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Eosinophil/Neutrophil/Platelet-to-Lymphocyte Ratios in Various Types of Immediate Hypersensitivity to NSAIDs: A Preliminary Study

Olga Branicka Barbara Rogala Joanna Glück

Department of Internal Diseases, Allergology and Clinical Immunology, Medical University of Silesia in Katowice, Katowice, Poland

Keywords

Eosinophil-to-lymphocyte ratio · Neutrophil-to-lymphocyte ratio · Platelet-to-lymphocyte ratio · Nonsteroidal anti-inflammatory drugs · Drug hypersensitivity

Abstract

Background: The eosinophil/neutrophil/platelet-to-lymphocyte ratios (ELR, NLR, and PLR) have been used as clinical markers of systemic inflammation. However, they have not yet been tested in various subtypes of immediate hypersensitivity to nonsteroidal anti-inflammatory drugs (NSAIDs). ***Objectives:*** To assess the ELR, NLR, and PLR in various types of hypersensitivity to NSAIDs. ***Materials and Methods:*** A retrospective analysis of complete blood cell count and the ELR, NLR, and PLR was performed. Appropriate types of hypersensitivity to NSAIDs were diagnosed based on the anamnesis and drug provocation tests. The analysis covered 97 patients. Twenty were diagnosed with NERD (NSAID-exacerbated respiratory disease), 20 with NECD (NSAID-exacerbated cutaneous disease), 38 with NIUA (NSAID-inducted urticaria/angioedema), and 19 with SNIUAA (single-NSAID-induced urticaria/angioedema or anaphylaxis). Two controls groups were included: the first covered 15 patients with bronchial asthma and the second 28 patients with chronic spontaneous urticaria without NSAID hypersensitivity. ***Results:*** The NLR did not differ significantly between the NSAID hypersensitivity types. The ELR was significantly higher in NERD patients, and the PLR was significantly lower in NECD patients than in patients with other types of NSAID hypersensitivity and in controls. ***Conclusions:*** The ELR and PLR may be useful in differentiating various types of immediate hypersensitivity to NSAIDs. Moreover, the ELR may be helpful in differentiating patients with bronchial asthma with and without NSAID hypersensitivity and PLR in differentiating patients with chronic spontaneous urticaria from NECD.

Introduction

Nonsteroidal anti-inflammatory drugs (NSAIDs) have high analgesic, anti-inflammatory, and antipyretic efficacy. Because of their easy availability, also over the counter, they are used by all age groups and often even overused. Incidence of hypersensitivity to NSAIDs has been reported between 0.6 and 5.7% of the general populations

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Olga Branicka
Department of Internal Disease, Allergology and Clinical Immunology
Medical University of Silesia in Katowice
Medyków 14, PL–40-752 Katowice (Poland)
o.branicka@gmail.com

[1]. Hypersensitivity reactions to NSAIDs belong to type B adverse drug reactions which are dose-independent, unpredictable, noxious, and unintended response to a drug taken at a dose normally used in humans. Moreover, hypersensitivity reactions occur in susceptible individuals [2, 3]. The reactions are divided depending on the mechanism into not immunological and immunological (IgE or T-cell mediated) and based on the time of reactions into immediate or delayed [4]. The first classification of hypersensitivity to NSAIDs presented by Stevenson et al. [5] in 2001 was based on clinical symptoms, the presence of chronic disease, and cross-reactivity with other COX-1 inhibitors. Up-to-date NSAID hypersensitivity is divided into 3 not immunologically mediated types: (1) NSAID-exacerbated respiratory disease (NERD), (2) NSAID-exacerbated cutaneous disease (NECD), and (3) NSAID-induced urticaria/angioedema (NIUA) and 2 immunologically mediated types: (1) single-NSAID-induced urticaria/angioedema or anaphylaxis (SNIUAA) and (2) single-NSAID-induced delayed hypersensitivity reactions (SNIRD) [5]. Diagnosis of hypersensitivity to NSAIDs is based on a detailed anamnesis and drug provocation tests (DPT). However, DPT are sometimes associated with a high risk of hypersensitivity reactions. Another impediment is the lack of laboratory indicators that would make the diagnosis of NSAID hypersensitivity easier. The only commercially available in vitro methods are estimation of serum IgE specific to pyrazolones and basophil activation test (BAT). However, they are very rarely used due to low sensitivity. They also do not allow us to allocate different cases of hypersensitivity to the appropriate type.

