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Research Article

Implications of Gastric Diverticulum in the Incidence of Metaplasia: An Analysis of 37 Cases

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Abstract

Aim: The present study aimed to investigate the potential association between gastric fundus diverticulum and metaplasia by retrospectively analysing patient data and biopsy results.

Material and Methods: 37 patients with gastric fundus diverticulum were examined, with their data compared to a control group of 50 patients without it. All diagnoses were made endoscopically. Demographic information, laboratory parameters, and endoscopic biopsy results were compared between the groups.

Results: No significant differences were identified between the two groups concerning several laboratory parameters. However, there were significant differences in lymphocytes, urea, albumin, Na, and K values ($p<0.05$). Helicobacter pylori and atrophy distributions did not differ between the groups ($p>0.05$), while a notable difference was seen in the distribution of metaplasia ($p<0.05$). Metaplasia positivity was found to be 16% in patients without gastric diverticulum and 43.2% in patients with gastric diverticulum.

Conclusions: This study found a higher prevalence of metaplasia positivity in patients with gastric diverticulum than those without. These findings suggest a potentially significant link between the gastric diverticulum and the occurrence of metaplasia, which warrants further research to better understand the underlying mechanisms and implications for patient management.

Keywords: Gastric diverticula, metaplasia, gastric biopsy, endoscopy, gastroenterology

INTRODUCTION

Gastric diverticula, while relatively rare, have been a topic of increased interest in recent years. Defined as herniations of the gastric mucosa through the muscular layer, and often discovered incidentally during endoscopic examinations (1,2). Recent advancements in endoscopic technology have improved our ability to identify and analyse the characteristics of gastric diverticula. They are typically asymptomatic but can occasionally present with non-specific symptoms such as abdominal pain, belching, bloating, and severe complications like bleeding or perforation (3-5).

Despite its rare occurrence, gastric diverticula hold potential implications in the onset of various gastrointestinal complications. Among these is metaplasia, a reversible transformation of one differentiated cell type to another, often as a response to chronic injury or irritation (6). While not malignant, this process has been associated with an increased risk of neoplastic transformation in various organs, including the stomach (7-10).

Recent studies have highlighted the possible connection between gastric diverticula and metaplasia (11). However, the specific mechanisms underlying this association remain elusive, suggesting the need for further investigation. Moreover, deepening our understanding of how this relationship can influence patient management and potential therapeutic approaches is crucial.

The present study aims to contribute to this growing

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body of research by conducting a retrospective analysis of patients diagnosed with gastric fundus diverticulum. By comparing these patients' laboratory and biopsy results with those of a control group, we seek to uncover potential differences that may indicate an increased risk of metaplasia among patients with gastric diverticulum.

MATERIAL AND METHOD

The local ethics committee of Giresun Training and Research Hospital approved the study protocol. Informed patient consent was waived due to the retrospective design of the study. This study was conducted on the relevant ethical principles of the Declaration of Helsinki, revised in 2013. The study was conducted at Giresun Training and Research Hospital in Giresun province.

This retrospective study was conducted on 87 patients who underwent upper gastrointestinal endoscopy at our institution from January 2020 to December 2022. Among them, 37 patients were diagnosed with gastric fundus diverticulum, while 50 patients with similar demographic characteristics but without gastric diverticulum served as the control group.

A gastric diverticulum was established using endoscopic examination, defined by the presence of a pouch protruding from the gastric wall. The location, size, and appearance of the diverticula were documented. The control group comprised patients who underwent endoscopy for similar complaints but were found not to have a gastric diverticulum.

Demographic information of the patients, including age and gender, was extracted from the patient records. Laboratory parameters including white blood cell (Wbc), haemoglobin (Hgb), hematocrit (Hct), mean corpuscular volume (MCV), platelet (Plt), glucose, alanine transaminase (ALT), aspartate transaminase (AST), calcium (Ca), lymphocytes (Lymp), creatine, urea, albumin, sodium (Na) and potassium (K) values were obtained from the laboratory records. Biopsies were taken from all patients during the endoscopy. The specimens were immediately fixed in 10% formalin and were sent for histopathological examination. Helicobacter pylori (H. pylori), atrophy, and metaplasia were evaluated and recorded by experienced pathologists blinded to the clinical data.

