JOURNAL OF
CONTEMPORARY MEDICINE

DOI: 10.16899/jcm.626167
J Contemp Med 2019;9(4):338-342

Original Article / Orjinal Araştırma

The prevalence of heterotopic gastric mucosa of the proximal esophagus and the relationship between clinical and endoscopic findings

Proksimal özofagusta heterotopik gastrik mukoza prevalansı ve klinik ve endoskopik bulgular arasındaki ilişki

Hatice Karagöz,[1] Ahmet Karaman[2]

[1]Department of Internal Medicine, Acıbadem Kayseri Hospital, Kayseri, Turkey
[2]Department of Gastroenterology, Acıbadem University Faculty of Medicine, İstanbul, Turkey

Abstract

Introduction: In this study, we aimed to investigate the prevalence of HGMPE and the relationship between clinical and endoscopic findings.

Methods: Between December 2013 and February 2018, a total of 4126 patients, 2091 women and 2035 men, who underwent esophagogastroduodenoscopy in the gastroenterology unit of Acıbadem Kayseri Hastanesi were retrospectively screened. Totally, 122 patients, 54 women and 68 men found to have heterotopic gastric mucosa and a control group of age and sex matched 241 patients, 107 women and 134 men who do not have heterotopic gastric mucosa were included the study.

Results: We found the prevalence of HGMPE 2.96% in our study. In the HGMPE + group, the three most common symptoms were stomach pain (48.4%), dyspepsia (16.4%) and reflux symptoms (13.1%). The three most common symptoms in the HGMPE - group were stomach pain (44.8%), dyspepsia (20.3%) and abdominal pain (11.2%). Dysphagia was significantly higher in the case group, whereas abdominal pain was higher in the control group (p=0.037 and p=0.024, respectively). No statistically significant difference was found between the HGMPE + and HGMPE - groups in terms of stomach ache, cough, dyspepsia, LPR symptoms, GIS bleeding, suspected GIS cancer and nausea and vomiting (p>0.05 for each).

Discussion and Conclusion: Despite the differences in the results of studies on the prevalence of HGMPE, we think that HGMPE may be a more common endoscopic finding if the endoscopist becomes more aware of this lesion. Although the controversies remain regarding the clinical significance of this entity, increasing number of cases of neoplastic transformation has further increased the importance of HGMPE.

Keywords: Cervical inlet patch; dysphagia; esophagus; heterotopic gastric mucosa; laryngopharyngeal reflux.

Özet

Amaç: Heterotopik gastrik mukoza (HGMPE), genellikle proksimal özofagusta lokalize olan ektopik gastrik mukoza adasıdır. HGMPE' nin klinik önemi esas olarak asit üretimi ve neoplastik dönüşüm kapasitesi ile ilişkilidir. Bu çalışmada HGMPE prevalansı ile klinik ve endoskopik bulgular arasındaki ilişkiyi araştırmayı amaçladık.

Gereç ve Yöntem: Aralık 2013 ile Şubat 2018 arasında Acıbadem Kayseri Hastanesi gastroenteroloji ünitesinde özofagogastroduodenoskopi yapılan 2091 kadın ve 2035 erkek toplam 4126 hasta retrospektif olarak tarandı. 54 kadın ve 68 erkekten oluşan toplam 122 HGMPE + hasta ile yaş ve cinsiyet açısından eşleştirilmiş 107 kadın ve 134 erkekten oluşan toplam 241 kişilik HGMPE - kontrol grubu çalışmaya dahil edildi.

Bulgular: Çalışmamızda HGMPE prevalansını %2,96 olarak saptadık. HGMPE + grupta en sık görülen üç semptom sırasıyla mide ağrısı (48,4%), dispepsi (16,4%) ve reflü semptomlarıyken (13,1%); HGMPE – grupta ise sırasıyla mide ağrısı (44,8%), dispepsi (20,3%) ve abdominal ağrıydı (11,2%). Disfaji, hasta grubunda anlamlı olarak yüksek iken, kontrol grubunda abdominal ağrı daha fazlaydı. HGMPE + ve HGMPE – gruplar arasında reflü özofajit, duodenal ülser ve alt özofageal sfinkter eksikliği açısından istatistiksel olarak anlamlı bir fark bulunmadı.

