

**DUODENAL DIVERTICULA MIGHT BE ASSOCIATED
WITH HIGHER SERUM INFLAMMATORY BIOMARKERS
AND *HELICOBACTER PYLORI* INFECTION: A
RETROSPECTIVE CROSS-SECTIONAL STUDY**

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Received on October 9, 2025

Presented by B. Petrunov, Member of BAS, on November 25, 2025

Abstract

Although it is not an extremely rare condition, less is known about the clinical features of duodenal diverticula (DD). This study aims to analyze laboratory and gastric histopathological features of DD, providing insights into this underexplored condition. A total of 152 patients undergoing upper gastrointestinal endoscopy for dyspepsia complaints were included in the study retrospectively, comprising 76 patients diagnosed with DD during the procedure and 76 control patients without DD. A comprehensive evaluation was conducted on the groups' clinical, laboratory, and gastrohistopathological characteristics. Statistical analyses were performed to ascertain whether significant differences existed between the groups. There were no significant differences in gender distribution or mean age between the groups. Patients with DD exhibited higher neutrophil, alkaline phosphatase, and C-reactive protein levels and lower platelet, lymphocyte, monocyte, calcium, and direct bilirubin levels. Although the diverticula group revealed a higher frequency of *Helicobacter pylori* (HP) infection (43.4% vs. 32.9%), none of the groups' gastric histopathological findings showed significant differences. The results of this study demonstrate notable laboratory and clinical variations in individuals with DD, with elevated inflammatory markers and HP infection rates, indicating potential implications

for disease pathophysiology. These findings provide a basis for future research and developing clinical management strategies related to DD.

Key words: duodenal diverticula, case series, endoscopy, inflammatory biomarkers, *Helicobacter pylori*, gastric histopathology

Abbreviations: CT: Computed scan; DD: Duodenal diverticula; HP: *Helicobacter pylori*; SPSS: Statistical Package for the Social Sciences; Med: Median; S.D.: Standard deviation; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; ALP: Alkaline phosphatase; CRP: C-reactive protein; MCV: Mean corpuscular volume.

Introduction. Although relatively uncommon, duodenal diverticula (DD) represent a significant clinical entity within the field of gastrointestinal pathology. These diverticula are outpouchings of the duodenal wall, most commonly localized in the second portion of the duodenum in the region of the ampulla of Vater [1]. The histological structure of DD comprises mucosa, submucosa, and, in some cases, muscular layers. However, they are typically classified as false diverticula due to the absence of a complete muscular layer. This classification is fundamental to understanding the condition's potential complications and clinical course [2,3].

From a physiological standpoint, the formation of DD is suggested to result from congenital or acquired weaknesses in the intestinal wall. An increased intraluminal pressure, particularly in older individuals, can further predispose patients to the development of DD, which often remains asymptomatic [4]. However, when clinical symptoms do appear, they are mainly nonspecific and may include abdominal discomfort, bloating, nausea, and, in more severe cases, complications such as diverticulitis, bleeding, or perforation [5,6].

From a pathological perspective, DD are frequently categorized according to their size and number, with the majority being solitary and relatively small [7]. The diverticula may vary in diameter from a few millimeters to several centimeters. The location of the diverticula in the duodenum also has implications for complications, particularly in relation to neighbouring structures such as the bile duct and pancreas [8].

From a clinical perspective, the majority of patients with DD present with no symptoms, which makes their detection a challenging endeavor. The criteria for suspicion frequently emerge incidentally during imaging studies, such as upper gastrointestinal endoscopy or computed tomography (CT) scans, which are performed for unrelated conditions. The diagnostic process largely relies on these imaging techniques, as endoscopy can directly visualize outpouchings, while CT scans provide more detailed information on the anatomical relationships and potential complications [7].

