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Research Article

Determination of the Frequency of Gastric Intestinal Metaplasia and Its Association with Helicobacter Pylori

Gastrik Intestinal Metaplazi Sıklığı ve Helikobakter Pilori ile İlişkisinin Belirlenmesi

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Abstract

Aim: Gastric intestinal metaplasia (IM) is a precancerous lesion in the pathway to gastric cancer. Helicobacter pylori (HP) is a bacterium that has been associated with an increase in the development of non-cardia gastric cancer and is involved in the development of gastric IM and atrophic gastritis. In this study, we aimed to determine the frequency of IM and its relationship with HP in patients undergoing endoscopic examination with the indication of dyspepsia.

Material and Method: The study included 2530 patients who underwent upper gastrointestinal system endoscopy and had gastric biopsy at the Karadeniz Technical University Farabi Hospital Gastroenterology Clinic due to dyspepsia between January 2019 and January 2020. Demographic characteristics of the patients such as age and gender, biopsy findings (presence of IM, HP, atrophy, dysplasia) were evaluated retrospectively.

Results: A total of 2530 cases, 1344 (53.1%) women and 1186 (46.9%) men, with a median age of 53 (18-93) years were included in the study. HP was detected in 27.8% of the cases and IM was detected in 26.8%. The median age of 677 patients with positive IM was 59 (19-92) years, and 29.7% (n=352) were male. While no significant difference was found between the sexes in terms of median age within the IM positive and negative groups (p=0.584, p=0.642, respectively), the median age and male sex ratio were higher in patients with IM positive than those with IM negative (p<0.001, p=0.002, respectively). While the rate of HP positivity among male patients was 31% (n=368), the same rate was 24.9% (n=334) among female patients (p=0.001). The male gender was significantly higher in HP positive patients (52.4% vs. 47.6%), and the median age was significantly lower in HP positive patients (p<0.001). There was no significant difference in HP positivity between IM positive and negative patient groups (p=0.341).

Conclusion: IM was more common in older and male patients. HP positivity was found more frequently in male and young patients. No significant difference was found in the frequency of IM and HP.

Keywords: Intestinal metaplasia, helicobacter pylori, gastric atrophy

Öz

Amaç: Gastrik intestinal metaplazi (IM) mide kanserine giden yolda prekanseröz bir lezyondır. Helikobakter pilori (HP) non-kardia mide kanseri gelişiminde artış ile ilişkilendirilen, gastrik IM ile atrofik gastrit gelişiminde rol alan bir bakteridir. Bu çalışma ile dispepsi endikasyonu ile endoskopik inceleme yapılan hastalarda IM sıklığını ve HP ile ilişkisini belirlemeyi amaçladık.

Materyal ve Metot: Çalışmada Ocak 2019-Ocak 2020 tarihleri arasında dispepsi nedeni ile Karadeniz Teknik Üniversitesi Farabi Hastanesi Gastroenteroloji Kliniği'nde üst gastrointestinal sistem endoskopisi yapılıp mide biyopsisi alınan 2530 hastanın yaş ve cinsiyet gibi demografik özellikleri ile biyopsi bulguları (IM, HP, atrofi, displazi varlığı) retrospektif taranarak değerlendirildi.

Bulgular: Çalışmaya median yaşı 53 (18-93) yıl olan 1344 (%53,1) kadın ve 1186 (%46,9) erkek toplam 2530 olgu dahil edildi. Olguların %27,8'inde HP ve %26,8'inde de İM tespit edildi. İM pozitif olan 677 hastaların median yaşı 59 (19-92)yıl idi ve %29,7'si (n=352) erkekti. IM pozitif ve negatif gruplar içinde cinsiyetler arasında median yaş açısından anlamlı farklılık saptanmazken (Sırasıyla p=0,584, p=0,642), IM pozitif saptanan hastalarda median yaş ve erkek cinsiyet oranı IM negatif olanlara nazaran daha yüksekti (Sırasıyla p<0,001, p=0,002). Erkek hastalar arasında HP pozitiflik oranı %31 (n=368) iken aynı oran kadın hastalar arasında %24,9 (n=334) (p=0,001) idi. HP pozitif hastalarda erkek cinsiyet belirgin olarak daha yüksek idi (%52,4'e karşılık %47,6) HP pozitif olanlarda median yaş anlamlı olarak daha düşük idi p<0,001). IM pozitif ve negatif saptanan hasta grupları arasında HP pozitifliği açısından anlamlı farklılık saptanmadı (p=0,341).

Sonuç: IM ileri yaşlarda ve erkek hastalarda daha fazla bulundu. HP pozitifliği erkek ve genç hastalarda daha fazla bulundu. IM ve HP sıklığı açısından anlamlı farklılık saptanmadı.