Sonuç: HGMPE prevalansı ile ilgili çalışmaların sonuçlarındaki farklılıklara rağmen, eğer endoskopistin bu lezyonla ilgili farkındalığı artarsa HGMPE'nin daha sık rastlanan bir endoskopik bulgu olabileceğini düşünüyoruz. Bu bulgunun klinik önemi ile ilgili tartışmalar devam etse de, artan sayıda neoplastik transformasyon HGMPE'nin önemini daha da artırmıştır.

Anahtar Sözcükler: Servikal inlet patch; disfaji; özofagus; heterotopik gastrik mukoza; laringofaringeal reflü.

Corresponding *(İletişim)*: Hatice Karagöz, Acıbadem Kayseri Hastanesi, İç Hastalıkları Kliniği, 38140 Melikgazi, Kayseri, Turkey
E-mail *(E-posta)*: haticeeverest@hotmail.com

Received *(Geliş Tarihi)*: 27.09.2019 **Accepted *(Kabul Tarihi)*:** 23.11.2019

Heterotopic gastric mucosa of the proximal esophagus (HGMPE), first described by Schumidt in 1805, is an island of ectopic gastric mucosa located in the proximal esophagus and commonly just below the upper esophagus sphincter.[1] It is also called as "inlet patch" or "cervical inlet patch".[2] Rarely, it can be found in the other parts of the esophagus[2,3] and also there are cases reported in the literature where it was seen in the gallbladder or cyctic duct,[4] duodenum,[5] ampulla of vater[6] and anus.[7] HGMPE is widely considered to be a congenital anomaly but recent studies have proposed that it might be an acquired condition.[1,8,9]

The incidence of HGMPE varies between 4–10% in different endoscopic studies.[10–14] The largest autopsy series in 1000 children found the incidence of HGMPE as 4.5%.[11]

Currently, there are three theories proposed for the development of HGMPE. The first and the most widely accepted theory is that: During the 10th week of gestational life, the esophagus is covered with columnar epithelium. At the 24 wk of gestation the squamous epithelium begins to appear in the middle 1/3 of the esophagus and from there it spreads distally and proximal. If this procedure is not completed, some columnar cells may be present at birth, and heterotopic gastric mucosa can be observed in the upper third of the esophagus.[1,2] The second theory is the metaplastic transformation of the squamous lining to columnar from chronic acid injury as seen in Barrett's esophagus.[8] The third theory involves rupture of proximal esophageal retention cystic glands.[9]

Based on clinical, endoscopic and histological characteristics, a clinico-pathologic classification has been described by von Rahden et al. for the categorization of HGMPE (Table1).[1]

The majority of patients found to have HGMPE are in group 1 and they are detected incidentally during evaluation for other gastrointestinal complaints. The patients with type II and III have symptoms probably related to the acid secretion of the patch. These include LPR symptoms (such as regurgitation, dysphagia, hoarseness, globus, throat dfiscomfort and chronic cough) and strictures and bleeding.[1,2]

The clinical significance of HGMPE is mainly related with its capacity to produce acid and neoplastic transformation.[15] There are also reports in the literature that inflammatory and pathologic changes such as atrophy, intestinal metaplasia, dysplasia and carcinoma can be seen.[2,16,17] HGMPE can be colonized by *Helicobacter pylori* (*H. pylori*) and even the prevalence has been reported to be as high as 82%.[18] There are many complications of HGMPE reported in the literature such as adenocarcinoma, intestinal metaplasia, stricture, web, ulceration and bleeding, fistula, perforation.[17,19–25]

Currently, there is not a consensus guideline established for the surveillance of HGMPE. Incidental identification of HGMPE does not require specific treatment but the symptomatic patients should be treated. For the detection of unsuspected findings or malignacy; the biopsies should be taken and the lesions must be evaluated by histological examinations.[26]

In this study, we aimed to investigate the prevalence of HGMPE and the relationship between clinical and endoscopic findings.