The neutrophil-to-lymphocyte ratio (NLR), eosinophil-to-lymphocyte ratio (ELR), and platelet-to-lymphocyte ratio (PLR) calculated for complete blood cell count (CBC) are markers of chronic inflammation that are known to be inexpensive and easy to calculate with usage of widely available methods. The usefulness of NLR, ELR, and PLR measurements has been reported in many diseases in oncology [6–8], cardiology [9,10], pulmonology [11, 12], and rheumatology [13, 14]. In allergic diseases, the usefulness of these ratios was evidenced in nasal polyposis [15–17], asthma [18, 19], and allergic rhinitis [20]. Moreover, high NLR and ELR have recently been found to serve as useful indicators of systemic inflammation in smokers [21]. In the present study, we aimed to assess if the NLR, ELR, and PLR may be useful in making diagnosis of various types of hypersensitivity to NSAIDs and to compare with control groups and C-reactive protein (CRP), which is the most commonly used marker of inflammation.

Methods

Study Design and Participants

The study was conducted at the Department of Internal Disease, Allergology and Clinical Immunology, University Clinical Hospital K. Gibińskiego, Katowice, Poland. We retrospectively analyzed data on all patients that had been hospitalized between January 2011 and December 2018 with the diagnosis with number D89.8 that describes in more detail the diagnosis of disorder involving the immune mechanism, and D89.9 that is a code used to specify a diagnosis of unspecified disorder involving the immune mechanism according to the International Classification of Diseases (ICD-10). These 2 codes were chosen because they were used to describe hypersensitivity reactions to the drugs. J45 and L50 were used as secondary codes. Then, we chose patients with confirmed hypersensitivity to NSAIDs during hospitalization. The typical allergological workup covered clinical history, and if the clinical history was not sufficient, DPT were used so as to diagnose an appropriate type of hypersensitivity to NSAIDs. Diagnosis of types of NSAID hypersensitivity was based on the anamnesis and DPT results [22]. Two control groups were formed from patients hospitalized in our department with diagnosis of well-controlled asthma without nasal polyps and with no anamnestic data on NSAID hypersensitivity (J45) and chronic spontaneous urticaria (L50), without history of NSAID hypersensitivity.

Clinical History

The detailed clinical history collected included pattern and chronology of symptoms, the interval between administration of the drug and the first symptoms, previous administration of NSAIDs, and other medications taken. To properly record the clinical history, we used a European Network for Drug Allergy (ENDA) Questionnaire on Drug Hypersensitivity [3, 23]. In the case of the history of 3 or more episodes of reaction to 2 different NSAIDs, the cross-reactive type of hypersensitivity was diagnosed and NERD or NECD was diagnosed if asthma or chronic urticaria was present. In the case of 2 or more reactions to the same NSAID with concomitant history of good tolerance to another NSAID, selective type of immediate hypersensitivity to NSAIDs was suspected, and further diagnosis was based on DPT [22].

Drug Provocation Test

DPT were performed in accordance with the EAACI/GA2LEN guidelines [3, 23]. Four increasing doses (27, 44, 117, and 312 mg) of aspirin were administered every 2 h until a cumulative dose of 500 (the patient with asthma) or 1,000 (the other patients) mg is reached [24]. If a patient shows no reaction after the last dose (total dose of 500 mg), another 500-mg aspirin could be given 1 h after the previous dose. The cumulative dose in that case would be 1,000 mg of aspirin. In selected cases, DPT and drug tolerance tests (DTT) with alternative NSAIDs were performed [24] according to the following scheme: 1/4, 1/4, and 1/2 of a single dose and then 1 dose every 1 h. Spirometry was performed before the test and after each drug administration in all patients with asthma and/or chronic rhinosinusitis with nasal polyps. A reaction was judged positive if a decrease in FEV1 by ≥20% of baseline occurred or when severe extrabronchial symptoms of aspirin hypersensitivity appear (e.g., profound rhinorrhea and nasal blockade even if FEV1 fall did not exceed 20%). A reaction was counted negative when the maximum cumulative dose of aspirin was reached without a drop in FEV1

Table 1. Characteristic of patients with various types of hypersensitivity to NSAIDs and controls

	Types of hypersensitivity to NSAIDs (n = 97)				Control groups (n = 43)	
	NERD	NECD	NIUAA	SNIUAA	C-AST	C-CSU
Patients, n (%)	20 (20)	20 (20)	38 (40)	19 (20)	15 (35)	28 (65)
Mean age ± SD, years	42.0±11.1	39.6±13.2	42.1±12.1	40.2±11.6	39.9±13.4	34.2±10.6
Male, n (%)	7 (35)	5 (25)	9 (24)	4 (21)	5 (33)	12 (43)
Female, n (%)	13 (65)	15 (75)	29 (76)	15 (79)	10 (67)	17 (57)
Comorbidity, n (%)						
Bronchial asthma	17 (85)	4 (20)	1 (2)	1 (5)	15 (100)	0 (0)
Allergic rhinitis	5 (25)	3 (15)	12 (31)	4 (21)	7 (46)	3 (10)
Nasal polyps	12 (60)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Chronic rhinosinusitis	7 (35)	0 (0)	1 (2)	0 (0)	2 (13)	0 (0)
Chronic spontaneous urticaria	0 (0)	19 (95)	6 (15)	0 (0)	0 (0)	28 (100)

NSAID, nonsteroidal anti-inflammatory drug; NERD, NSAID-exacerbated respiratory disease; NECD, NSAID-exacerbated cutaneous disease; SNIUAA, single-NSAID-induced urticaria/angioedema or anaphylaxis; C-AST, group of patients with well-controlled asthma without nasal polyps and with no anamnestic data on NSAID hypersensitivity; C-CSU, group of patients with chronic spontaneous urticaria.