Statistical Analysis

Data was analysed using the Statistical Package for the Social Sciences (SPSS) 26.0 Statistics package program. The suitability of the numerical variables of the patients to the normal distribution was determined by looking at the skewness values. Except for glucose, urea, ALT and albumin values, it was observed to comply with the rules of normal distribution. The reference value in the normal distribution is between ±1.5. The chi-square test was used to compare patients' descriptive features and pathology findings with and without gastric diverticulum. The Independent Sample T Test or Mann Whitney U test was used to compare patients' age and laboratory parameters with and without gastric diverticulum. Pearson or Spearman Correlation tests were used to examine the relationships between gastric diverticulum disease and age, gender, laboratory and pathology findings. Correlation coefficient; A relationship between 0.00-0.30 was considered as low, between 0.30-0.70 as a medium level, and between 0.70-1.00 as a high-level relationship. Logistic regression analysis results were used to estimate the probability of having a gastric diverticulum. The significance levels were carried out in the study by considering the values of 0.05 and 0.01.

RESULTS

Eighty-seven patients were included in the study. 57.5% of the patients were without gastric diverticulum, and 42.5% were patients with gastric diverticulum. Of the patients without gastric diverticulum, 70% (35 patients) were female, 30% (15 patients) were male, and of the patients with gastric diverticulum, 62.2% (23 patients) were female, 37.8% (14 patients) were male. Of the patients without gastric diverticulum, 52% (26 patients) were under 60 years of age, 48% (24 patients) were 60 years and older, and 51.4% (19 patients) of patients with gastric diverticulum were younger than 60 years, 48%, 6 (18 patients) are 60 years old and above. In addition, the mean age of patients without gastric diverticulum is 58.90 years, and that of patients with gastric diverticulum is 62.89 years. These results showed that the gender and age distribution of patients with and without gastric diverticulum did not differ ($p>0.05$). In other words, the gender and age distributions of the patients in both groups are homogeneous. All gastric diverticulums were in fundus localisation. The comparison of the characteristics of patients with and without gastric diverticulum is shown in Table 1.

In the comparison of laboratory parameters of patients between the two groups, there was no significant difference between Wbc, Hgb, Htc, MCV, Plt, glucose, creatine, ALT, AST and Ca values of patients with and without gastric diverticulum ($p>0.05$). There was a significant difference between the lymphocytes, urea, albumin, Na and K values of patients with and without gastric diverticulum ($p<0.05$). The comparison of laboratory parameters of patients with and without gastric diverticulum is shown in Table 2.

The distribution of H. pylori and atrophy in patients with and without gastric diverticulum did not differ ($p>0.05$). Metaplasia positivity is 16% in patients without gastric diverticulum and 43.2% in patients with gastric diverticulum. According to these findings, metaplasia positivity in patients with gastric diverticulum was considerably higher than in patients without gastric diverticulum. The pathology findings of patients with and without gastric diverticulum are shown in Table 3.

Regression analysis was performed to estimate the probability of having a gastric diverticulum. The patients' lymphocyte, urea, albumin, Na, K and metaplasia parameters were determined as independent variables.

The created logistic regression model was found to be statistically significant (χ2(6)=37.82, p=0.000, p<0.01). Independent variables explain 35.6, according to Cox & Snell and 47.8, according to Nagelkerke, of the changes in the probability of gastric diverticulum. When lymphocyte and albumin variables and the effects of other independent variables were controlled, it was seen that there was no significant variable in estimating the probability of gastric diverticulum in the patient (p>0.05). Urea, Na, K and metaplasia variables were significant in estimating the patient's gastric diverticulum probability when the effects of other independent variables were controlled (p<0.05). When beta coefficients are examined, It was observed that the most influential variable on gastric diverticulum, from largest to smallest, was K, metaplasia, Na and urea. In this context, the logistic regression analysis results for estimating the probability of gastric diverticulum are shown in Table 4.

