

# Comparison of intestinal metaplasia and Helicobacter pylori positivity in patients from different age groups with antral gastritis

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## Ethics Committee Approval

The study was approved by the Institutional Board of Nisa Private Hospital (date: 01.04.2019). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

## Conflict of Interest

No conflict of interest was declared by the authors.

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## Abstract

**Background/Aim:** Gastric carcinoma (GC) is the fourth most common cancer worldwide and the second most common cause of cancer death. Primary prevention for GC includes healthy diet, eradication of Helicobacter pylori (HP), chemoprevention and early diagnosis. For this reason, finding out the HP incidence in patients with suspected antral gastritis in various age groups can lead to forming a treatment strategy to prevent development of GC. The aim of this study is to find out the HP incidence in patients with a proven antral gastritis diagnosis in various age groups and form different treatment strategies.

**Methods:** This study included 1589 patients aged between 15-91 years who underwent diagnostic upper gastrointestinal endoscopy due to complaints of dyspepsia. The demographic characteristics, such as age and sex, and histopathological HP score (HPS) and IM score (IMS) were recorded. The patients were divided into three groups according to age: 15-29 years, 30-64 years, and 65 years and above.

**Results:** In the 15–29-year age group, IM positivity was significantly lower and HP positivity was significantly higher compared to other age groups ( $P<0.01$ ). In the age group of 65 years and above, HP positivity was significantly lower than in the other groups ( $P<0.01$ ). The incidence of IM was significantly higher and that of HP was significantly lower in male patients aged 65 years and older ( $P<0.01$  for both). IM positivity was significantly higher in HP negative patients than in HP positive patients ( $P=0.02$ ).

**Conclusion:** The most important risk factors for the development of IM are male gender and being aged 65 years and older. HP positivity is higher among the young population and IM prevalence is higher in advanced ages. There is no correlation between HP positivity and the presence of IM.

**Keywords:** Endoscopy, Gastrointestinal system, Intestinal metaplasia, Helicobacter pylori

## Introduction

Gastric carcinoma (GC) is the fourth most common cancer worldwide and the second most common cause of cancer death. Primary prevention for GC includes healthy diet, eradication of *Helicobacter pylori* (HP), chemoprevention and early diagnosis [1].

HP is a gram-negative bacterium found in the stomach and detected in 50% of population [2]. In 1994, HP was classified as a class I carcinogen by the International Agency for Research on Cancer [3]. The Maastricht III Guidelines recommend treating the *H. pylori* infections [4]. In chronic HP infections, a multistep process of atrophy, intestinal metaplasia (IM), and dysplasia develops, which leads to GC [2, 5]. Therefore, IM is considered a precancerous lesion for gastric carcinoma [6]. It is known that the most important risk factor for developing IM is HP [2, 7]. However, the effect of the presence of HP on the development of IM is still debated [2]. Studies on the frequency and the effects of HP infections may significantly contribute to early diagnosis and treatment of GC and survival [6].

In this study, the aim was to determine the frequency of and relationship between IM and HP in different age groups.

## Materials and methods

Patients who underwent upper GI endoscopy between January 1, 2017 and March 22, 2019 were retrospectively evaluated. This study included 1589 patients aged between 15-91 years who underwent diagnostic upper gastrointestinal endoscopy due to complaints of dyspepsia. The demographic characteristics, such as age and sex, and histopathological scoring of HP score (HPS) and IM score (IMS) were recorded. The patients were divided into three groups according to age: 15-29 years, 30-64 years, and 65 years and above. Biopsies were obtained from antrum. The samples were histopathologically graded from 0 to 3 according to the severity of IMS and HPS. IMS and HPS were evaluated as 0=none, 1=mild, 2=moderate and 3=severe. In statistical analysis, IMS and HPS scores were evaluated as mild and moderate/severe.

The endoscopy and pathology results of 1842 patients who underwent upper GIS endoscopy for dyspeptic complaints were reviewed retrospectively. Among them, 1589 patients with endoscopic and histopathologic findings of antral gastritis were included. A total of 253 patients were excluded from the study based on the results of control gastroscopy, along with a 107-year-old patient who had a previous pathology of antral gastritis (gastric cancer, Maltoma, etc.), who had previously undergone HP eradication therapy and control gastroscopy. The presence and correlation of IM and HP were compared only in patients with antral gastritis. Therefore, only antrum biopsies were considered. This study was not planned primarily to reveal the incidence of HP.

Since the number of patients with IMS and HPS 3 was very low and did not indicate statistical significance, IMS / HPS: 3 patients were categorized as moderate / severe with 2 patients and statistically evaluated.

## Endoscopy technique

All upper gastrointestinal mucosa, from oropharynx to second part of the duodenum, were examined under direct vision with Pentax EPK 100-p brand endoscopy device in the Endoscopy Unit after at least 8 hours of fasting and under sedo-anesthesia (propofol). Antral mucosal biopsy was performed in all patients.

