

## History of Nonsteroidal Anti-inflammatory Hypersensitivity and Gastromucosal Evaluation; Cross-Sectional Study

Arzu AYRALER<sup>1\*</sup>, Ahmet Cumhuri DÜLGER<sup>2</sup>, Aslı DIKMEN<sup>1</sup>

<sup>1</sup>Giresun University, Faculty of Medicine, Training and Research Hospital, Department of Family Medicine, Giresun

<sup>2</sup>Giresun University, Faculty of Medicine, Training and Research Hospital, Department of Internal Medicine, Giresun

\*Sorumlu yazar (Corresponding author): [ayraler7@hotmail.com](mailto:ayraler7@hotmail.com)

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### Abstract

There is limited research evaluating gastrohistopathologic findings in individuals with a history of Nonsteroidal Anti-inflammatory Drug (NSAID) Hypersensitivity. In this study, we aimed to evaluate the biochemical parameters and endoscopic findings of individuals with a history of NSAID hypersensitivity. Patients with a history of NSAID hypersensitivity and those without a history of NSAID hypersensitivity were retrospectively divided into two groups from the file records of individuals who applied to the gastroenterology outpatient clinic and underwent endoscopy. Data on endoscopy results, *Helicobacter pylori* (*H.pylori*), metaplasia, atrophy and biochemical results were evaluated. The mean age of the participants was  $57.20 \pm 16.27$  years. *H.pylori* positivity in the gastrohistopathology of individuals with NSAID allergy was 61.50% (n=16) and 24.40% in the control group (n=10). *H.pylori* negativity was 75.60% in the group without NSAID allergy (n=31) and 38.50% in the group with allergy (n=10). *H. pylori* positivity in the group with NSAID allergy was statistically significant compared to the control group (p=0.002). Considering the public health importance of NSAID allergy, this review provides an evaluation in terms of metaplasia, atrophy and *H.pylori*.

**Keywords:** NSAID Hypersensitivity History, Endoscopy, *H. pylori*

## 1. Introduction

Drug allergy is an unpredictable condition that covers the spectrum of immunologically mediated hypersensitivity reactions and has various mechanisms and clinical presentations (Warrington et al., 2018). Nonsteroidal anti-inflammatory drugs (NSAIDs) are widely used in all levels of medicine due to their analgesic, antipyretic and anti-inflammatory properties (Ali et al., 2022). The diagnosis of drug allergy requires a detailed history and the identification of physical findings and symptoms consistent with the characteristics and timing of drug-related allergic reactions (Warrington et al., 2018). Acetylsalicylic acid/aspirin and other NSAIDs are commonly used drugs that can cause hypersensitivity reactions in a significant proportion of patients (Terzioğlu et al., 2020). Side effect profiles differ in terms of gastro-intestinal, renal and hepatic complications (Farkouh et al., 2021). A study of patients with chronic diarrhea demonstrated the use of aspirin and non-steroidal anti-inflammatory drugs (Yen et al., 2022). The widespread use of NSAIDs increases the risk of drug side effects, including gastrointestinal (GI) damage. The risk of gastric mucosal defect (erosion or petechiae) has been reported to be approximately 50% in patients with long-term use of NSAIDs (Shim et al., 2019). A study showed an inverse linear relationship between the use of NSAIDs, including aspirin and non-aspirin NSAIDs, the duration of NSAIDs and the risk of gastric cancer (Huang et al., 2017). In this study, we aimed to contribute to the literature by evaluating the gastromucosal evaluation of individuals with a history of NSAID hypersensitivity.

## 2. Materials and Methods

The retrospective records of the individuals who applied to the Gastroenterology outpatient clinic in Giresun Training and Research Hospital were obtained from the hospital automation system. Those with NSAID allergy were randomized into two groups. Power analysis method was used to form the research sample. With the power analysis, the total number of samples was determined as 67, 26 in the experimental group and 41 in the control group, with 95% confidence ( $1-\alpha$ ), 80% test power ( $1-\beta$ ) and  $d=0.71$  effect size according to the two-tailed independent samples t test analysis (Martins et al., 2005), (Hofmann et al., 2010).

### Statistical method

All analyses were evaluated with a threshold of  $p < 0.05$  for statistical significance and were performed on IBM SPSS Statistics for Windows, Version 25.0 (IBM, NY, USA). The Kolmogorov-Smirnov test was used to check normality. Categorical variables were summarized as number and percentage, and continuous measures were summarized as mean and standard deviation. Independent sample t test was applied to determine the difference between groups in continuous measurements. The relationship between variables in categorical measurements was evaluated by chi-square test. Statistical significance level was taken as  $p < 0.05$  for all measurements.

## 3. Results

A total of 70 individuals, 55 females (78.5%) and 15 males (21.4%) were included in the study. The mean age was  $57.20 \pm 16.27$  years. Biochemical parameters of participants Table 1.

