ORIGINAL ARTICLE

Eastern Journal of Medicine

East J Med 30(2): 261-267, 2025
DOI: 10.5505/ejm.2025.80707

# Gastrointestinal and Biochemical Characteristics in Dyspeptic Patients with Anaphylaxis: A Comparative Study

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**ABSTRACT**

The objective of this study was to evaluate the gastrointestinal and biochemical characteristics of dyspeptic patients with documented drug allergies in comparison to a control group of dyspeptic patients without drug allergies. By examining the demographic data, blood haemogram, biochemical parameters, and gastric antrum biopsy results, we sought to gain further insight into the impact of drug-induced anaphylaxis on these patients.

A total of 122 patients presenting with dyspeptic symptoms and documented drug allergies, who were referred to gastroenterology outpatient clinics from internal medicine and general surgery outpatient clinics, were included in the analysis. A control group of 100 dyspeptic patients without drug allergies was also included for comparison. The demographic data, blood haemogram, biochemical parameters, and gastric antrum biopsy results (*Helicobacter pylori*, intestinal metaplasia, atrophy) were collected and subjected to analysis. Statistical comparisons were conducted between the anaphylaxis group and the control group, as well as within the anaphylaxis group itself.

The study included 122 patients with drug allergies (73.8% female, mean age 53.12±15.73 years) and 100 controls. No significant differences were identified in the prevalence of *Helicobacter pylori*, metaplasia, or atrophy across different allergy types. However, patients with a cephalosporin allergy exhibited significantly elevated calcium levels in comparison to individuals with other allergy types ($p<0.05$). In comparison to the control group, the anaphylaxis group was characterised by a higher proportion of females, a lower mean age, and higher leukocyte and lymphocyte values.

It can be concluded that dyspeptic patients with drug-induced anaphylaxis exhibit distinct gastrointestinal and biochemical characteristics in comparison to those without drug allergies. These findings emphasise the necessity for tailored clinical management and further research into the underlying mechanisms driving these differences.

**Keywords:** Dyspepsia, anaphylaxis, drug allergies, Helicobacter pylori, gastric antrum biopsy

## Introduction

Dyspepsia, a prevalent gastrointestinal disorder, affects a significant portion of the global population, often resulting in considerable healthcare utilisation and a reduction in quality of life. Dyspepsia is characterised by upper abdominal discomfort, bloating, nausea and early satiety. It can have a variety of aetiologies, including functional disturbances, peptic ulcer disease and *Helicobacter pylori* (*H. pylori*) infection. The intricate interplay between gastrointestinal physiology and external factors, such as medications and allergens, introduces an additional layer of complexity to the diagnosis and management of dyspeptic symptoms (1).

One area of literature that has been relatively underexplored is the impact of drug-induced anaphylaxis on gastrointestinal health, particularly in patients with pre-existing dyspeptic symptoms. Anaphylaxis is a severe systemic hypersensitivity reaction that is most commonly triggered by medications, foods, and insect stings (2,3). Among the medications that have been identified as potential triggers are non-steroidal anti-inflammatory drugs (NSAIDs), antibiotics (such as penicillins and cephalosporins), and analgesics like Novalgin® (4,5). The gastrointestinal manifestations of anaphylaxis, including nausea,

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**Received:** 14.12.2024, **Accepted:** 02.02.2025

vomiting, diarrhoea and abdominal pain, are well documented. Nevertheless, the long-term consequences of recurrent drug allergies on the structure and function of the gastrointestinal system, particularly in the context of dyspepsia, remain inadequately elucidated.

Previous studies have indicated that drug allergies may contribute to or exacerbate gastrointestinal conditions by altering mucosal integrity, modifying inflammatory responses, or influencing the gastric microbiome. For example, NSAIDs are known to cause damage to the gastric mucosa, leading to the formation of ulcers and bleeding. This process may be further complicated by an allergic response. Similarly, antibiotics such as penicillins and cephalosporins have the potential to disrupt the gut microbiota, which could result in dysbiosis and the onset of gastrointestinal symptoms (6). However, the precise impact of these drug-induced reactions on dyspeptic patients, particularly in regard to histopathological alterations such as intestinal metaplasia and atrophy and their correlation with *H. pylori* infection, remains largely unstudied (7).