## Histopathological examination

Gastric mucosal biopsy specimens were fixed in 10% formaldehyde and followed by routine tissue follow-up. After being embedded in paraffin, 4-5-micron thick sections were removed from the specimens. They were stained with Hematoxylin-Eosin and histological examination was performed. The other sections were stained with modified Giemsa and HP was investigated. Histopathological examination was performed according to Sydney classification [8], and they were evaluated for inflammation, activation, intestinal metaplasia, atrophy, and *Helicobacter pylori* presence in 4 degrees (0: None, 1: Mild, 2: Moderate, 3: Severe).

## Statistical analysis

IBM SPSS Statistics V23.0 package software was used to analyze the data. Central and prevalence criteria such as number, percentage, mean, median, range of distribution, standard deviation were used to present descriptive data. The conformity of numerical variables to normal distribution was evaluated with visual (histogram) and analytical (Shapiro Wilk test) tests. Pearson's Chi-square test was used to determine the differences between categorical variables and Spearman Correlation tests were used to determine those between numerical variables. A value of  $P < 0.05$  was considered statistically significant.

## Results

This study included 1589 patients aged 15-91 years. There were 267 patients in the 15–29-year age group, 1088 patients in the 30-64-year age group and 234 patients in the 65-year and above age group. Of the patients, 38.21% were female and 61.79% were male. The mean age of patients was 46.23 years. IM and HP positivity rates were 8.62% and 34.61%, respectively.

In the 15–29-year age group, IM positivity was significantly lower and HP positivity was significantly higher in comparison with other age groups ( $P < 0.01$ ). In the group of 65 years and above, HP positivity was significantly lower than in the other groups ( $P < 0.01$ ). Comparison of the age groups of patients with IM and HP positivity is presented in Table 1.

Table 1: Comparison of age groups of patients with IM and HP positivity

	15-29		Age groups 30-64		65 and over		X <sup>2</sup>	P-value**
	n	%	n	%	n	%		
IM positivity								
Negative	259	97.0	989	90.9	204	87.2	16.3	<0.01
Positive	8	3.0	99	9.1	30	12.8		
HP positivity								
Negative	151	56.6	693	63.7	195	83.3	43.9	<0.01
Positive	116	43.4	395	36.3	39	16.7		

\* Column percentage. \*\* Chi-square tests

No significant difference was found between the age groups in terms of IM and HP scores ( $P > 0.05$ ). The incidence of IM was significantly higher and that of HP was significantly lower in male patients aged 65 and above than other age groups ( $P < 0.01$  for both). While the frequency of HP was significantly

lower in female patients aged 65 and older ( $P < 0.01$ ), there was no significant difference in terms of IM frequency ( $P > 0.05$ ). Comparison of IM and HP positivity among age groups in male and female patients is shown in Tables 2 and 3.

Table 2: Comparison of IM and HP positivity among age groups in male patients

	15-29		Age groups 30-64		65 and over		X <sup>2</sup>	P-value**
	n	%	n	%	n	%		
IM positivity								
Negative	98	98.0	378	91.3	76	81.7	15.7	<0.01
Positive	2	2.0	36	8.7	17	18.3		
HP positivity								
Negative	48	48.0	251	60.6	76	81.7	23.9	<0.01
Positive	52	52.0	163	39.4	17	18.3		

\* Column percentage, \*\* Chi-square tests

Table 3: Comparison of IM and HP positivity among age groups in female patients

	15-29		Age groups 30-64		65 and over		X <sup>2</sup>	P-value**
	n	%	n	%	n	%		
IM positivity								
Negative	161	96.4	611	90.7	128	90.8	6	>0.05
Positive	6	3.6	63	9.3	13	9.2		
HP positivity								
Negative	103	61.7	442	65.6	119	84.4	22.1	<0.01
Positive	64	38.3	232	34.4	22	15.6		

\* Column percentage, \*\* Chi-square tests

In terms of gender, HP positivity was significantly higher among male patients compared to female patients ( $P = 0.02$ ), however, IM positivity was similar ( $P > 0.05$ ). Comparison of gender with IM and HP positivity in patients is shown in Table 4.

IM positivity was significantly higher in HP negative patients than in HP positive patients ( $P = 0.02$ ). Comparison of HP and intestinal metaplasia positivity in patients is shown in Table 5. There was no significant correlation between HPS and IMS ( $P > 0.05$ ).