**Table 1.** Biochemical parameters

Parameter	Group		p
	Allergy	Control	
	Mean±S. Deviation	Mean±S. Deviation	
Wbc	7,73±1,81	44,30±130,32	0,080
Hgb	13,25±1,60	22,20±35,60	0,116
Mcv	87,13±5,19	144,87±214,01	0,092
Plt	259,12±75,80	267,02±80,24	0,689
Lymp	2,54±0,78	10,38±34,80	0,157
Urea	29,66±10,64	35,44±29,50	0,341
Creatine	0,73±0,15	3,35±15,81	0,402
Alt	18,08±10,84	15,22±9,63	0,263
Ast	19,83±8,87	18,27±6,00	0,391
Alb	46,25±3,01	51,78±81,10	0,794
Sodium	139,88±2,29	140,41±3,33	0,480
Potassium	4,48±0,43	6,94±9,28	0,097
Calcium	9,64±0,35	14,17±19,33	0,157
Crp	3,39±3,56	28,23±111,91	0,192

\*Independent Sample T-Test

The mean biochemical parameters were not statistically significant in allergy and control groups ( $p > 0.05$ ). Gastromucosal

evaluation findings of the participants Table 2.

**Table 2.** Gastromucosal findings of the participants

		Allergy	Control	p
<i>H.pylori</i>	are	16(61,50)	10(24,40)	0,002
	none	10(38,50)	31(75,60)	
Metaplazi	are	5(19,20)	9(22,00)	0,79
	none	21(80,80)	32(78,00)	
Atrofi	are	3(11,50)	4(9,80)	0,56
	none	23(88,50)	37(90,20)	

\*Chi-Square Test

The differences in the presence of *H. pylori* in the allergy and control groups were statistically significant. Accordingly, 61.50% of the group with a history of allergy had *H.pylori* positivity while 24.40% of the control group had *H.pylori* positivity.

#### 4. Discussion

In this study, we found that individuals with a history of NSAID hypersensitivity were more infected with *H. pylori*. There are few studies on Gastromucosal Evaluation of Individuals with a History of Hypersensitivity and Gastromucosal Evaluation. NSAIDs commonly used in the treatment of rheumatoid arthritis may cause gastric mucosal lesions (Tsujimoto et al., 2018). In a

study conducted in Japan, it was reported that only half of NSAID users with gastric ulcer were infected with *H. Pylori* (Matsukawa et al., 2003). In another study conducted in Japan, it was reported that the rate of *H. pylori* infection in NSAID-associated gastric ulcers was significantly lower than in non-NSAID-associated gastric ulcers (Kamada et al., 2006). In addition, aspirin use has been reported to inhibit the replication and growth of *H. Pylori* (Wang et al., 2003). In a study conducted in Romania with 1552 patients, NSAID treatment in patients with positive *H. pylori* status was found to be statistically significant in the *H. pylori* group (Negovan et al., 2022). In this study, the fact that NSAID treatment and severe endoscopic

lesions were statistically significantly more frequent in *H. pylori* positive biopsies indicated the importance of *H. pylori* eradication in reducing peptic ulcer bleeding and the development of NSAID-related mucosal lesions (Negovan et al., 2022). In addition, due to its widespread use, low-dose aspirin causes a significant amount of peptic ulcer disease (Sarri et al., 2019). In this study, *H. Pylori* positivity was found to be statistically significant in individuals with a history of NSAID hypersensitivity in accordance with the literature. It is not known why individuals with NSAID hypersensitivity acquire it and what the triggers are (Thong, 2018) 1.9-3.5% of the general adult population have reported hypersensitivity reactions to NSAIDs (Trinh et al., 2021). This has not been well characterized in epidemiological/cohort studies. None of the other cofactors known to trigger anaphylaxis (including physical factors) have been identified in relation to NSAID hypersensitivity (Thong, 2018). NSAIDs have harmful and beneficial effects on the large intestine, including protection against colorectal cancer and reduction in the size of colonic polyps (Sohail et al., 2023). Approximately 30% to 50% of NSAID users among the population in the Aseer region in southern Saudi Arabia reported endoscopic lesions, including subepithelial hemorrhages, erosions and ulcerations, but these lesions have no clinical impact and resolve spontaneously with long-term use (Alhammadi et al., 2022). However, endoscopic abnormalities (mucosal erosions, ulceration and subepithelial bleeding) were reported in up to 70% of patients with long-term NSAID intake, despite dyspeptic symptoms alone (Tai and McAlindon, 2021). In this study, there was no difference in gastromucosal metaplasia and atrophy between those with and without a history of hypersensitivity. More studies are needed to contribute to the literature on gastro mucosal evaluation of patients with a history of NSAID hypersensitivity.

## 5. Conclusion

The eradication of *H. pylori* in patients with a history of hypersensitivity and the role of family medicine in the diagnosis and treatment process with a holistic approach in this regard.

## Ethics approval and consent to participate

This cross-sectional study was conducted at Giresun Training and Research Hospital between May 1, 2023 and June 15, 2023. Approval dated 19.06.2023 and numbered (CREC-113) was obtained from Giresun Training and Research Hospital Clinical Research Ethics Committee. Approval numbered E-5393568-929-219096365 was obtained from the Provincial Health Directorate. It was conducted in accordance with the Declaration of Helsinki.

## Declaration of Author Contributions

The authors declare that they have contributed equally to the article. All authors declare that they have seen/read and approved the final version of the article ready for publication.

## Declaration of Conflicts of Interest

All authors declare that there is no conflict of interest related to this article.

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