Table 1. Comparison of characteristics of patients with and without gastric diverticulum

Patients' characteristics		Patient without gastric diverticulum (n:50)		Patient with gastric diverticulum (n:37)		p
		Number	%	Number	%	
Gender	Female	35	70.0	23	62.2	0.591
	Male	15	30.0	14	37.8	
Age	< 60	26	52.0	19	51.4	1.000
	≥ 60	24	48.0	18	48.6	
		Med±SD Med (Min-Max)		Med±SD Med (Min-Max)		
Age[t]		58.90±16.15 58.5 (22-86)		62.89±19.34 59 (27-96)		0.298

*p<0.05, **p<0.01, χ2: chi-square test (categorical data), t: independent sample T test, Med: median, SD: standart deviation. Min: minimum. Max: maximum

Table 2. Comparison of laboratory parameters of patients between groups

Laboratory parameters	Patient without gastric diverticulum (n:50)	Patient with gastric diverticulum (n:37)	p
	Med±SD	Med±SD	
Wbc[t]	6935.80±1869.00	7125.68±3107.62	0.743
Hgb[t]	12.61±1.76	12.18±2.03	0.298
Htc[z]	38.32±4.70 39.05 (25.5-45)	37.01±5.47 39 (23-48.70)	0.196
MCV[t]	85.09±7.22	87.16±4.82	0.134
Plt[t]	264.74±79.42	253.81±65.91	0.498
Lymp[t]	2.09±0.61	1.74±0.71	**0.015***
Glucose[z]	108.82±32.58 100 (65-245)	126.86±57.48 102 (54-254)	0.424
Urea[z]	29.40±8.91 28 (12-59)	43.70±31.75 33 (15-179)	**0.008****
Creatine[t]	.74±0.19	.80±0.21	0.239
ALT[z]	16.64±8.91 15 (6-55)	15.22±10.28 12 (5-55)	0.104
AST[t]	19.52±5.73	20.08±9.21	0.745
Albumin	44.22±7.47 44 (4.5-52.2)	38.66±8.81 41 (10-49)	**0.000****
Na[t]	140.82±2.30	139.46±2.91	**0.017***
K[t]	4.48±0.36	4.19±0.39	**0.001****
Ca[t]	9.54±0.42	9.30±0.74	0.062

*p<0.05, **p<0.01, Med: median, SD: standart deviation, t: independent sample T test, z: Mann Whitney U test (mean and standard deviation values of the data, as well as median, minimum and maximum values are given)

Table 3. Comparison of pathology findings of patients between groups

Pathology findings		Patient without gastric diverticulum (n:50)		Patient with gastric diverticulum (n:37)		p
		Number	%	Number	%	
H.pylori	Negative	38	76.0	29	78.4	0.998
	Positive	12	24.0	8	21.6	
Atrophy	Negative	47	94.0	31	83.8	0.234
	Positive	3	6.0	6	16.2	
Metaplasia	Negative	42	84.0	**21**	56.8	**0.010****
	Positive	8	16.0	16	43.2	

*p<0.05, **p<0.01, $\mathcal{X}2$: chi-square test

Table 4. Results of regression analysis for estimating the probability of gastric diverticulum occurrence in patients

Predictive variable	β	SE	p	Odds ratio	Confidence intervals 95 C.I.for OR	
					Lower	Upper
Lymphocytes	-0.387	0.447	0.387	0.679	0.283	1.631
Urea	0.054	0.027	**0.050**	1.055	1.000	1.113
Albumin	-0.019	0.038	0.614	0.981	0.911	1.056
Na	-0.300	0.147	**0.041**	0.741	0.556	0.987
K	-2.492	0.804	**0.002**	0.083	0.017	0.400
Metaplasia	1.396	0.622	**0.025**	4.040	1.193	13.682
Constant value	52.014	21.253	0.014	$3.8x10^{22}$		