Given the rarity of symptomatic cases, it is essential to employ evidence-based diagnostic criteria [9]. The current literature emphasizes the necessity for a comprehensive review of the patient history, clinical symptoms, and imaging findings when there is a suspicion of DD [10]. Furthermore, developments in endoscopic

and radiological techniques have facilitated more precise detection and classification of these diverticula. Early recognition is of primary importance for preventing complications and the guidance of appropriate clinical management, particularly in cases where surgical or endoscopic intervention may be indicated [2].

This study presents a comprehensive analysis of DD's clinical, laboratory, and gastric histopathological features based on a case series and a comparative approach. Our objective is to contribute to understanding this condition by providing novel insights from a large patient cohort coupled with evidence-based review findings that reflect the current state of the literature.

Methods. The local ethics committee of Giresun Training and Research Hospital approved the study protocol with the decision numbered 13.06.2024/10. The study was retrospective; therefore, informed consent was waived. This study was conducted in accordance with the relevant ethical principles of the Declaration of Helsinki, revised in 2013.

The reports of patients who applied to internal medicine, general surgery, and gastroenterology outpatient clinics with dyspeptic complaints between 1 January 2020 and 30 June 2024 and underwent upper gastrointestinal tract endoscopy were analyzed. These patients were divided into two groups: those with duodenal diverticulum (Group DD) and those without DD (control group). The control group was assigned randomly except for the similar age and gender distribution with the patient group. Patients with acute infection and a history of rheumatological diseases, autoimmune diseases, and oncological diseases were excluded since acute phase reactants could be found false positive due to these underlying diseases. The demographic data, including age and sex, laboratory parameters, and gastric histopathological results, such as HP status, presence of atrophy, and intestinal metaplasia, were recorded. The results were compared between the two groups.

The gastric biopsy specimens were evaluated with the histopathological examinations conducted by the same experienced pathologist blinded to the clinical data. Therefore, the interobserver variability risk was excluded. The presence of HP was assessed pathologically by using hematoxylin and eosin staining. Endoscopy was performed by the same gastroenterologist, with the mucosal changes evaluated using high-resolution electronic endoscopy equipment (Fujifilm® EPX3500 HD series).

Statistical analysis. Statistical analysis of the data was performed using the SPSS version 22.0 (SPSS for Windows, Statistical Package for the Social Sciences, IBM Corp., Armonk, NY). The normality of the variables was evaluated using the Shapiro–Wilk test. Continuous variables are expressed as mean $\pm$ standard, while categorical variables were given as frequency and percentage (n , %). The comparisons between the two groups were made using the Mann–Whitney U test, Chi-square test, and Fisher's exact test. The $p < 0.05$ values were considered statistically significant.

Results. There was no significant difference in the gender and age distribution of the groups ($p > 0.05$). The mean age of the Group DD was 65.8 years, while that of the control group was 62.1 years. These data clearly show that the gender and age distribution of the groups are homogeneous. Table 1 shows the comparison of gender and age variables of the groups.

T a b l e 1
Comparison of demographic data of the groups

Variables		Duodenal diverticulum group (<i>n</i> :76)		Control group (<i>n</i> :76)		<i>p</i>
		Number	%	Number	%	
Gender	Female	33	43.4	33	43.4	1.000
	Male	43	56.6	43	56.6	
Age	65 years and younger	40	52.6	38	50.0	0.871
	Over 65 years old	36	47.4	38	50.0	
Age ^t		Med.±S.D (Min.-Max.) 65.8±14.20 (33-98)		Med.±S.D (Min.-Max.) 62.1±16.87 (22-89)		0.142

* $p < 0.05$, ** $p < 0.01$, χ^2 : Chi-square test (Categorical data), t: Independent Sample T Test.
Med: Median, Min: Minimum, Max: Maximum, S.D.: Standard deviation

Regarding the laboratory tests, there was no significant difference in aspartate aminotransferase (AST), alanine aminotransferase (ALT), sodium, potassium, glucose, urea, creatinine, leukocyte, hemoglobin, total bilirubin, alkaline phosphatase (ALP), and gamma-glutamyl transferase (GGT) values between the groups ($p > 0.05$). The group DD had lower platelet, lymphocyte, monocyte, calcium, and direct bilirubin levels while higher neutrophil and CRP levels. Table 2 presents a comparison of the laboratory parameters of the groups.