Table 1. Clinico-pathological classification for heterotopic gastric mucosa of the proximal esophagus

Category	Description	Symptoms/findings
I	Asymptomatic	None
II	Symptomatic	Laryngopharyngeal reflux
III	Symptomatic with benign complications	Strictures/webs/ fistula/bleeding
IV	Intra-epithelial dysplasia	None/non-specific
V	Malignant transformation	Asymptomatic/dysphagia

Materials and Method

Between December 2013 and February 2018, a total of 4126 patients, 2091 women and 2035 men, who underwent esophagogastroduodenoscopy in the gastroenterology unit of Acibadem Kayseri Hospital were retrospectively screened, using the hospital records. This study was approved by the Acibadem University Ethics Committee. All patients were performed esophagogastroduodenoscopy with a white light video endoscopy using high definition system (Olympus Evis Exera II CV180, NBI).

Totally, 122 patients, 54 women and 68 men found to have HGM (HGMPE +) were included the study. After removal of 122 patients from 4126 patients, a control group of 241 patients, 107 women and 134 men (HGMPE - group), was formed from the remaining patients, similar in age and gender to the individual case group.

Statistical Analyses

For statistical analysis, the Statistical Package for the Social Sciences [SPSS] v 20 was used. We reported continuous variables as mean±standard deviation. Categorical variables were defined as numbers (n) and percentages (%). Fisher's exact test or chi-square test were used to analyze symptom differences between the HGMPE + and HGMPE - groups. P-values <0.05 were considered significant.

Results

Among 122 patients included in the study, 54 (44.3%) were females and 68 (55.7%) were males. The mean age of the females in the patient group was 39.46±12.,71 and the males was 38.76±13.23.

Among 241 patients in the control group, 107 (44.4%) were females, and 134 (55.6%) were males.

The mean age of the females in the conrol group was 39.85±12.45 and the males was 38.63±13.08. There was no statistically significant differences among the groups according to the age and gender (p>0.05).

We found the prevalence of HGMPE 2.96% in our study and

Table 2. The prevalence of symptoms reported in HGMPE + and HGMPE – patients

Symptoms reported	Prevalence %		p value
	HGMPE +	HGMPE -	
LPR symptoms	13.1%	8.7%	NS
Dyspepsia	16.4%	20.3%	NS
Stomach pain	48.4%	44.8%	NS
Dysphagia	9.0%	3.7%	p=0.037
GIS bleeding	5.7%	5.0%	NS
Nausea-vomiting	0.00%	2.5%	NS
Abdominal pain	4.1%	11.2%	P=0.024
Cough	0.8%	0.8%	NS
Suspected GIS cancer	2.5%	2.9%	NS

HGMPE: Heterotopic gastric mucosa of the proximal esophagus; LPR: Laryngopharyngeal reflux; GIS: Gastrointestinal system; NS: not significant.

also observed 14 (11.47%) patients that have more than single lesion.

The lesion sizes were as follows: 22 (%18.9) of the lesions were found to be between 0–10 mm, 74 (%63.2) were between 10–30 mm and 21 (%17.9) were higher than 30 mm.

The symptoms of patients were categorized in nine main groups. These were: stomach pain, dyspepsia, laryngopharyngeal reflux (LPR) symptoms, dysphagia, abdominal pain, gastrointestinal system (GIS) bleeding, cough, suspected GIS cancer and nausea and vomiting.

In the HGMPE + group, the three most common symptoms were stomach pain (48.4%), dyspepsia (16.4%) and reflux symptoms (13.1%). The three most common symptoms in the HGMPE - group were stomach pain (44.8%), dyspepsia (20.3%) and abdominal pain (11.2%).

Dysphagia was significantly higher in the case group, whereas abdominal pain was higher in the control group (p=0.037 and p=0.024, respectively).

No statistically significant difference was found between the HGMPE + and HGMPE - groups in terms of stomach ache, cough, dyspepsia, LPR symptoms, GIS bleeding, suspected GIS cancer and nausea and vomiting (p>0.05 for each).

The prevalence of symptoms reported in HGMPE + and HGMPE – patients are shown in Table 2.