Furthermore, biochemical abnormalities are frequently observed in patients with drug-induced anaphylaxis, in addition to the aforementioned gastrointestinal symptoms. An increase in white blood cell count is a common occurrence in allergic reactions, with eosinophils and basophils being particularly elevated (8,9). Nevertheless, the broader implications of these hematological changes, including their potential impact on gastrointestinal health, remain largely speculative. It is imperative that these relationships are understood to develop more effective management strategies for patients who experience both dyspeptic symptoms and drug allergies.

This study aims to address this gap in the literature by conducting a comprehensive examination of the gastrointestinal and biochemical characteristics of dyspeptic patients with documented drug allergies, with a comparison to a control group without such allergies. By analysing a range of parameters, including demographic data, blood haemogram, biochemical profiles, and gastric antrum biopsy results (including *H. pylori* status, intestinal metaplasia, and atrophy), we aim to provide new insights into how drug-induced anaphylaxis influences the clinical presentation and outcomes of dyspepsia.

## Material and Methods

A total of 122 patients with a history of drug allergy who presented to the internal medicine, general surgery and gastroenterology outpatient clinics of Giresun Training and Research Hospital with dyspeptic symptoms and underwent endoscopy were included in the study between 1 January 2022 and 1 May 2023. The study protocol was reviewed and approved by the local ethics committee of Giresun Training and Research Hospital in accordance with the ethical principles set forth in the Declaration of Helsinki, revised in 2013. Patient confidentiality was rigorously maintained, with all data anonymised before analysis.

The study population consisted of adult patients aged between 18 and 87 years old who presented with dyspeptic symptoms and were subsequently referred to gastroenterology outpatient clinics. Patients were required to have a documented history of drug allergies, specifically to NSAIDs, penicillins, cephalosporins, Novalgin®, and paracetamol. Patients were excluded from the study if they had undergone major gastrointestinal surgery, were diagnosed with an active malignancy, had chronic liver or kidney disease, or had autoimmune disorder. Furthermore, long-term corticosteroids or immunosuppressive therapy patients were excluded to avoid confounding effects on the study outcomes.

The study population was randomly selected and met the pre-established criteria. A tissue biopsy was employed as the diagnostic method of choice for *H. pylori*, the most reliable diagnostic technique. The patients were divided into five groups according to the drugs to which they had developed an allergy: NSAIDs, penicillins, cephalosporins, Novalgin® and paracetamol. A comparison was made between the groups in terms of age, gender, eosinophil, basophil and calcium levels, as well as the histopathological results of antrum mucosal biopsies. A further comparison was conducted between 122 patients with drug allergies and 100 patients who underwent endoscopy with similar presenting symptoms. In this comparison, the laboratory parameters analysed included leukocytes (WBC), lymphocytes, eosinophils, basophils, haemoglobin (Hgb), haematocrit (Htc), mean corpuscular volume (MCV), platelets, urea, creatinine, sodium, potassium, calcium, albumin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), C-reactive protein (CRP).

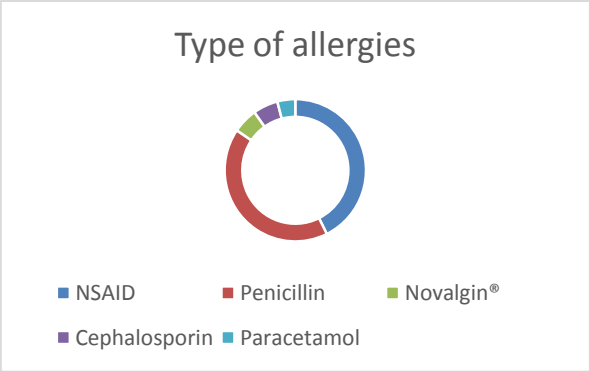


**Fig. 1.** Distribution Scheme According To Allergy Types

The gastric biopsy specimens were evaluated for intestinal metaplasia, atrophy, and H. pylori, with the histopathological examinations conducted by experienced pathologists blinded to the clinical data. The presence of *H. pylori* was evaluated pathologically through the use of hematoxylin and eosin staining.

Endoscopy was performed by gastroenterologists, with the mucosal changes evaluated using high-resolution electronic endoscopy equipment (Fujifilm® EPX3500 HD series).

