.000
None	400 (97.09)	679 (98.98)	1,079	
Positive	12 (2.91)	7 (1.02)	19	

the distribution of IS, IA, HPI, IM and ED of stomach according to the grade of CAG was shown. There was a significant correlation between CAG and all the other study variables (P<0.05). A notable increase in IM and ED was shown in association with more sever grade of CAG (*Table 5*). There were 178 patients (16.21% of total cases) with IM, 52.25% of them had simultaneous CAG. The *Table 6* shows the distribution of IA, IS, HPI, CAG and ED according to the grading of IM. There's a significant correlation between IM and IA, IS, HPI, CAG and ED (P<0.05). A total of 19 cases (1.73 % of total cases) had ED. A total of 57.89% of them had simultaneous IM, 36.84% were HPI positive, and 42.11% had GAC. ED significantly correlates with IA (P=0.020), GAC (P=0.000) and IM (P=0.000) (*Table 7*). We conducted a binary logistic regression test on the IA, HPI, CAG, IM and ED everyone with each other. As presented in *Table 8*, IA significantly (P=0.05) adds to the odd of HPI (OR =12.863, 95% CI: 9.573-17.283) and inversely increase in HPI cause a probable enhancement of IA (OR =12.863, 95% CI: 9.573-17.283). Moreover, binary logistic regression analysis of coupled CAG-IM, CAG-ED and IM-ED showed that CAG adds to odds of IM (OR =12.150, 95% CI: 8.340-17.702) and ED (OR =4.147, 95% CI: 1.643-10.468) and similarly IM and ED add to the odd of CAG by an equivalent extent of OR. Finally, increase in IM leads to a probable enhancement of ED (OR =7.509,

Table 5 The distribution of inflammatory severity, inflammatory (neutrophil) activity, *H. pylori* infection intestinal metaplasia and dysplasia according to the grade of gastric atrophy

Characteristics	Gastric atrophy (%)				Total	P value
	None	Mild	Moderate	Sever		
Cases (N)	929	126	35	8	1,098	
Gender						0.872
Male	528 (56.84)	74 (58.73)	18 (51.43)	5 (62.50)	625	
Female	401 (43.16)	52 (41.27)	17 (48.57)	3 (37.50)	473	
Inflammatory activity						0.000
Inactive	326 (35.09)	65 (51.59)	15 (42.86)	6 (75.00)	412	
Active	603 (64.91)	61 (48.41)	20 (57.14)	2 (25.00)	686	
Inflammatory severity						0.001
None	600 (64.59)	106 (84.13)	27 (77.14)	7 (87.50)	740	
Mild	146 (15.72)	10 (7.94)	1 (2.86)	0 (0.00)	157	
Moderate	41 (4.41)	4 (3.17)	2 (5.71)	1 (12.50)	48	
Sever	142 (15.29)	6 (4.76)	5 (14.29)	0 (0.00)	153	
H. pylori infection						0.000
None	305 (32.83)	68 (53.97)	19 (54.29)	5 (62.50)	397	
Mild	462 (49.73)	46 (36.51)	10 (28.57)	1 (12.50)	519	
Moderate	99 (10.66)	7 (5.56)	3 (8.57)	1 (12.50)	110	
Sever	63 (6.78)	5 (3.97)	3 (8.57)	1 (12.50)	72	
Intestinal metaplasia						0.000
None	844 (90.85)	62 (49.21)	13 (37.14)	1 (12.50)	920	
Mild	80 (8.61)	50 (39.68)	11 (31.43)	3 (37.50)	144	
Moderate	0 (0.00)	5 (3.97)	11 (31.43)	1 (12.50)	17	
Sever	5 (0.54)	9 (7.14)	0 (0.00)	3 (37.50)	17	
Dysplasia						0.000
None	918 (98.82)	119 (94.44)	35 (100.00)	7 (87.50)	1,079	
Positive	11 (1.18)	7 (5.56)	0 (0.00)	1 (12.50)	19	

95% CI: 2.976-18.947) and reversely ED adds to the odd of IM by the same extent of OR.

Discussion

More than half of the world's population have *H. pylori* colonization in their stomachs that is known as a key factor in pathogenesis of some gastro duodenal diseases (17). In 1994, the International Agency for Research on Cancer classified *H. pylori* as a type I carcinogen agent that means a definite cause of cancer in human beings (18). In spite of recently emerging evidences that confirms decrease in the prevalence of *H. pylori* in all age groups, the image of its attributable diseases continues to change. GC development is considered as multistep progression which begins with a sequence of chronic gastritis development to GA, IM to dysplasia, and finally invasive cancer (19), this process could be triggered by chronic HPI. In our study analysis of HPI distribution by 20 years age groups Chi-square test revealed a significant correlation between increase in age and increase in HPI prevalence and intensity as demonstrated in *Table 1*, but the binary logistic regression test showed just alteration from juvenile to early adulthood may possibly add to rate of HPI (OR =1.831, CI: 1.093-3.067). Our results confirmed the results of other studies that indicated HPI increase with age in developing and developed countries (20,21). A recent study by Chen *et al*. which has similarity in method they used to ours, found that the incidence of HPI decreased