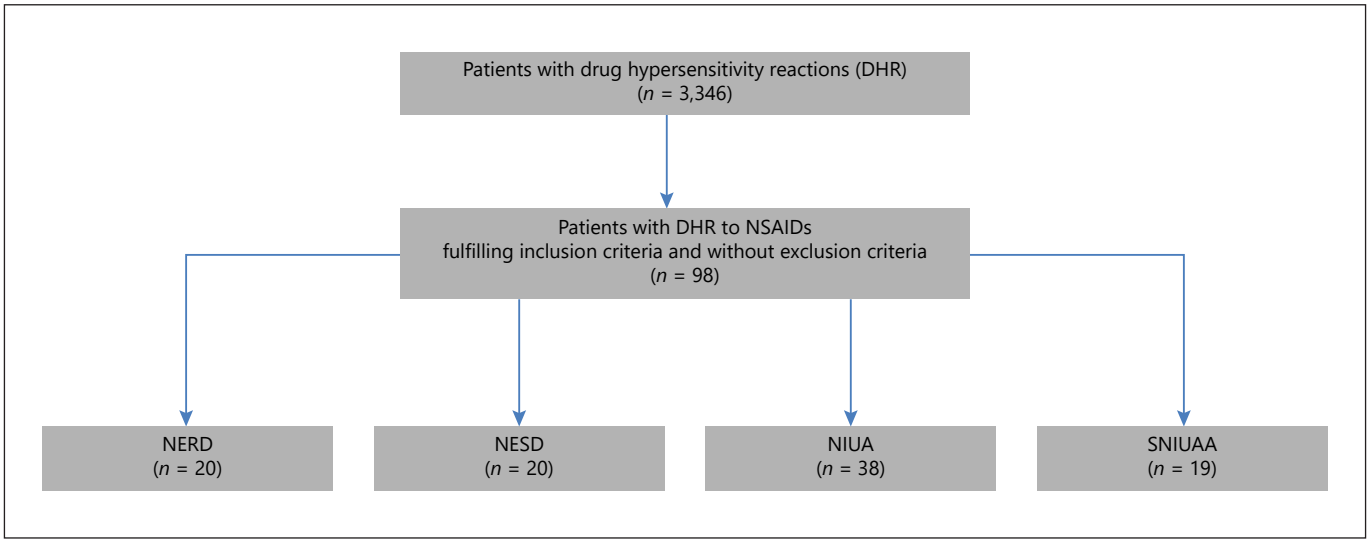

Fig. 1. Flowchart of qualification to the study. DHR, drug hypersensitivity reactions; NSAID, nonsteroidal anti-inflammatory drug; NERD, NSAID-exacerbated respiratory disease; NECD, NSAID-exacerbated cutaneous disease; SNIUAA, single-NSAID-induced urticaria/angioedema or anaphylaxis.

≥20% and without other symptoms of aspirin hypersensitivity. If a patient with an underlying chronic urticaria developed wheals and/or angioedema after DPT, the diagnosis was NECD. If such symptoms developed in a patient without other allergic diseases, NIUA was diagnosed. SNIUAA was diagnosed based on an anamnesis and negative DPT with aspirin.

Exclusion Criteria

The exclusion criteria included associated diseases unrelated to the basic diagnosis of hypersensitivity to drugs that could affect the results of laboratory tests. Those included all chronic inflammatory diseases (thyroid dysfunction, diabetes mellitus, coronary artery disease, hypertension, heart failure, chronic kidney disease, chronic lung disease, connective tissue disease, metabolic syndrome, and anemia), acute upper respiratory tract infection diagnosed within the previous 4 weeks, parasite infestation, pregnancy, and chronic medical treatment including systemic steroid and use of antiplatelet drugs. Any significant hematological, biochemical, or serological abnormalities were also excluded.