Anahtar Kelimeler: İntestinal metaplazi, helikobakter pilori, gastrik atrofi

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INTRODUCTION

Gastric cancer ranks third among cancer-related deaths in the world (1). Gastric intestinal metaplasia (IM) is a precancerous lesion found in Correa's cascade, a model on the pathway to gastric cancer, and is histologically defined as the alteration of the oxyntic and antral mucosa to the intestinal mucosa consisting of panin, absorptive, and goblet cells (2) (Figure 1).

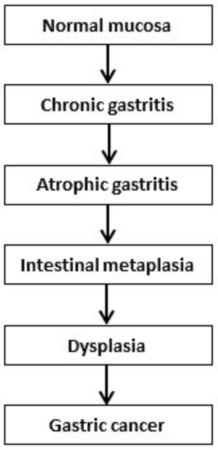

Figure 1. Correa's cascade

Gastric IM rarely causes specific symptoms. It is usually discovered incidentally in patients undergoing upper gastrointestinal endoscopy for dyspepsia.

Helicobacter pylori (HP) is a gram-negative bacterium classified by the World Health Organization (WHO) as a type 1 carcinogen, associated with a 3-fold increase in the development of non-cardia gastric cancer, and involved in the development of gastric IM and atrophic gastritis (3,4). It is estimated that nearly half of the world's population is infected with this pathogen (5). The Maastricht IV guidelines recommend HP infection treatment (6).

In this study, we aimed to determine the frequency of IM and its relationship with HP in different age and sex groups who underwent endoscopic examination with the indication of dyspepsia.

MATERIAL AND METHOD

The Ethics Committee of the Faculty of Medicine of Karadeniz Technical University approved the study under the number 2020/192. In the study, the data of 2530 patients who underwent upper gastrointestinal tract endoscopy (GIT) due to dyspepsia in the Endoscopy Department of Gastroenterology Clinic of Karadeniz Technical University Farabi Hospital, and who underwent gastric biopsy were retrospectively analyzed. Patients under 18 years of age and patients who had undergone gastric surgery were excluded from the study. First-time endoscopy results of patients with repeat endoscopies were included in the study, and subsequent endoscopy results were not included in the study (Figure 2).

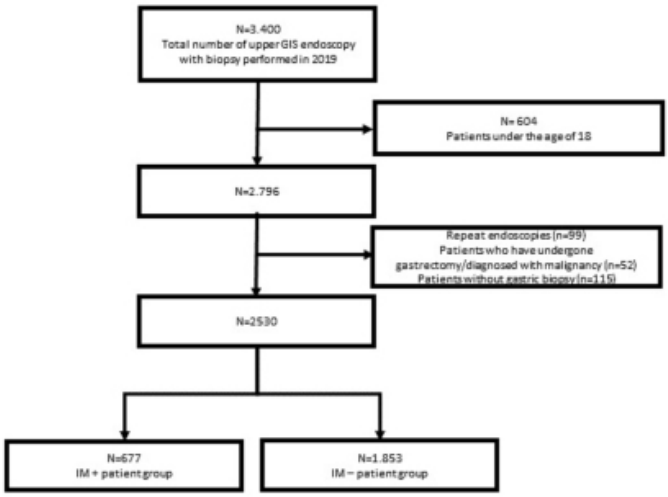

Figure 2. Flowchart of patients included in the study

Patient demographic characteristics such as age and sex, the regions where the gastric biopsy was taken (antrum, corpus, fundus, cardia), and biopsy findings (presence of IM, HP, atrophy, dysplasia) were evaluated.

Pentax, Olympus, or Fuji fiberoptic gastroscopes were used for the upper GI endoscopic procedures performed with sedoanalgesia after at least 8 hours of fasting. During the procedure, 2 biopsies were taken from at least one region of the antrum, corpus, fundus, and/or cardia of the stomach and placed in containers containing 5 ml formalin. The biopsy material was analyzed by the Giemsa method for HP and by the histochemical reaction PAS / AB pH 2.5 for IM.

Statistical analysis

Statistics 22.0 (IBM Corp., Armonk, NY, USA) for Windows package program was used for statistical tests. Continuous variables were evaluated with the histogram and Q-Q plot in terms of normal distribution, while they were evaluated with Shapiro-Wilk or Kolmogorov-Smirnov tests, depending on the number of variables. Normally distributed continuous variables were presented throughout the study as mean ± standard deviation, and the t-test for independent variables was used to compare the two groups. Other continuous variables were presented as median (minimum-maximum or IQR), and the nonparametric Mann-Whitney U test was used to compare the groups. Categorical variables were presented as frequency and percentage, and the Pearson chi-square test or Fischer's exact probability test was used to compare the groups. Tests with a p-value of 0.05 or less at the 95 percent confidence interval were considered statistically significant.