Table 4: Comparison of gender with IM and HP positivity in patients

	Sex				X <sup>2</sup>	P-value**
	Male		Female			
	n	%	n	%		
IM positivity						
Negative	552	90.9	900	91.6	0.2	0.62
Positive	55	9.1	82	8.4		
HP positivity						
Negative	375	61.8	664	67.6	5.6	0.02
Positive	232	38.2	318	32.4		

\* Column percentage, \*\* Chi-square tests

Table 5: Comparison of HP and intestinal metaplasia positivity in patients

	IM positivity		X <sup>2</sup>	P-value**
	Negative	Positive		
	n	%	n	%
HP positivity				
Negative	937	90.2	102	9.8
Positive	515	93.6	35	6.4

\* Column percentage, \*\* Chi-square tests

## Discussion

In some histopathological studies, chronic atrophic gastritis, IM, dysplasia, and carcinoma development period beginning with chronic active gastritis due to HP is reported as 16-24 years [9]. Therefore, early detection and treatment of HP presence are clinically important to prevent the development of GC. In our study, there was a significant difference in HP positivity in the 15-29-year age group compared to the other age groups, and all patients underwent HP eradication.

There are numerous studies showing regression in IM with HP eradication therapy, whereas some other studies report otherwise [2, 6, 10-14]. The results of these studies lead to debates about HP eradication. In a study conducted by Rokkas et al. [15], GC development was prevented if HP was eradicated in the case of atrophic and non-atrophic gastritis. On the other hand,

once IM and dysplasia developed, eradication therapy did not prevent the development of GC. Hwang et al. [16] conducted a study on 598 patients with a 10-year follow-up period and showed that HP eradication caused regression in IM and atrophic gastritis. It was reported as a preventive strategy for the development of intestinal type GC. These results demonstrate the importance of early diagnosis and treatment of HP in preventing the development of GC. In our study, considering the high presence of HP among the younger population, we consider that detecting the presence of HP and its treatment are important, especially in patients with complaints of dyspepsia at younger ages.

IM is more commonly present in advanced ages. However, there are some studies showing that HP is more common in advanced ages, while in some other studies it is higher in the earlier ages. In a study conducted by Craanen et al. [9], HP positivity was more common in the elderly population, while Kesici [2] reported that it was more common in the younger population. In our study, HP positivity was significantly higher especially in earlier ages and gradually decreased in advanced ages. In studies conducted by Craanen et al. [9] and Kesici [2], IM presence was more common in advanced ages. In our study, the presence of IM increased with age, and it was significantly higher in the group aged 65 years and older, which is consistent with the results of these studies.

In the literature, the rates of IM vary considerably. This may be because patients in different studies have different age and gender ratios. In their study conducted on 3301 patients in Turkey, Ozdil et al. [17] reported the HP positivity as 71.3% and IM presence as 17.8%. In our study, the HP positivity and IM rates were 34.61% and 8.62%, respectively. The rate of IM was 19.8% in a study by Ajdarkosh et al. [18] and 11.5% in a study by Kesici [2]. In the study of Jiang et al. [19] on 28745 patients in the Chinese population, the most important risk factors for the development of IM were 40-70-year age range, male gender, gastric ulcer, bile reflux, HP infection and severe chronic inflammation. In our study, similar to the results of this study, the most important risk factor for developing IM was being male and being aged 65 years and above. In a study by Ozdil et al. [17], HP infection decreased, and the prevalence of IM increased with age. In our study, in line with these results, HP positivity decreased with age and the presence of IM increased with it.

While some studies in the literature have reported a significant relationship between HP positivity and IM presence, some other studies have not identified a significant relationship. In a study by Uemura et al. [20], a significant relationship was found between HP positivity and development of IM, whereas Topal et al. [21] and Kesici [2] reported otherwise. In our study, no significant relationship was found between HP positivity and the presence of IM. However, the presence of IM in HP negative patients was significantly higher than in HP positive patients. The lack of correlation between concurrent HP and IM presence in our study did not indicate that HP is not a risk factor for development of IM. Although HP is highly prevalent in the young population, the lack of correlation in concurrent investigations should be considered a possible outcome since development of IM takes a long period of time. Due to the low HP positivity rate in advanced ages, long-term exposure to HP

and the lack of timely eradication treatment, the fact that there is no correlation between IM and HP depending on high IM development can be considered a possible result.

### Conclusion

The most important risk factor for the development of IM is male gender and being aged 65 years and above. HP positivity is higher in young population and IM prevalence is higher in advanced ages, and there is no correlation between HP positivity and the presence of IM. By taking the results of this study and other studies in the literature into account and considering that cancer develops within 16-24 years in the presence of HP, since HP positivity is more common in patients with complaints of dyspepsia, especially in the 15-29 age group, it is believed that early detection and eradication of HP play an essential role to prevent the development of cancer in this group. However, due to the multifactorial nature of cancer development, we believe that more studies are needed to reveal the relationship between HP and IM. Multi-center studies are needed to reveal the incidence.

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