Laboratory Measurements

CBC and the CRP test were routinely performed in all patients admitted to the department. Blood samples were collected in a hematologic sample tube containing an anticoagulant, and neutrophil, lymphocyte, eosinophil, and platelet absolute counts were recorded using a Sysmex XN-350 hematology analyzer (Sysmex Europe Corporation, Norderstedt, Germany). Using these data, neutrophil, eosinophil, and platelet absolute numbers were divided by the lymphocyte absolute number, and NLR (neutrophil absolute number/lymphocyte absolute number), ELR (eosinophil absolute number/lymphocyte absolute number), and PLR (platelet absolute number/lymphocyte absolute number) values were calculated. The obtained data were compared among patients with NERD, NECD, NIUA, and SNIUAA.

Statistical Analysis

The results of CBC were expressed as absolute number and percentages. The NLR, ELR, and PLR were presented as median and interquartile range. The χ^2 test was used to analyze differences in nominal variables between groups. Nonparametric Kruskal-Wallis ANOVA and post hoc tests were used to compare the studied groups. All analyses were performed with a software package (Statistica 13.3, StatSoft Poland, Kraków, Poland). p values <0.05 were considered significant.

Results

Between 2011 and 2018, 3,346 patients were hospitalized with a diagnosis of drug hypersensitivity. After considering exclusion criteria, 97 patients (female: 72, 73%) were included to the final analysis. The mean age was 40.2 years (range 19–70). Twenty patients (20.5%) were diagnosed with NERD, 20 patients (20.5%) with NECD, 38 patients (39.2%) with NIUA, and 19 patients (19.5% with SNIUAA) (Fig. 1). The control group contained 43 patients were divided into 2 subgroups: the first group covering patients with well-controlled asthma without nasal polyps and with no anamnestic data on NSAID hypersensitivity (C-AST) to compare with the NERD group and the second group covering patients with chronic spontaneous urticaria (C-CSU) to compare with NECD, NIUA, and SNIUAA groups. C-AST included 15 patients, mean age 39.9 years (range 21–66), and C-CSU included 28 patients, mean age 34.2 years (range 22–59). The groups were comparable in terms of age and sex distribution ($p > 0.05$) (Table 1). No cases of SNIRD and NSAID-exacerbated food allergy (NEFA) were diagnosed. Patients did not take any medicines systemically. DPT had been performed with appropriate nonselective NSAIDs (acetylic acid, ketoprofen, diclofenac, naproxen, and metamizol) in 61 patients, acetaminophen in 57 patients, and preferential inhibitors of COX-2 (nimesulid) in 8 patients, and DTT had been performed with a selective inhibitor of COX-2 (celecoxib) in 77 patients.

Table 2. Median values and interquartile ranges of CBC and NLR, ELR, and PLR in patients with various types of hypersensitivity to NSAIDs and in control groups

	Normal values	NERD	NECD	NIUAA	SNIUAA	C-AST	C-CSU	*p* value
Leukocyte count, $\times 10^3/\mu L$	4.0–10.0	6.8 (5.1–7.8)	7.0 (5.7–8.0)	6.4 (5.2–7.3)	5.8 (5.2–7.8)	6.3 (5.3–6.7)	6.0 (5.3–7.8)	0.77
Platelet count, $\times 10^3/\mu L$	130.0–400.0	252.0 (222.0–315.0)	264.0 (219.0–292.5)	256.0 (216.0–290.0)	231.0 (196.0–288.0)	229.0 (202.0–280.0)	230.0 (205.0–274.5)	0.76
Neutrophils, %	45.0–70.0	53.3 (48.1–60.6)	59.4 (55.7–69.8)	56.7 (52.5–68.6)	59.1 (55.0–64.1)	57.0 (48.9–65.0)	60.45 (51.0–66.4)	0.33
Neutrophil count, $\times 10^3/\mu L$	2.5–5.0	3.2 (2.9–4.3)	4.0 (2.9–5.6)	3.5 (2.9–4.9)	3.2 (2.9–4.5)	3.2 (2.65–4.22)	3.5 (2.9–5.0)	0.79
Lymphocytes, %	20.0–45.0	32.3 (26.7–35.0)	34.2 (22.3–38.0)	30.5 (24.2–36.3)	33.0 (27.0–36.9)	29.4 (26.3–40.7)	30.0 (25.7–37.2)	0.97
Lymphocyte count, $\times 10^3/\mu L$	1.5–3.5	1.9 (1.5–2.6)	2.1 (1.6–2.3)	1.8 (1.6–2.5)	1.9 (1.5–2.4)	1.97 (1.65–2.27)	2.0 (1.7–2.2)	0.98
Eosinophils, %	1.0–5.0	6.9 (3.7–8.0)	2.4 (1.9–3.1)	3.0 (2.0–4.4)	2.3 (1.7–4.0)	2.5 (2.1–3.7)	2.2 (1.6–4.0)	**0.0002**
Eosinophil count, $\times 10^3/\mu L$	0.04–0.4	0.3 (0.2–0.6)	0.1 (0.11–0.2)	0.1 (0.13–0.2)	0.1 (0.1–0.2)	0.16 (0.13–0.21)	0.16 (0.11–0.25)	**0.0002**
ELR		0.2 (0.1–0.2)	0.08 (0.06–0.1)	0.08 (0.6–0.1)	0.08 (0.05–0.1)	0.08 (0.06–0.09)	0.07 (0.05–0.10)	**0.0003**
NLR		1.6 (1.3–2.2)	1.6 (1.4–3.1)	1.8 (1.4–2.7)	1.8 (1.5–2.3)	1.9 (1.1–2.5)	2.0 (1.4–2.4)	0.94
PLR		131.5 (99.2–181.5)	65.3 (45.0–94.2)	129.1 (105.0–173.2)	122.4 (101.4–157.9)	116.2 (100.0–168.2)	121.3 (95.8–159.5)	**0.00001**
CRP, mg/dL	0.0–5.0	1.7 (1.0–4.2)	1.5 (1.0–5.3)	1.1 (1.0–2.9)	1.3 (1.0–3.1)	1.3 (0.9–2.9)	1.0 (0.5–2.3)	0.27