RESULTS

A total of 2530 cases, 1344 (53.1%) women and 1186 (46.9%) men, with a median age of 53 (18-93) years, were included in the study. HP was detected in 27.8% of cases and IM in 26.8% (Table 1).

Table 1. Sex, HP, and IM status of cases

	Number of patients (%)
Total	2530 (100)
Female	1344 (53.1)
Male	1186 (46.9)
HP +	702 (27.8)
HP -	1828 (72.2)
IM +	677 (26.8)
IM -	1853 (73.2)

The median age of the 677 patients with positive IM was 59 (19-92) years, and 29.7% (n=352) were male (Table 2). While there was no statistically significant difference in median age between male and female sexes in IM positive and negative groups (p=0.584 and p=0.642, respectively), median age and male sex ratio were significantly higher in IM positive patients than in IM negative patients (p<0.001 and p=0.002, respectively) (Table 2).

Table 2. Relationship between IM status and gender and age

	Total	IM +	IM -	p
Female, n (%)	1344 (100)	325 (24,2)	1019 (75.8)	**0.002**
Male, n (%)	1186 (100)	352 (29.7)	834 (70.3)	
Total	2530	677	1853	**<0.001**
Age (min-max)		59 (19-92)	50 (18-93)	

*IM: Intestinal metaplasia

HP was positive in 27.7% (n=702) of patients. While the rate of HP positivity in male patients was 31% (n=368), the same rate in female patients was 24.9% (n=334) (p=0.001). Among HP-positive patients, the male gender was significantly more prevalent (52.4% vs. 47.6%). The median age was significantly lower in HP positive patients (p<0.001) (Table 3).

Table 3. Relationship of HP with gender and age

	All patients	HP +	HP -	P
Total	2530 (100)	702 (27.7)	1828(72.3)	**0.001**
Male, n (%)	1186 (46,9)	368 (31)	818 (69)	
Female, n (%)	1344 (53.1)	334 (24.9)	1010 (75.1)	**<0.001**
Age, median (IQR)		48 (23)	55 (22)	

*HP: Helicobacter pylori

HP was positive in 26.3% (n=178) of the 677 patients who tested positive for IM. While no statistically significant difference was found between genders in HP positivity for this subject (p=0.162), the median age was significantly lower in HP positive patients (p<0.001) (Table 4).

HP was positive in 28.3% (n=524) of patients in whom IM was negative. While the HP positivity rate was 32% (n=267) in IM-negative men and 25.2% (n=257) in women, the HP positivity rate was significantly higher in men than in women (p=0.001). The median age of HP-positive patients was significantly lower (p<0.001, median age 46 in HP-positive patients, 53 in HP-negative/positive patients) (Table 4).

Table 4. Gender and age relation according to HP positivity/negativity of intestinal metaplasia positive or negative patients

		HP +	HP -	p (IM +/-)
IM +, n (%)		178 (26.3)	499 (73.7)	
	Female	77 (23.7)	248 (76.3)	0.162
	Male	101 (28.7)	251 (71.3)	
IM -, n (%)		524 (28.3)	1329 (71.7)	
	Female	257 (25.2)	762 (74.8)	**0.001**
	Male	267 (32)	567 (68)	
IM +, Age (IQR)		54 (20)	61 (19)	<0.001
IM -, Age (IQR)		46 (24)	53 (23)	<0.001

*IM: Intestinal metaplasia, HP: Helicobacter pylori

There was no significant difference between IM positive and negative patient groups in terms of HP positivity (p=0.341) (Table 5). There was no significant relationship between dysplasia and Helicobacter positivity and male/female gender (p=0.374 and p=0.283, respectively).

Table 5. Relationship between HP and intestinal metaplasia

	All patients	IM +	IM -	p
HP +	702 (27.7)	178 (25.4)	524 (74.6)	0.341
HP -	1828 (72.3)	499 (27.3)	1329 (72.7)	
Total	2530 (100)	677 (26,8)	1853 (73.2)	

*IM: Intestinal metaplasia, HP: Helicobacter pylori

In the cases in which atrophy could be evaluated as pathologic, the frequency of atrophy was 0.9%. As expected, the frequency of atrophy was significantly higher at older ages (median (IQR) 62 (17), 53 (24), p=0.022, respectively). There was no significant difference between genders in terms of the frequency of atrophy (p > 0.05).

Dysplasia was significantly higher in patients with IM positive than in negative patients (p=0.004). 1.3% (n=9) of patients with IM positive had dysplasia and 1.2% (n=8) had atrophy, while atrophy could not be assessed in 31.8% (n=215). Dysplasia was found in 0.3% (n=5) of IM negative patients, while atrophy was found in 0.3% (n=6) and could not be assessed in 39.8% (n=737). Median age was higher in patients with dysplasia (median age (IQR) 66 (8), 53 (23), p<0.001, respectively).