**Statistical Analysis:** In the statistical analysis section of the study, descriptive statistics for categorical variables (demographic characteristics) are presented as frequencies and percentages, and for numerical variables as mean and standard deviation. The suitability of the numerical variables for normal distribution was checked with the "Shapiro-Wilk Test". For normally distributed data, numerical descriptive statistics of the variables are given with mean and standard deviation values. "Independent Sample t-Test" was used for the data between two independent groups that were compatible with normal distribution. When examining the relationships between categorical variables (2x2), "Fisher's Test" was applied when at least one of the expected values of the cells was less than 5, "Yates Chi-Square" when it was between 5-25, and "Pearson Chi-Square Independence Test" when it was greater than 25. The margin of error in the evaluation of statistical hypothesis tests was taken as 5%. The findings were evaluated using IBM SPSS 26 program.

## Results

A comparative analysis was conducted to examine the characteristics of the anaphylaxis and control groups. The mean age of the patients in the anaphylaxis group was found to be significantly lower than that of the control group. Additionally, the female sex ratio was observed to be significantly higher in the anaphylaxis group compared to the control group (Table 1).

The WBC, lymphocyte, and eosinophil values of patients in the anaphylaxis group were significantly higher than those of the control group (Table 2).

No notable discrepancy was observed in the blood biochemical parameters of patients in the anaphylaxis and control groups (Table 3).

The analysis revealed no statistically significant correlation between the prevalence of H. pylori and atrophy in the anaphylaxis and control groups.

The prevalence of metaplasia was significantly higher in the control group (Table 4).

In study, drug allergy types are given in (figure 1).

A statistically significant difference was observed in calcium levels between the various allergy types. The posthoc Dunn's test, performed to ascertain the statistical significance, revealed that calcium levels in patients with a cephalosporin allergy were significantly higher than those in patients with an NSAID allergy (p=0,017), a penicillin allergy (p=0,001), an allergy to novalgin® (p=0,009) and an allergy to paracetamol (p=0,048). No statistically significant difference was observed in calcium levels between other allergy types (p> 0.05) (Table 5).

No statistically significant difference was observed in the rates of H. pylori, metaplasia and atrophy between the various allergy types (Table 6).

## Discussion

The present study offers a comprehensive examination of the gastrointestinal and biochemical characteristics of dyspeptic patients with drug-induced anaphylaxis in comparison to a control group of dyspeptic patients without drug allergies. Our findings contribute to the growing body of literature that seeks to elucidate the intricate relationship between drug allergies, gastrointestinal pathology, and biochemical alterations in dyspeptic patients.

One of the principal findings of this study is the significant discrepancy in the mean age and gender distribution between the anaphylaxis and control groups. The patients in the anaphylaxis group were younger and predominantly female, a pattern

**Table 1:** Comparison of Demographics Between Anaphylaxis and Control Groups

| Variables | | Anaphylaxis (n: 122) | | Control (n:100) | | |
|---|---|---|---|---|---|---|
| | | Number | % | Number | % | p |
| GenderK | Female | 90 | 73.7 | 55 | 55.0 | 0.005K** |
| | Male | 32 | 26.3 | 45 | 45.0 | |
| | | Med.±SD | | Med.±SD | | |
| Aget | | 53.050 ± 15.788 | | 62.290 ± 15.828 | | <0.001t ** |

*p<0.05; **p<0.01; K: Pearson Chi-square test; t: Independent Sample T-Test; Med: Median, SD: Standart deviation

**Table 2:** Comparison of Anaphylaxis and Control Group Blood Haemogram Parameters

| Parameters | Anaphylaxis (n: 122) | Control (n:100) | p |
|---|---|---|---|
| | Med.±S.D | Med.±S.D | |
| WBCt | 7.66 ± 2.15 | 6.95 ± 1.89 | 0.011* |
| Lymphocytet | 2.30 ± 0.79 | 1.97 ± 0.60 | 0.001* |
| Eosinophilt | 0.22 ± 0.23 | 0.17 ± 0.1 | 0.033* |
| Basophilt | 0.031 ± 0.017 | 0.032 ± 0.016 | 0.619 |
| Hgbt | 12.75 ± 1.87 | 12.61 ± 2.05 | 0.597 |
| MCVt | 85.50 ± 6.59 | 85.21 ± 8.0 | 0.775 |
| Plateletst | 265.808 ± 79.03 | 262.700 ± 76.78 | 0.769 |