Bold type denotes significance. CBC, complete blood cell count; NSAID, nonsteroidal anti-inflammatory drug; NLR, neutrophil-to-lymphocyte ratio; ELR, eosinophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; NERD, NSAID-exacerbated respiratory disease; NECD, NSAID-exacerbated cutaneous disease; SNIUAA, single-NSAID-induced urticaria/angioedema or anaphylaxis; C-AST, group of patients with well-controlled asthma without nasal polyps and with no anamnestic data on NSAID hypersensitivity; C-CSU; group of patients with chronic spontaneous urticaria; CRP, C-reactive protein.

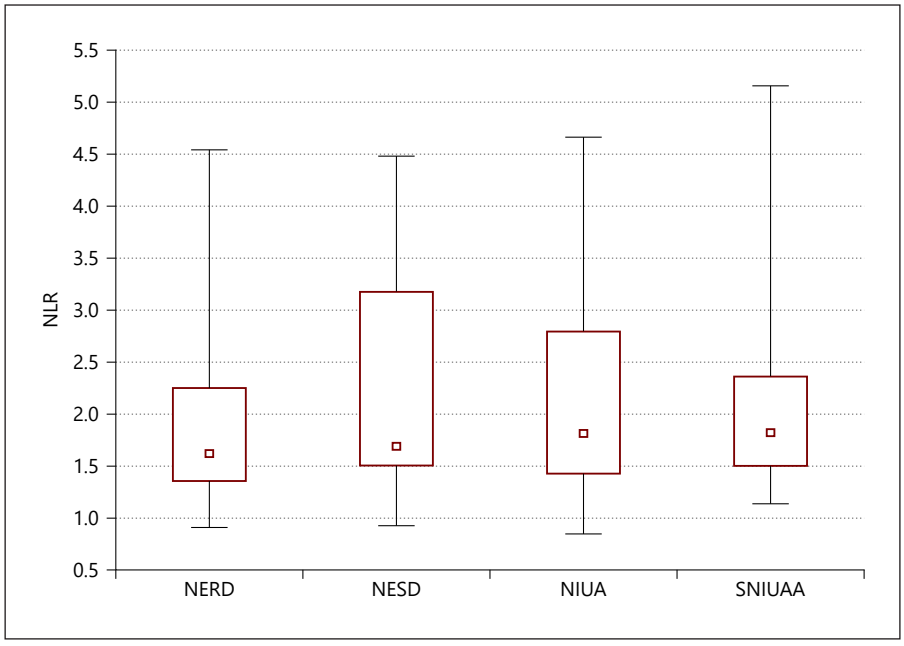

Fig. 2. Median values and interquartile and total range of NLR in patients with different types of NSAID hypersensitivity. There were no statistically significant differences among the groups. NSAID, nonsteroidal anti-inflammatory drug; NLR, neutrophil-to-lymphocyte ratio; NERD, NSAID-exacerbated respiratory disease; NECD, NSAID-exacerbated cutaneous disease; SNIUAA, single-NSAID-induced urticaria/angioedema or anaphylaxis.