DISCUSSION

Gastric cancer, the incidence of which is gradually decreasing, was the leading cause of cancer-related deaths in many European countries about 50 years ago (7,8). Although the incidence of gastric cancer has decreased because of the focus on diagnosis and eradication of HP after it was recognized as a type 1 carcinogen by the WHO it still causes more than 700,000 deaths per year in the world (9). Early diagnosis and treatment of HP play an important role in preventing the development of gastric cancer, as

some studies have shown that the development of chronic atrophic gastritis, IM, dysplasia, and carcinoma takes 16-24 years from the onset of HP-induced chronic active gastritis (10). Although it is said that the most important risk factor for the occurrence of IM is HP, discussions on this topic continue due to conflicting publications. There are different data from our country and different regions of the world about the incidence of IM, HP, and atrophy.

In the study conducted by Kösekli in the Denizli region, the frequency of IM was 16%, the frequency of atrophy was 0.2%, and IM and atrophy were observed more frequently in males ($p < 0.001$ and $p=0.006$, respectively) (11). In the study conducted by Tosun et al. in the Şanlıurfa region, the frequency of IM was 8.9% and atrophy 5.1% (12), while Özdil et al. found the frequency of IM to be 17.8% (13). In one study, the frequency of IM was found to be 18.1% in Konya (14), 8.62% in Istanbul, and more frequent in men (15). In our study, the frequency of IM was 26.8%, the frequency of atrophy was 0.9%, and IM and atrophy were more common in males ($p=0.002$).

Considering the frequency of IM and atrophy in relation to age, Tosun et al. found that the mean age of cases was significantly higher at IM (12). In contrast, Kösekli et al. found that the frequency of IM and atrophy was higher in patients older than 40 years (11), and Kesici et al. found that the frequency of IM was higher in patients older than 65 years ($p < 0.01$) (15). In our study, the median age of patients with IM and atrophy was significantly higher ($p < 0.001$), lwhich is consistent with the literature.

While Kösekli found the frequency of HP to be 71% (11), Tosun et al. 43.9% (12), Bor et al. 75.7% (16), Kesici et al. 34.61% (15), Korkmaz et al. 40% (14), Özdil et al. 71.3% (13). In the 2010 study by Erkut et al., the frequency of HP in the Trabzon region was reported to be 40.4% (17). Interestingly, the frequency of HP in our study was 27.7%, which was lower than that reported in the literature. The fact that no data could be obtained on whether patients had previously received HP eradication treatment and the increased frequency of patients who had received possible eradication treatment based on the recent history of our study may explain the low rate of HP positivity.

When the association between HP and gender was investigated, no significant gender difference was found in the study by Kösekli (11). In contrast, Kesici et al. found that the frequency of HP was higher in men (15). Our study observed HP more frequently in males ($p=0.001$).

When we look at the relationship between HP and age, the median age of HP-positive patients was significantly higher than that of HP-negative patients ($p<0.001$). In their study, Kesici et al. found that the prevalence of HP was lower at the age of 65 years compared to other age groups ($p<0.01$) (15).

In the study conducted by Tosun et al. it was found that the rate of atrophy was high in IM positive patients ($p<0.01$) (12). In our study, it was found that the rate of atrophy was higher in IM positive patients ($p=0.034$).

In the literature, there are publications with different results about the relationship between HP and IM. Tosun et al. and Topal et al. found no significant association between IM and HP ($p > 0.05$) (12,18). Studies by Crannen et al. and Aydın et al. found that IM was higher in HP positive cases than in negative cases (10,19). In contrast, Kesici et al. found that the frequency of IM was higher in HP -negative patients than in HP -positive patients (15). In our study, no statistically significant difference was found between HP and IM ($p=0.341$).

The main limitations of our study are that it was a single-center and retrospective study. In addition, the IM subgroups were not specified in the histopathology reports, and atrophy could not be assessed in some patients due to inadequate biopsy. Despite all this, we believe that such studies are necessary and useful to collect local data on HP and IM and to perform general evaluation and planning. Our study has once again demonstrated the need for multicenter prospective studies that address these limitations and provide standardization in the endoscopic and histopathologic evaluation (Sydney classification) of the biopsy and also consider potential risk factors and comorbidities. We hope that our study will not only enrich the local data in our country but also be a positive stimulus in this regard.

CONCLUSION

IM was more common in older and male patients. HP positivity was found more frequently in male and young patients. There was no significant difference in HP frequency in IM positive and negative patients. Atrophy was more common in IM positive patients.

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Conflict of Interest: *The authors declare that they have no competing interest.*

Ethical approval: *The Ethics Committee of the Faculty of Medicine of Karadeniz Technical University approved the study under the number 2020/192.*

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