Table 6 The distribution of inflammatory severity, inflammatory (neutrophil) activity, *H. pylori*, gastric atrophy and dysplasia according to the presence or absence of intestinal metaplasia

Characteristics	Intestinal metaplasia (%)				Total	P value
	None	Mild	Moderate	Sever		
Cases (N)	920	144	17	17	1,098	
Gender						0.675
Male	521 (56.63)	87 (60.42)	8 (47.06)	9 (52.94)	625	
Female	399 (43.37)	57 (39.58)	9 (52.94)	8 (47.06)	473	
Inflammatory activity						0.000
Inactive	314 (34.13)	74 (51.39)	10 (58.82)	14 (82.35)	412	
Active	606 (65.87)	70 (48.61)	7 (41.18)	3 (17.65)	686	
Inflammatory severity						0.005
None	603 (65.54)	107 (74.31)	14 (82.35)	16 (94.12)	740	
Mild	150 (16.30)	6 (4.17)	1 (5.88)	0 (0.00)	157	
Moderate	39 (4.24)	8 (5.56)	1 (5.88)	0 (0.00)	48	
Sever	128 (13.91)	23 (15.97)	1 (5.88)	1 (5.88)	153	
H. pylori infection						0.000
None	293 (31.85)	79 (54.86)	13 (76.47)	12 (70.59)	397	
Mild	465 (50.54)	49 (34.03)	0 (0.00)	5 (29.41)	519	
Moderate	97 (10.54)	11 (7.64)	2 (11.76)	0 (0.00)	110	
Sever	65 (7.07)	5 (3.47)	2 (11.76)	0 (0.00)	72	
Gastric atrophy						0.000
None	844 (91.74)	80 (55.56)	0 (0.00)	5 (29.41)	929	
Mild	62 (6.74)	50 (34.72)	5 (29.41)	9 (52.94)	126	
Moderate	13 (1.41)	11 (7.64)	11 (64.71)	0 (0.00)	35	
Sever	1 (0.11)	3 (2.08)	1 (5.88)	3 (17.65)	8	
Dysplasia						0.000
None	912 (99.13)	134 (93.06)	17 (100.00)	16 (94.12)	1,079	
Positive	8 (0.87)	10 (6.94)	0 (0.00)	1 (5.88)	19	

with age (22). Eighty four point forty percent of our HPI positive patients had simultaneously IA and Chi-square test revealed a significant correlation between HPI and IA and the results of binary logistic regression test of HPI and IA confirmed this correlation (OR =12.863, 95% CI: 9.573-17.283). In line of our study, Parsonnet *et al*. reported that in a series of patients with gastroduodenal disorders, cases with *H. pylori* developed GC (23). Mizuno *et al*. revealed that the presence of HP infection and atrophic gastritis determines by serological evaluation has a predictive value in risk of individuals for GC (24). Our results are consistent with those of Chen *et al*. (22) and Tanko *et al*. (25) who demonstrated HPI may result in neutrophil activation and chronic gastritis. Our study showed a 45.56% prevalence of HPI in CAG positive patients which was not significantly low comparing with 21.01 % that was found in the similar study by Chen *et al*. (22). In a study by Haziri *et al*., the very high percentage of HPI among patients with precancerous lesions (IM: 71.7% and ED: 71.4%) was determined (26). Since atrophy may reverse after effective eradication therapy, eradication therapy of *H. pylori* after detection of atrophy is recommended (5). Applying Chi-square test, CAG significantly correlated with HPI but by binary logistic regression test no remarkable OR (0.409) was found in comparison with Weck *et al*. study who reported OR of 2.9% (95% CI: 2.3-3.6) and with Fontham *et al*. (OR =6.4) (11,27). So in contrast with other studies, our results didn't support the positive association between HPI and CAG,

Table 7 The distribution of inflammatory severity, inflammatory (neutrophil) activity, *H. pylori* infection, gastric atrophy and intestinal metaplasia according to the presence or absence of dysplasia