Dependent variable: having gastric diverticulum, β: beta coefficient, SE: standart error, +: positivity, OR: odds ratio

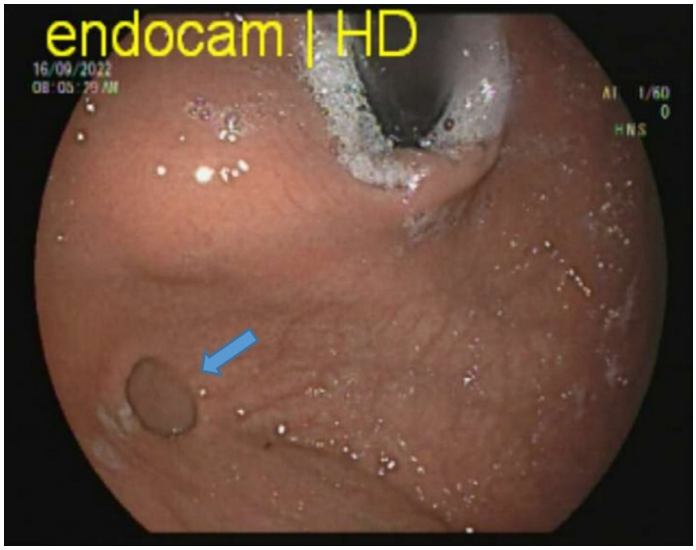

Figure 1. Endoscopic view of the gastric fundus diverticulum

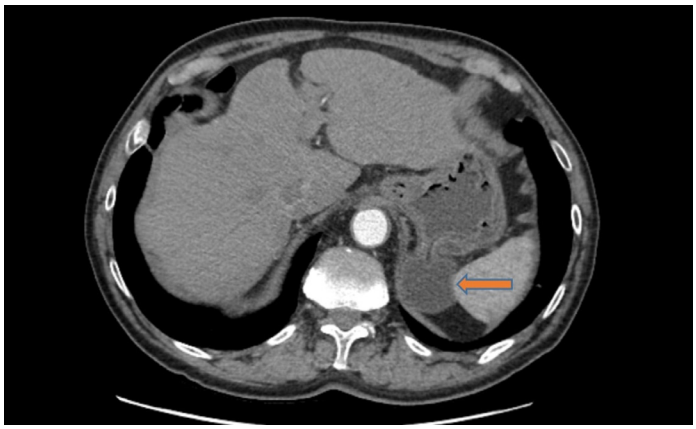

Figure 2. Computed tomography image of gastric fundus diverticulum

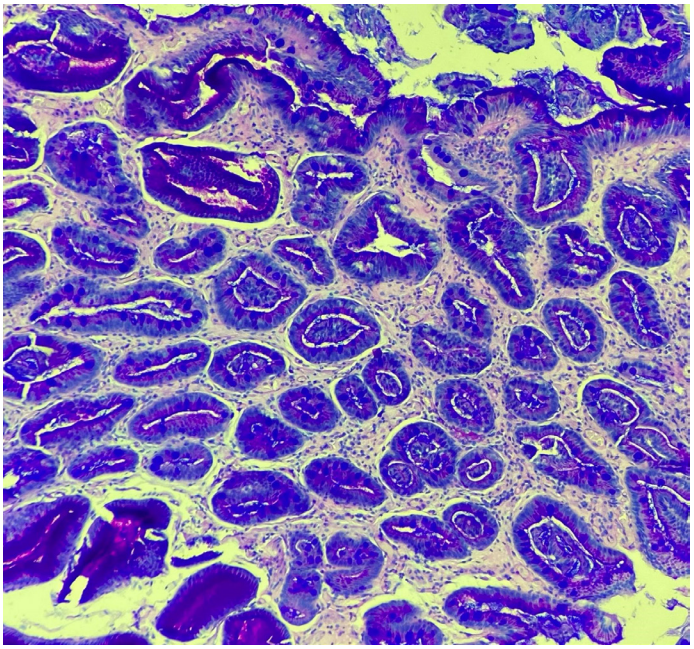

Figure 3. Gastric biopsy showing intestinal metaplasia. Magnification 100×

DISCUSSION

This study is one of the first to explore the relationship between gastric fundus diverticulum and metaplasia in English literature. The significant association between gastric diverticula and metaplasia uncovered in our study is noteworthy, given the established link between metaplasia and the progression to gastric cancer, one of the most lethal malignancies worldwide. While the exact mechanism behind this relationship remains unclear, it is plausible that the diverticulum's structure might promote

bacterial overgrowth, inflammation, and subsequent metaplastic changes. It aligns with the 'Correa cascade', a widely accepted pathogenic model of gastric cancer development, where chronic inflammation can lead to atrophic gastritis, intestinal metaplasia, dysplasia, and eventually, cancer (12).

One could speculate that the altered anatomy and physiology in the area of the diverticulum might lead to the stagnation of gastric contents, promoting metaplasia (13-15). Alternatively, the diverticulum could result from a weakened gastric wall in response to a prolonged inflammatory stimulus, such as H. pylori infection, also known as a risk factor for metaplasia. Although our study found no significant difference in the distribution of H. pylori between the two groups, previous literature described a link between H. pylori infection and gastric metaplasia (12). Given H. pylori's known role in the pathogenesis of gastric cancer, future research could further investigate the relationship between H. pylori, gastric diverticulum, and metaplasia.

A similar mechanism has been suggested in the case of intestinal diverticulosis, where inflammation within the diverticula has been associated with colonic mucosal dysplasia and adenocarcinoma (16). Other instance, colorectal diverticula have been associated with an increased risk of colorectal neoplasia, a pathogenesis thought to result from chronic inflammation (17). These parallel observations underscore the potential significance of gastric diverticulum and metaplasia and the need for further research.