*p<0,05; t: Independent Sample T-Test; Med:Median; S.D:Standard deviation WBC:White Blood Count Hgb:Hemoglobin: MCV:Mean Corpuscular Volume

**Table 3:** Comparison of Anaphylaxis and Control Group Blood Biochemical Parameters

| Parameters | Anaphylaxis (n: 122) | Control (n:100) | p |
|---|---|---|---|
| | Med.±S.D | Med.±S.D | |
| Ureat | 29.38 ± 13.93 | 28.43 ± 10.04 | 0.677 |
| Creatininet | 0.79 ± 0.20 | 0.73 ± 0.19 | 0.170 |
| Sodiumt | 140.19 ± 2.73 | 140.17 ± 2.45 | 0.960 |
| Potassiumt | 4.36 ± 0.43 | 4.43 ± 0.44 | 0.439 |
| Calciumt | 9.63 ± 0.59 | 9.61 ± 0.42 | 0.805 |
| Albumint | 44.50 ± 6.28 | 52.77 ± 55.11 | 0.225 |
| ALT t | 16.70 ± 7.36 | 17.04 ± 9.41 | 0.826 |
| ASTt | 20.18 ± 6.75 | 18.73 ± 7.04 | 0.252 |
| CRP t | 7.27 ± 19.88 | 4.36 ± 6.26 | 0.309 |

*p<0,05; t: Independent Sample T-Test; Med:Median; S.D:Standard deviation ALT:Alanin Aminotransferaz AST:Aspartat Aminotransferaz CRP:C-reaktif protein

that aligns with previous research indicating that women are more likely to develop both dyspeptic symptoms and drug allergies (10,11). This gender disparitymay be related to hormonal influences on immune response and gastrointestinal function, as well as differences in healthcare-seeking behaviour between men and women.

The elevated white blood cell (WBC) and lymphocyte counts observed in the anaphylaxis group are consistent with the known immunological responses associated with allergic reactions. The presence of elevated eosinophil levels, although not statistically significant, provides further evidence of the involvement of an allergic inflammatory process in these patients. Similar findings have been reported in studies examining eosinophilic oesophagitis and other allergic gastrointestinal disorders, where elevated eosinophil counts are a hallmark feature (12,13). This study contributes to the existing literature by

**Table 4:** Comparison of Pathology Findings of Patients Between Groups

| Pathology findings | | Anaphylaxis (n: 122) | | Control (n:100) | | |
|---|---|---|---|---|---|---|
| | | Number | % | Number | % | p |
| H.pylori | Negative | 69 | 56.5 | 61 | 61.0 | 0.439 |
| | Positive | 53 | 43.5 | 39 | 39.0 | |
| Atrophy | Negative | 112 | 91.8 | 89 | 89.0 | 0.660 |
| | Positive | 10 | 8.2 | 11 | 11.0 | |
| Metaplasia | Negative | 108 | 88.5 | 76 | 76.0 | 0.016 K* |
| | Positive | 14 | 11.5 | 24 | 24.0 | |

*p<0,05, **p<0,01, K: Pearson Chi-square test H.pylori:Helicobacter pylori

**Table 5:** The Evaluation of Laboratory Results According To The Classification of Allergies

| | NSAID | Penicillin | Novalgin® | Cephalosporin | Paracetamol | |
|---|---|---|---|---|---|---|
| | Med. ± S.D | Med. ± S.D | Med. ± S.D | Med. ± S.D | Med. ± S.D | p |
| Eosinophil | 249.81±280 | 216.67±221.09 | 177.14±95.87 | 155.71±93.96 | 214±142.58 | 0.982 |
| Basophil | 30.19±15.9 | 31.18±13.66 | 32.14±14.1 | 55.71±38.23 | 30±18.71 | 0.126 |
| Calcium | 9.69±0.49 | 9.51±0.56 | 9.47±0.32 | 10.12±0.31 | 9.56±0.47 | 0.015* |

Kruskal Wallis Test *p<0.05 Med:Median; S.D:Standard deviation NSAİD: Non-steroidal anti-inflammatory drugs