In this study, we also examined the endoscopic findings of the patients as well as symptoms. Reflux esophagitis was found in 8.2%[10] patients in the HGMPE + group and 4.1%[10] patients in the HGMPE - group but it was not a statistically significant difference (p=0.1).

Duodenal ulcer was found in 17.2%[21] patients in the HGMPE + group and 10.8%[26] patients in the HGMPE - group but it was not a statistically significant difference (p=0.08).

Lower esophageal sphincter (LES) deficiency was found in 24.6%[30] patients in the HGMPE + group and 22%[53] patients in the HGMPE - group but it was not a statistically significant difference (p=0.578).

Discussion

HGMPE, is an island of ectopic gastric mucosa located in the proximal esophagus.[1] Compared to the other esophageal disorders, there are few numbers of publications on this entity and the controversies remain regarding the clinical significance of this entity.[15] The reported prevalence of HGMPE varies in different studies. We found the prevalence of HGMPE 2.96% in our study. This was 1.1% in the study of Avidan et al.,[8] 0.1% in the study of Neumann et al.,[27] 10% in the study of Borhan-Manesh et al.,[3] 5.6% in the study of Chong et al.,[28] 11% in the study of Weickert et al.,[29] and 4.9% in the study of Jacobs et al.[30]

The prevalence of HGMPE reported in different studies from Turkey were as folows: 1% in the study of Alagozlu et al.,[19] 1.8% in the study of Yuksel et al.,[31] 1.67% in the study of Akbayır et al.[16] and 3.6% in the study of Poyrazoglu et al.[32]

The symptoms reported were not consistent between the studies. The prevalence rate of LPR symptoms has been reported to be as high as 73.1% in a study of Chong et al. and all of the LPR symptoms including chronic cough, sore throat/hoarseness, globus, regurgitation and heartburn were found to be significantly higher in the HGMPE + group compared to the HGMPE – group.[28] Akbayır et al. found the prevalence of LPR symptoms as 45% but they did not find statistical significance between the HGMPE + and HGMPE – groups.[16] In our study, we found the LPR symptoms prevalence as 13.1% in the HGMPE + group and 8.7% in the HGMPE – group and there was no statistically significant difference among the groups (p>0.05).

In our study, the prevalence of dysphagia was found to be higher in the HGMPE + group. It was 9.0% in HGMPE + group and 3.7 in HGMPE – group and this was statistically significant (p=0.037). This was not a surprising result when we think about the close proximity of HGMPE with the laryngopharyngeal complex. Similarly, there are reports in the literature showing the high prevalences of dysphagia in the patients with HGMPE. Baudet et al.,[33] Porazoglu et al.[32] and Neumann et al.[27] also reported that dysphagia was found to be higher in the patients with HGMPE +.

We found dyspepsia prevalence as 16.4% in HGMPE + group and 20.3% in HGMPE – group but there was not statistically significant difference among the groups (p>0.05). Alagözlü et al. also reported that dyspepsia prevalences were not statistically significant between the HGMPE + and HGMPE – groups.[19] We did not find any statistically significant difference between the HGMPE + and HGMPE - groups in terms of stomach ache, cough, dyspepsia, LPR symptoms, GIS bleeding, suspected GIS cancer and nausea and vomiting (p>0.05 for each).

We examined and compared the groups also for the endoscopic findings. In our study; we did not find any statistically significant difference between the HGMPE + and HGMPE -

groups in terms of reflux esophagitis, duodenal ulcer and LES deficiency.

In the literature, there are also reports on the associations between HGMPE and other endoscopic findings but the results vary between studies. For example, Avidan et al. reported significantly more reflux esophagitis, Barrett's esophagus, hiatus hernia and gastric ulcer in their study.[8] Similarly, Neumann et al. reported more reflux esophagitis, Barrett's mucosa and adenocarcinoma arising from Barrett's mucosa.[27] Jacobs et al. also reported significantly more reflux esophagitis but they did not find any significant difference for hiatus hernia, Barrett's esophagus and any gastric or duodenal ulcer.[30] On the other hand, Borhan-Monesh et al. did not find any significanct difference for reflux esophagitis and Barrett's esophagus.[3] Similarly Chong et al.[28] and Weickert et al.[29] did not show any significant difference for reflux esophagitis, Barrett' s esophagus, hiatus herni, duodenal ulcer or gastric ulcer.