It is also worth noting that there were significant differences in some laboratory parameters between the groups, namely lymphocytes, urea, albumin, Na, and K values. These findings could suggest a systemic influence of gastric diverticulum, possibly related to inflammation, nutritional status, or electrolyte balance. However, further studies are needed to elucidate the potential implications of these variations.

Study Limitations

While our study presents novel insights into the potential association between gastric fundus diverticulum and metaplasia, it is important to acknowledge its limitations.

Firstly, the retrospective nature of our study may introduce selection bias and limit the ability to establish a causal relationship between gastric diverticulum and metaplasia. Secondly, although our sample size is larger than many previous studies on this topic, it remains relatively small, given the rarity of the gastric diverticulum. This limited sample size may reduce our findings' statistical power and the results' generalizability to the broader population. Thirdly, due to the design of our study, we could not account for potential confounding factors such as the patients' dietary habits, medication use, and other lifestyle factors that might influence the risk of metaplasia. Lastly, the lack of follow-up data in our study means we cannot ascertain whether the patients with metaplasia progressed to dysplasia or gastric cancer, which limits our understanding of the clinical implications of our findings.

CONCLUSION

This study uncovers a novel association between gastric fundus diverticulum and increased metaplasia positivity, potentially implicating gastric diverticulum as a risk factor in gastric cancer development. This highlights the importance of vigilant surveillance in patients with gastric diverticulum and invites further investigation into the underlying mechanisms. The identified discrepancies in laboratory parameters further extend the potential clinical implications of this condition. Future prospective studies with larger cohorts are warranted to corroborate these findings and pave the way for improved patient care and prognosis.

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

Ethical approval: *The study was conducted in accordance with the Helsinki Declaration principles and was approved by our Corporate Ethics Committee Giresun Training and Research Hospital (2023/KAEK-93).*

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