**Table 6:** Evaluation of the Biopsy Results According To The Type of Allergy

| | | NSAID | Penicillin | Novalgin® | Cephalosporin | Paracetamol | |
|---|---|---|---|---|---|---|---|
| | | n (%) | n (%) | n (%) | n (%) | n (%) | p |
| H.pylori | Negative | 25 (%48.1) | 32 (%62.7) | 4 (%57.1) | 5 (%71.4) | 3 (%60) | 0.585 |
| | Positive | 27 (%51.9) | 19 (%37.3) | 3 (%42.9) | 2 (%28.6) | 2 (%40) | |
| Atrophy | Negative | 49 (%94.2) | 45 (%88.2) | 7 (%100) | 7 (%100) | 4 (%80) | 0.472 |
| | Positive | 3 (%5.8) | 6 (%11.8) | 0 (%0) | 0 (%0) | 1 (%20) | |
| Metaplasia | Negative | 43 (%82.7) | 47 (%92.2) | 7 (%100) | 7 (%100) | 4 (%80) | 0.362 |
| | Positive | 9 (%17.3) | 4 (%7.8) | 0 (%0) | 0 (%0) | 1 (%20) | |

demonstrating that these immunological markers are also elevated in the context of drug-induced anaphylaxis among dyspeptic patientIt is noteworthy that our analysis did not identify any significant differences in the prevalence of H.pylori infection or gastric atrophy between the anaphylaxis and control groups. This is in contrast with the findings of some previous studies that have suggested a potential link between H. pylori infection and allergic conditions (14). The absence of an association in the present study may be attributed to the specific population under investigation or the potential influence of other confounding factors, such as dietary habits, smoking, or regional variations in the prevalence of H. pylori. However, the significantly higher prevalence of intestinal metaplasia in the control group gives rise to significant questions regarding the protective or predisposing factors that differentiate these two patient populations. It is possible that patients with drug allergies, particularly those with anaphylaxis, may experience a different disease course or have a distinct pathophysiological mechanism that mitigates the progression to metaplasia (15,16).

Another significant finding is the considerable variation in calcium levels observed among patients with different drug allergies, particularly the elevated calcium levels noted in patients with cephalosporin allergies. This observation is intriguing and has not been extensively documented in the existing literature. Elevated calcium levels may be indicative of a range of physiological or pathological processes, including altered parathyroid function, modifications in calcium metabolism associated with the allergic response, or even a direct impact of cephalosporins on calcium homeostasis (17). Further research is required to elucidate this relationship and determine whether this finding

has clinical significance in managing patients with drug allergies.

In conclusion, our study highlights the necessity of considering drug-induced anaphylaxis as a factor in the clinical management of dyspeptic patients. The differences in age, gender distribution, and certain immunological markers between the anaphylaxis and control groups suggest that these patients may represent a distinct clinical subgroup that requires tailored diagnostic and therapeutic approaches. Furthermore, the observed biochemical differences, particularly in calcium levels, warrant further investigation to clarify their underlying mechanisms and potential clinical implications.

**Study Limitations:** Although this study offers valuable insights into the gastrointestinal and biochemical characteristics of dyspeptic patients with drug-induced anaphylaxis, it is not without limitations. The sample size, particularly about specific allergy subtypes, may limit the generalisability of the findings to broader populations. Furthermore, the cross-sectional design of the study precludes the establishment of causal relationships between drug allergies and the observed gastrointestinal and biochemical changes. Further research involving larger, more diverse cohorts and longitudinal follow-up is required to validate the findings presented here and to explore the potential mechanisms underlying the observed associations.

This study demonstrates that patients presenting with dyspepsia and drug-induced anaphylaxis exhibit distinct clinical and biochemical characteristics compared to those without drug allergies. These characteristics are particularly evident in terms of age, gender distribution, and immune markers. The observed variations, including elevated calcium levels in cephalosporin-allergic patients, emphasise the necessity for a nuanced approach to the management of these patients, given their distinctive profiles. These findings contribute to our understanding of the relationship between drug allergies and gastrointestinal health, while also emphasising the importance of personalised management strategies for this population. Further research is required to elucidate the underlying mechanisms and potential therapeutic implications of these differences.

**Acknowledgement:** N/A

**Conflict of Interest:** The authors declare no conflict of interest to disclose

**Funding:** This study did not receive financial support

**Data Availability:** Data used in this study can be provided on reasonable request

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