Characteristics	Dysplasia (%)		Total	P value
	None	Positive		
Cases (N)	1,079	19	1,098	
Gender				0.931
Male	614 (56.90)	11 (57.89)	625	
Female	465 (43.10)	8 (43.11)	473	
Inflammatory activity				0.215
Inactive	400 (37.07)	12 (63.16)	412	
Active	679 (62.93)	7 (36.84)	686	
Inflammatory severity				0.020
None	724 (67.10)	16 (84.21)	740	
Mild	157 (14.55)	0 (0.00)	157	
Moderate	48 (4.45)	0 (0.00)	48	
Sever	150 (13.90)	3 (15.79)	153	
H. pylori infection				0.056
None	385 (35.68)	12 (63.16)	397	
Mild	512 (47.45)	7 (36.84)	519	
Moderate	110 (10.19)	0 (0.00)	110	
Sever	72 (6.67)	0 (0.00)	72	
Gastric atrophy				0.000
None	918 (85.08)	11 (57.89)	929	
Mild	119 (11.03)	7 (36.84)	126	
Moderate	35 (3.24)	0 (0.00)	35	
Sever	7 (0.65)	1 (5.26)	8	
Intestinal metaplasia				0.000
None	912 (84.52)	8 (42.11)	920	
Mild	134 (12.42)	10 (52.63)	144	
Moderate	17 (1.58)	0 (0.00)	17	
Sever	16 (1.48)	1 (5.26)	17	

this maybe because of the hypothesis that attributes lower sensitivity of HPI detecting methods in presence of CAG to a low *H. pylori* density in the presence of atrophy (11,12) or as a result of HPI declining prevalence due to improvement in the standard of living in economically rapidly developing counties (28). In the current study, the presence of IM and ED was remarkably higher in CAG positive patients than CAG negatives (55.03% and 4.73% to 9.15% and 1.18%). According to the results of Chi-square test, prevalence and intensity of IM significantly correlates with IA, HPI, and CAG. Binary logistic regression test showed CAG significantly cause probable increase in prevalence of IM (OR =12.150, 95% CI: 8.340-17.702) and ED (OR =4.147, 95% CI: 1.643-10.468). These results match with those of demonstrated by Chen *et al*. (22) and Rugge *et al*. (29). Beside the very high Iranian's rate of HPI comparing with other populations, age of infection seems to be very low (30). Few studies with different methods are fulfilled on CAG and other GC precancerous lesions in Iran, for instance CAG prevalence varies from 21.9% of cardiac and 39.3% of cardiac species from Ardebil (Northwest of Iran) by histologic method (31) to 53% in Babol (North of Iran) by the serologic pepsinogen I/II method (32). A cross sectional study by Malekzadeh *et al*. showed prevalence of 8.7% and 0.2% for IM and ED in Ardabil in Northwest of Iran (31). So as a conclusion of our carrier, HPI incidence in Iran that

Table 8 The results of binary logistic regression analysis of inflammatory (neutrophil) activity, *H. pylori* infection, gastric atrophy and intestinal metaplasia by each other

Characteristics	Inflammatory type			Inflammatory activity			*H. pylori* infection			Gastric atrophy			Intestinal metaplasia			Dysplasia		
	P	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P	OR	95% CI
Gender	0.934	0.946	0.253-3.541	0.570	0.931	0.728-1.191	0.204	1.176	0.916-1.509	0.892	0.977	0.702-1.361	0.658	0.929	0.671-1.286	0.931	0.960	0.383-2.406
Inflammatory activity	0.087	3.365	0.837-13.526	–	–	–	0.000	12.863	9.573-17.283	0.000	0.522	0.375-0.726	0.000	0.423	0.306-0.586	0.026	0.344	0.134-0.880
H. pylori infection	0.073	3.570	0.888-14.355	0.000	12.863	9.573-17.283	–	–	–	0.000	0.409	0.293-0.570	0.000	0.333	0.239-0.462	0.019	0.324	0.126-0.829
Gastric atrophy	0.572	0.634	0.131-3.078	0.000	0.522	0.375-0.726	0.000	0.409	0.293-0.570	–	–	–	0.000	12.150	8.340-17.702	0.003	4.147	1.643-10.468
Intestinal metaplasia	0.625	0.675	0.139-3.275	0.000	0.423	0.306-0.586	0.000	0.333	0.239-0.462	0.000	12.150	8.340-17.702	–	–	–	0.000	7.509	2.976-18.947
Dysplasia	0.999	13588106.337	0.000	0.026	0.344	0.134-0.880	0.019	0.324	0.126-0.829	0.003	4.147	1.643-10.468	0.000	7.509	2.976-18.947	–	–	–

OR, odds ratio; CI, confidence interval.

resembles a pattern of HPI distribution in the developing countries, increases in the first years of human life then its increase rate slows down in the early adulthood and turns to diminish in the rest of life. In contrast to HPI, CAG and IM steadily progress whole the life with an additive rate of increase in the adulthood. In this study unlike former studies which supported the evident role of HPI in the development of gastric precancerous lesions, our study showed HPI does not own a significant direct effect on the incidence of mentioned lesions but CAG alone, makes a considerable risk for occurrence of IM and ED.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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