The studies from Turkey also report different results. Yüksel et al.[31] found significantly more reflux esophagitis and histologically proven Barrett's esophagus but no difference in hiatus hernia. Alagozlu et al.[19] reported significantly more endoscopic Barrett' s esophagus in patients with HGM but not with reflux esophagitis. Akbayır et al.[16] and Poyrazoglu et el.[32] also did not show any significant difference for reflux esophagitis, Barrett's esophagus, hiatus herni, duodenal ulcer or gastric ulcer similar to our study.

Our study has some limitations. First limitation is the retrospective nature of our study so we could not perform control endoscopies and do not know about the current situation. The second limitation of our study is that no biopsies have been taken of any of the patients and therefore we do not know about the presence of H. pylori colonization, atrophy, dysplasia or adenocarcinoma in the HGM specimens.

Conclusion

Despite the differences in the results of studies on the prevalence of HGMPE, we think that HGMPE may be a more common endoscopic finding if the endoscopist becomes more aware of this lesion. We found the prevalence of HGMPE 2.96% in our study. The majority of patients are asymptomatic and are detected incidentally but also symptomatic cases can interfere with the other upper digestive disorders. Similarly, in our study, the prevalence of dysphagia was significantly higher in the HGMPE + group. The symptomatic patients should be treated and followed up for the complications. In recent years, the increasing number of cases of neoplastic transformation has further increased the importance of HGMPE. Currently, there are still many unresolved and unknown areas of HGMPE and further researches are required.

Funding: There was no specific funding for this study.

Conflict of interest: There are no relevant conflicts of interest to disclose.

References

1. von Rahden BH, Stein HJ, Becker K et al. Heterotopic gastric mucosa of the esophagus: literature-review and proposal of a clinicopathologic classification. Am J Gastroenterol 2004; 99: 543–551.
2. Chong VH. Heterotopic gastric mucosal patch of the proximal esophagus. Gastrointestinal Endoscopy 2011; 125–148
3. Borhan-Manesh F, Farnum JB. Incidence of heterotopic gastric mucosa in the upper oesophagus. Gut 1991; 32: 968–972
4. Orizio P, Villanacci V, Bassotti G et al. Heterotopic gastric mucosa in the cystic duct. Int. J. Surg. Pathol 2011; 19: 364–365
5. Mann NS, Mann SK, Rachut E. Heterotopic gastric tissue in the duodenal bulb. J. Clin. Gastroenterol 2000; 30: 303–306
6. Jarry J, Rault A, Sa Cuhna A et al. Acute recurrent pancreatitis by heterotopic fundic mucosa at the ampulla of vater. Pancreas 2009; 38: 351–353
7. Rifat Mannan AA, Kahvic M, Bharadwaj S etal. Gastric heterotopia of the anus: report of two rare cases and review of the literature. Indian J. Pathol. Microbiol 2008; 51: 240–241
8. Avidan B, Sonnenberg A, Chejfec G et al. Is there a link between cervical inlet patch and Barrett's esophagus? Gastrointest Endosc 2001; 53: 717–721
9. Meining A, Bajbouj M. Erupted cysts in the cervical esophagus result in gastric inlet patches. Gastrointest Endosc 2010; 72: 603–605
10. Takeji H, Ueno J, Nishitani H. Ectopic gastric mucosa in the upper esophagus: prevalence and radiologic findings. Am. J. Roentgenol 1995; 164: 901–904
11. Rector LE, Connerly ML. Aberrant mucosa in the esophagus in infants and in children. Arch. Pathol 1941; 31: 285–294
12. Truong LD, Stroehlein JR, McKechnie JC. Gastric heterotopia of the proximal esophagus: a report of four cases detected by endoscopy and review of literature. Am. J. Gastroenterol 1986; 81: 1162–1166
13. Schroeder WW, Myer III CM, Schechter GL. Ectopic gastric mucosa in the cervical esophagus. Laryngoscope 1987; 97: 131–135
14. Taylor AL. The epithelial heterotopias of the alimentary tract. J. Pathol 1927; 30: 415–449
15. Chong VH. Clinical significance of heterotopic gastric mucosal patch of the proximal esophagus. World J Gastroenterol 2013; 193): 331-338
16. Akbayir N, Alkim C, Erdem L et al. Heterotopic gastric mucosa in the cervical esophagus (inlet patch): endoscopic prevalence, histological and clinical characteristics. J Gastroenterol Hepatol 2004; 19: 891–896
17. Lauwers GY, Scott GV, Vauthey JN. Adenocarcinoma of the upper esophagus arising in cervical ectopic gastric mucosa: rare evidence of malignant potential of so-called "inlet patch" Dig. Dis. Sci 1998; 43: 901–907
18. Gutierrez O, Akamatsu T, Cardona H et al. Helicobacter pylori and hetertopic gastric mucosa in the upper esophagus (the inlet patch) Am J Gastroenterol 2003; 98: 1266–1270
19. Alagozlu H, Simsek Z, Unal S et al. Is there an association between Helicobacter pylori in the inlet patch and globus sensation? World J. Gastroenterol 2010; 16: 42–47
20. Ward EM, Achem SR. Gastric heterotopia in the proximal esophagus complicated by stricture. Gastrointest Endosc 2003; 57: 131–133
21. Buse PE, Zuckerman GR, Balfe DM. Cervical esophageal web asso-