There was no difference in the distribution of atrophy, HP, and intestinal metaplasia between the groups ($p > 0.05$). However, these data show that *H. pylori* rates are higher in patients with duodenal diverticulum. Table 3 presents the comparison of gastric biopsy results of the groups.

According to the results of the analysis, the presence of duodenal diverticulum had a significantly increasing effect on neutrophil count ($B = 0.87$, $p = 0.003$), ALP ($B = 24.33$, $p = 0.000$) and CRP ($B = 7.60$, $p = 0.027$) levels. The effect on ALP levels was particularly strong ($\beta = 0.37$, $R^2 = 0.140$), indicating that duodenal diverticulum may cause a significant increase in alkaline phosphatase levels. In contrast, the presence of duodenal diverticulum caused a significant decrease in monocyte ($B = -0.24$, $p = 0.000$), lymphocyte ($B = -0.40$, $p = 0.002$), platelet ($B = -27.28$, $p = 0.012$), calcium ($B = -0.25$, $p = 0.013$) and direct bilirubin ($B = -0.06$, $p = 0.008$) levels. The effect on monocyte levels showed the strongest

T a b l e 2

Comparison of laboratory parameters between the groups

Parameters	Duodenal diverticulum group (<i>n</i> :76)	Control group (<i>n</i> :76)	<i>p</i>
	Mean.±S.D	Mean.±S.D	
Leukocyte ^t (10 ³ /μL)	7.66 ± 2.52	7.10 ± 1.91	0.121
Hemoglobin ^t (g/dL)	12.30 ± 2.08	12.74 ± 2.11	0.203
MCV ^z (fL)	86.86 ± 6.69	85.24 ± 8.78	0.876
Platelet ^z (10 ³ /μL)	237.32 ± 53.44	264.59 ± 77.87	0.010**
Lymphocyte ^z (10 ³ /μL)	1.88 ± 0.90	2.28 ± 0.66	0.000**
Neutrophil ^t (10 ³ /μL)	4.92 ± 2.20	4.05 ± 1.39	0.004**
Monocyte ^t (10 ³ /μL)	0.18 ± 0.13	0.42 ± 0.18	0.000**
Glucose ^z (mg/dL)	112.52 ± 25.94	104.76 ± 28.15	0.066
Urea ^z (mg/dL)	37.49 ± 20.87	31.21 ± 10.92	0.129
Creatinine ^z (mg/dL)	0.96 ± 0.63	0.79 ± 0.25	0.095
ALT ^z (U/L)	18.77 ± 12.72	16.51 ± 9.18	0.440
AST ^z (U/L)	21.73 ± 10.94	19.08 ± 5.82	0.522
Sodium ^z (mmol/L)	140.00 ± 3.94	140.65 ± 2.32	0.086
Potassium ^t (mmol/L)	4.36 ± 0.53	4.42 ± 0.44	0.431
Calcium (mg/dL)	9.24 ± 0.78	9.49 ± 0.42	0.014*
Total bilirubin ^z (mg/dL)	0.55 ± 0.40	0.58 ± 0.32	0.118
Direct bilirubin ^z (mg/dL)	0.20 ± 0.12	0.26 ± 0.15	0.017*
ALP ^z (mg/dL)	90.00 ± 35.87	65.67 ± 25.91	0.000**
GGT ^z (U/L)	26.96 ± 27.08	24.13 ± 18.90	0.238
CRP ^z (mg/L)	12.35 ± 27.10	4.76 ± 11.96	0.000**

* $p < 0.05$, ** $p < 0.01$, χ^2 : Chi-square test (Categorical data), t: Independent Sample T-Test, z: Mann Whitney U Test, Med: Median, S.D.: Standard deviation ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, ALP: Alkaline phosphatase, GGT: Gamma glutamyl transferase, CRP: C-reactive protein, MCV: Mean corpuscular volume

negative association ($\beta = -0.60$, $R^2 = 0.365$), suggesting that monocyte levels may be significantly lower in patients with duodenal diverticulum (Table 4).