The NLR in the NERD group was 1.62 (1.3–2.2); NECD, 1.69 (1.4–3.1); NIUA, 1.81 (1.4–2.7); SNIUAA, 1.82 (1.5–2.3); and in C-AST, 1.97 (1.1–2.5) and C-CSU, 2.03 (1.4–2.4). No statistically significant difference was found between the 4 groups with NSAID hypersensitivity and control groups ($p > 0.05$) (Table 2; Fig. 2). The ELR in the NERD group was 0.23 (0.1–0.2); NECD, 0.08 (0.06–0.1); NIUA, 0.09 (0.6–0.1); SNIUAA, 0.09 (0.05–0.1), C-AST, 0.08 (0.06–0.09); and C-CSU, 0.076 (0.05–0.10). The ELR was significantly higher in the NERD group than in the NECD ($p = 0.0009$), NIUA ($p = 0.0001$), and SNIUAA ($p = 0.0007$) groups and then in control groups C-AST ($p = 0.0008$) and C-CSU ($p = 0.0008$) (Table 2; Fig. 3). PLR values were significantly lower in the NECD group ($p = 0.0013$) than in the NERD ($p = 0.00004$), NIUA ($p = 0.000001$), and SNIUAA (0.00003) groups and then in control groups C-AST ($p = 0.0002$) and C-CSU ($p = 0.000009$). The PLR in the NECD group was 65.30 (25.5–140.0); NERD, 131.58 (77.4–250.8); NIUA, 129.10 (55.6–234.2); and SNIUAA, 122.40 (68.0–237.6); and in C-AST, 116.24 (100.0–168.2) and C-CSU, 121.35 (95.8–159.5) (Table 2; Fig. 4). The CRP value statistically significantly correlated with NLR ($r_s = 0.26$; $p < 0.05$) but not with ELR ($r_s = 0.16$) and PLR ($r_s = 0.04$) in all patients with NSAID hypersensitivity.

Discussion

In this study, we tried to assess if some peripheral blood cell ratios may be helpful to subcategorize NSAID-hypersensitive patients. Thus, we conducted a retrospective analysis in which we evaluated the NLR, ELR, and PLR as potential diagnostic indicators in groups of patients with various types of NSAID hypersensitivity. We found that the NLR was comparable in all examined groups, the ELR was significantly higher in patients with NERD, and the PLR was significantly lower in patients with NECD (shown in Fig. 2–4; Table 2). We compared the results with controls. We chose 2 control groups. The first one included the patients with well-controlled bronchial asthma without nasal polyps and with self-reported good tolerance to NSAIDs, and the second group included patients with chronic spontaneous urticaria with self-reported good tolerance to NSAIDs. Thanks to these control groups we could assess if higher ELR was characteristic only for NERD patients or for the whole group of patients with asthma, and in parallel, we looked if lower PLR was typical only for urticaria exacerbated by NSAIDs (NECD) or also for another type of urticaria, namely chronic spontaneous urticaria.

The higher ELR in NERD patients than in NECD, NIUA, and SNIUAA patients and then control groups C-AST and C-CSU seems to be easy to explain. Most patients with NERD have nasal polyps associated with eo-