ciated with a patch of heterotopic gastric mucosa. Abdom Imaging 1993; 18: 227–228
22. Bataller R, Bordas JM, Ordi J et al. Upper gastrointestinal bleeding: a complication of "inlet patch mucosa" in the upper esophagus. Endoscopy 1995; 27: 282
23. Katsanos KH, Christodoulou DK, Kamina S et al. Diagnosis and endoscopic treatment of esophago-bronchial fistula due to gastric heterotopy. World J. Gastrointest Endosc 2010; 2: 138–142
24. García AO, Mazzadi SA, Raffo L et al. Heterotopic gastric mucosa in the upper esophagus: report of a case with a fistula. Dis Esophagus 2002; 15: 262–265
25. Righini CA, Faure C, Karkas A et al. Spontaneous perforation in the upper oesophagus resulting from ulcer in heterotopic gastric mucosa. Rev. Laryngol Otol Rhinol (Bord) 2007; 128: 197–200
26. Sahin G, Adas G, Koc B et al. Is Cervical Inlet Patch Important Clinical Problem? Int J Biomed Sci 2014; 10(2): 129-35
27. Neumann WL, Luján GM, Genta RM. Gastric heterotopia in the proximal oesophagus ("inlet patch"): Association with adenocarcinomas arising in Barrett mucosa. Dig Liver Dis 2012; 44: 292–296
28. Chong VH, Jalihal A. Heterotopic gastric mucosal patch of the esophagus is associated with higher prevalence of laryngopharyngeal reflux symptoms. Eur Arch Otorhinolaryngol 2010; 267: 1793–1799.
29. Weickert U, Wolf A, Schröder C et al. Frequency, histopathological findings, and clinical significance of cervical heterotopic gastric mucosa (gastric inlet patch): a prospective study in 300 patients. Dis Esophagus 2011; 24: 63–68
30. Jacobs E, Dehou MF. Heterotopic gastric mucosa in the upper esophagus: a prospective study of 33 cases and review of literature. Endoscopy 1997; 29: 710–715
31. Yüksel I, Usküdar O, Köklü S et al. Inlet patch: associations with endoscopic findings in the upper gastrointestinal system. Scand J Gastroenterol 2008; 43: 910–914
32. Poyrazoglu OK, Bahcecioglu IH, Dagli AF et al. Heterotopic gastric mucosa (inlet patch): endoscopic prevalence, histopathological, demographical and clinical characteristics. Int J Clin Pract 2009; 63: 287–291
33. Baudet JS, Alarcón-Fernández O, Sánchez Del Río A et al. Heterotopic gastric mucosa: a significant clinical entity. Scand J Gastroenterol 2006; 41:1398–1404.