Discussion. This study represents the first comprehensive analysis of the clinical, laboratory, and gastric histopathologic features of patients with duodenal diverticula, with a comparison group serving as the control. The findings of this study offer significant insights into the physiological and biochemical alterations associated with duodenal diverticula. By examining 76 patients with duodenal diverticula and 76 control patients without diverticula, our findings reveal distinct differences in several laboratory markers and clinical characteristics, some of which have potential implications for understanding the pathophysiology of this condition.

T a b l e 3

Comparison of the gastric histopathological findings between the groups

Variables		Duodenal diverticulum group (n:76)		Control group (n:76)		<i>p</i>
		Number	%	Number	%	
HP	Negative	43	56.6	51	67.1	0.242
	Positive	33	43.4	25	32.9	
Intestinal metaplasia	Negative	63	82.9	59	77.6	0.541
	Positive	13	17.1	17	22.4	
Gastric atrophy	Negative	69	90.8	69	90.8	1.000
	Positive	7	9.2	7	9.2	

* $p < 0.05$, ** $p < 0.01$, χ^2 : Chi-square test (Categorical data), HP: *Helicobacter pylori*

T a b l e 4

Pathway analysis results investigating the effect of the presence of duodenal diverticulum on various blood findings in patients

Dependent variable	Path	Independent variable	<i>B</i>	S.E.	β (Beta)	<i>p</i>	R^2
Neutrophil	←	Presence of duodenal diverticulum	0.87	0.30	0.23	0.003**	0.054
Monocyte	←	Presence of duodenal diverticulum	-0.24	0.03	-0.60	0.000**	0.365
Lymphocyte	←	Presence of duodenal diverticulum	-0.40	0.13	-0.25	0.002**	0.061
Platelets	←	Presence of duodenal diverticulum	-27.28	10.8	-0.20	0.012**	0.041
Calcium	←	Presence of duodenal diverticulum	-0.25	0.10	-0.20	0.013**	0.040
Direct bilirubin	←	Presence of duodenal diverticulum	-0.06	0.02	-0.22	0.008**	0.046
Alkaline phosphatase	←	Presence of duodenal diverticulum	24.33	5.31	0.37	0.000**	0.140
C-reactive protein	←	Presence of duodenal diverticulum	7.60	3.44	0.18	0.027*	0.034

B: Unstandardized path coefficient, β (Beta): Standardized path coefficient, S.E.: Standard error * $p < 0.05$, ** $p < 0.01$, R^2 : Ratio of variance explained in dependent factors

The most remarkable finding of this study is the elevated level of CRP and neutrophils in patients with duodenal diverticula. These biomarkers are widely acknowledged as indicators of systemic inflammation and have previously been associated with gastrointestinal pathologies, including diverticular colon disease. Elevated CRP levels have been linked to an increased inflammatory response, which may explain the elevated risk of complications such as diverticulitis in some

patients. Furthermore, the neutrophil count, another marker of acute inflammation, provides additional evidence that duodenal diverticula may trigger both localized and systemic inflammatory responses [11]. Nevertheless, the precise relationship between duodenal diverticula and inflammation remains under-explored and requires further investigation.