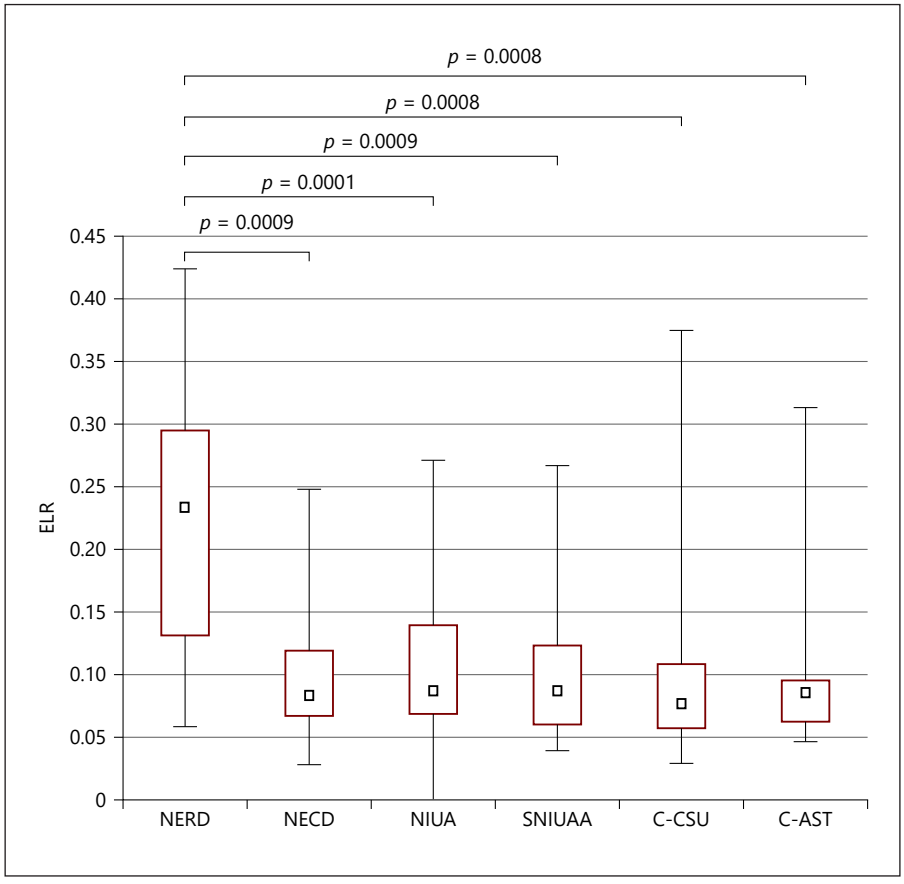

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Fig. 3. Median values and interquartile and total range of ELR in patients with different types of NSAID hypersensitivity and control groups. NSAID, nonsteroidal anti-inflammatory drug; ELR, eosinophil-to-lymphocyte ratio; NERD, NSAID-exacerbated respiratory disease; NECD, NSAID-exacerbated cutaneous disease; SNIUAA, single-NSAID-induced urticaria/angioedema or anaphylaxis; C-AST, group of patients with well-controlled asthma without nasal polyps and with no anamnestic data on NSAID hypersensitivity; C-CSU; group of patients with chronic spontaneous urticaria.

sinophilia. We have also found that both absolute number and percentage of eosinophils in peripheral blood were significantly higher in NERD patients than in others. Thus, higher ELR may simply result from NERD pathophysiology. The important and practical finding of our study is that the ELR was significantly higher in patients with NERD but not in asthma without polyps and with normal tolerance to NSAIDs. If we know the cutoff value of ELR value characteristic for NERD, it will be helpful in initially distinguishing patients with asthma with unclear clinical history of NSAID hypersensitivity before performing DPT. However, we could bear in mind that there are patients with bronchial asthma and nasal polyps with good tolerance to NSAIDs; thus, our results should also be compared with this group of asthmatic patients in future.

More difficult to explain is lower PLR in NECD than in other types of NSAID hypersensitivity. The absolute number and percentage of platelets and lymphocytes were comparable among all types of NSAID hypersensitivity [24, 25]. In our study, most patients with NECD also had chronic spontaneous urticaria, which was asymptomatic at the time of the study. Patients did not have other autoimmune disease that could affect the number of platelets in the blood. Data on the role of platelets in chronic urticaria are conflicting. In patients with chronic urticaria and hypersensitivity to acetylic acid (ASA), platelet activation was increased as compared with urticaria patients tolerating ASA [25]. However, the results of studies on platelet indices such as mean platelet volume, platelet count, and distribution width, as well as markers of platelet aggregation in chronic urticaria, were equivocal. We compared the PLR values in NECD patients with patients with CSU-C and found statistically lower PLR values only in NECD patients. Thus, low PLR values seem to be characteristic for NECD patients and may be a clinically helpful tool in management of patients with chronic urticaria and unclear tolerance to NSAIDs, particularly while considering dietary restrictions. However, this phenomenon needs further investigations with larger groups of patients with NECD and CSU. It should be underlined that no patients with CSU had positive ANA results.