In contrast, patients without duodenal diverticula exhibited higher platelets, lymphocytes, monocytes, calcium, and direct bilirubin levels. These findings are intriguing, particularly given that elevated platelet and lymphocyte counts are often associated with chronic inflammatory states or conditions such as infection and malignancy. The elevated calcium and direct bilirubin levels observed in the control group may indicate underlying metabolic or hepatic conditions. However, no direct association between these levels and duodenal diverticula has yet been established in the literature. The lack of notable variations in most liver function tests (e.g., ALT, AST) between the groups indicates that the observed biochemical alterations may be more indicative of systemic rather than localized processes [12]. Further investigation is required to better understand the broader metabolic implications for patients with duodenal diverticula.

Another important aspect of this study was the analysis of the results of endoscopic biopsies. Although no significant differences were observed between the groups regarding atrophy, HP infection, or intestinal metaplasia, the prevalence of HP in the DD group was notable. HP has been associated with various gastrointestinal disorders, including peptic ulcer disease and gastritis, and may play a direct role in mucosal inflammation of the duodenum. Although no statistically significant association between HP and duodenal diverticulum was found in our study, most studies have emphasised that HP should be considered a potential co-factor in upper gastrointestinal disorders [13]. Further research is required to elucidate the role of this bacterium in the development and clinical course of DD.

A comparison of patients with DD reveals that age is a significant factor. Our findings indicate that a substantial proportion of patients with duodenal diverticula are over the age of 65, which is consistent with previous reports suggesting that diverticular disease is predominantly a condition of older adults [14]. The age-related weakening of the intestinal wall, coupled with changes in motility and increased intraluminal pressure, may predispose older individuals to the development of diverticula [14].

Regarding clinical management, our findings highlight the necessity for a case-by-case approach. The elevated inflammatory markers observed in patients with duodenal diverticula suggest that some individuals may be at an increased risk of developing complications, such as diverticulitis or perforation, particularly those with pre-existing comorbidities. This knowledge raises the question of whether anti-inflammatory or antibiotic therapy should be considered a preventive measure in selected patients, particularly those with recurrent symptoms. As reviewed by CAPASSO et al. [15], the current literature suggests that early intervention may

reduce the risk of severe complications. Further randomized controlled trials are required to confirm this in the context of duodenal diverticula.

It is essential to acknowledge the limitations of this study. Firstly, despite the relatively large sample size for a rare condition like duodenal diverticula, the study population may not fully capture the variability of this condition across different demographics or clinical settings. The lack of number, size, and anatomical localization data of DDs complicates our understanding of how the variability of these lesions affects the clinical course of the patients. Furthermore, the retrospective design introduces selection bias since the patients were identified through endoscopic findings rather than broader clinical screening. Due to the retrospective nature of our study, clinical conditions such as hypertension, obesity, smoking, and medication use, which are associated with systemic inflammatory response, could not be assessed and existed as confounding factors. The lack of long-term follow-up limits our ability to determine the progression of symptoms or complications over time. While laboratory biomarkers and endoscopic biopsy results were analyzed, more advanced imaging or histopathological techniques could have provided more profound insights into duodenal diverticula's structural and functional aspects.

Conclusion. This study offers valuable insights into the clinical and biochemical characteristics of duodenal diverticula, underscoring notable distinctions in inflammatory biomarkers and HP infection frequency between patients with and without the condition. The elevated CRP and neutrophil levels observed in the diverticula group suggest a potential role for inflammation in the condition's pathophysiology. Moreover, the higher platelet and lymphocyte levels observed in the control group point to underlying systemic differences. These findings improve our understanding of duodenal diverticula and provide a foundation for future research to improve diagnostic and therapeutic approaches.

Authors' contributions. Conceptualization, E.K.; Investigation, A.M., K.I., S.A.; Data curation, E.K, E.C., S.A., G.A., and A.C.D.; Formal analysis, E.C., A.M.; Methodology, E.C., A.C.D.; Project administration, E.K., E.C. and A.C.D.; Validation, G.A, A.C.D.; Visualization, A.M., A.C.D.; Writing – original draft, E.K., Writing – review editing, K.I., A.C.D.

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