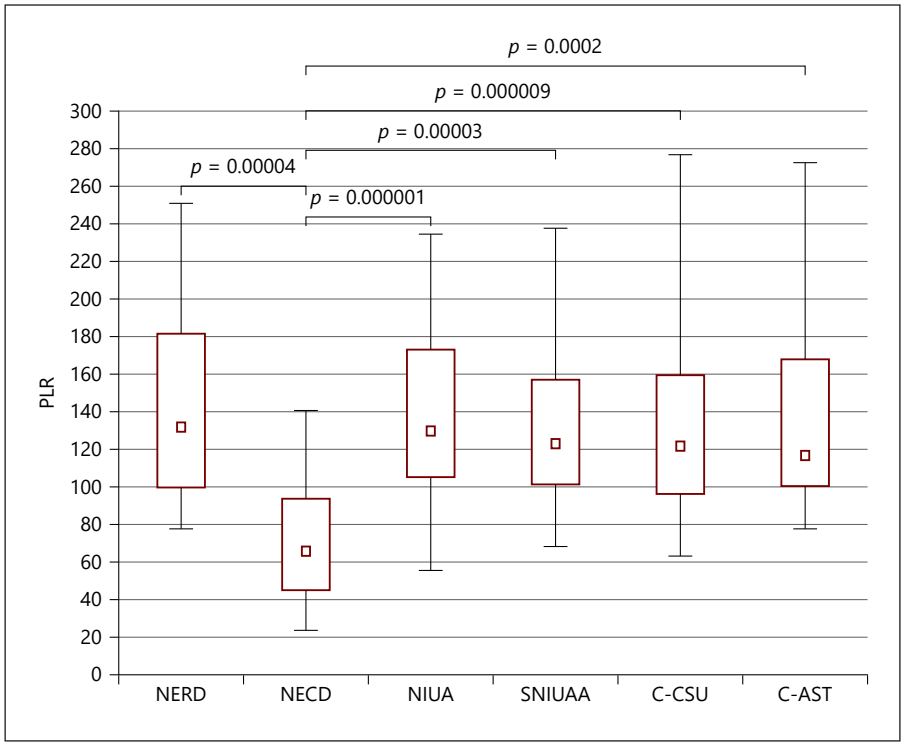

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Fig. 4. Median values and interquartile and total range of PLR in patients with different types of NSAID hypersensitivity and control groups. NSAID, nonsteroidal anti-inflammatory drug; PLR, platelet-to-lymphocyte ratio; NERD, NSAID-exacerbated respiratory disease; NECD, NSAID-exacerbated cutaneous disease; SNIUAA, single-NSAID-induced urticaria/angioedema or anaphylaxis; C-AST, group of patients with well-controlled asthma without nasal polyps and with no anamnestic data on NSAID hypersensitivity; C-CSU; group of patients with chronic spontaneous urticaria.

The usefulness of ELR, NLR, and PLR has not yet been studied in hypersensitivity to NSAIDs and neither in hypersensitivity to other drugs. However, the NLR, ELR, and PLR were assessed in other allergic diseases. Mochimaru et al. [18] reported the correlation between the NLR and increased probability for an episode of severe asthma exacerbation within the next year. Gungen and Aydemir [19] reported positive correlation of the NLR in patients with controlled asthma and with state of uncontrolled asthma. Yenigun et al. [20] reported correlation between the ELR and allergic rhinitis with positive skin prick tests in children. In some studies, the means of NLR and ELR were significantly higher in patients with chronic rhinosinusitis with nasal polyps (CRSwNP) whose disease recurred than in those remaining disease-free after surgery [15]. Moreover, the mean ELR was significantly higher in patients with CRSwNP with other clinical conditions such as (allergy, asthma, and ASA intolerance) and with recurrence of the disease than in patients without allergies [15]. Other data came from studies in different immunologically mediated diseases. Gasparyan et al. [14] summarized publications on the PLR in rheumatic disease and reported positive correlation between exacerbation of rheumatic disease and PLR and decrease in the PLR in response to anti-inflammatory therapies. In other diseases such as cancer processes or with atherosclerotic background and in some chronic diseases [6–10], the usefulness of the NLR has been confirmed.

Moreover, in our study the correlations between the ratios and CRP were calculated. CRP did not significantly differ among patients with various type of NSAID hypersensitivity, but its value correlated only with the NLR in the whole group of patients. This observation may suggest that the NLR together with CRP may be an auxiliary laboratory tool while neutrophilic inflammation is suspected.

There are some limitations of our study. First, the population sizes of groups with individual types of hypersensitivity to NSAIDs were relatively small. It makes impossible to assess the cutoff value of ELR and PLR and sensitivity and specificity in relation to data from the interview and the result of DPT in false-positive and false-negative patients.

The strengths of this study are that only the patients with proper diagnosis of hypersensitivity to NSAIDs based on the medical history and DPT were included into the study. Of special importance is the fact that their comorbid chronic diseases and chronic or acute infections which could affect NLR, ELR, or PLR values were exclusion criteria. The influence of systemically used drugs was excluded as well.

On the other hand, strict exclusion criteria may be a drawback of our project as in real life most patients with NSAID hypersensitivity have coexisting diseases that can influence the CBC ratios Thus, while interpreting the CBC ratios, the possible changes of them caused by other diseases should be taken into consideration.

One can assume that the ELR in NERD and the PLR in NECD could be used as a helpful indicator although it will probably not replace the diagnostic gold standard of drug hypersensitivity workup, that is, DPT. Further studies covering more numerous groups of patients are warranted in order to establish the diagnostic value of ELR and PLR in NSAID hypersensitivity. The most valuable results of our study seem to be the finding on higher ELR in NERD than in NSAID-tolerated asthma and in lower values of PLR in NECD than in CSU as they both may have practical application.

Conclusions

The ELR and PLR may be helpful in differentiating various types of hypersensitivity to NSAIDs and in some allergic diseases with good NSAID tolerance. The NLR seems not to be useful in this field. However, further studies with larger patient groups are required to confirm our initial findings.

Statement of Ethics

This paper is exempt from ethics committee approval because all examinations were routinely performed in all patients admitted to the department.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Author Contributions

Olga Branicka: acquisition, analysis, or interpretation of data for the work; drafting the work; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Barbara Rogala: substantial contributions to the design of the work; revising manuscript critically for important intellectual content; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Joanna Glück: substantial contributions to the conception or design of the work, interpretation of data for the work; revising the work critically for important intellectual content; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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