

HEMATOLOGIC INDICES AS POTENTIAL BIOMARKERS IN URTICARIA: A COMPARATIVE CASE-CONTROL STUDY IN ALBANIAN POPULATION

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Abstract: Urticaria is primarily a mast cell-mediated inflammatory disorder in which basophils, eosinophils, platelets, and multiple inflammatory mediators contribute to its pathophysiology. Routinely available hemogram-derived inflammatory indices may provide inexpensive and objective measures of systemic inflammatory alterations and may have potential value as biomarkers of disease activity, particularly in chronic urticaria, where disease assessment relies substantially on subjective patient-reported outcomes. Although several hematological ratios and indices have been investigated in urticaria, data from the Albanian population remain limited. This study evaluated selected hematological parameters in hospitalized patients with high disease activity urticaria compared with controls and assessed their associations with C-reactive protein (CRP). This cross-sectional retrospective case-control study included 113 patients hospitalized with diagnosis urticaria at the main tertiary hospital center in Tirana and 398 controls who underwent hemogram testing as part of routine health examinations in private practice. The median age was 50 (32–57) years in the urticaria group and 42 (32–54) years in controls with no statistical difference between groups, while females comprised 83 (73.45%) and 269 (67.59%), respectively. Acute urticaria was diagnosed in 55 (48.67%) patients and chronic urticaria in 58 (51.33). All evaluated hematological parameters differed significantly between patients with urticaria and controls ($p < 0.001$). Patients with urticaria had statistically significant lower absolute eosinophil, basophil, and lymphocyte counts and PDW (platelet distribution width), while MPV (mean platelet volume) and NLR (neutrophil to lymphocyte ratio) were higher. Undetectable eosinophil and basophil counts were observed in 79 (69.91%) and 99 (87.61%) urticaria patients, respectively. Spearman's rank correlation analysis showed that NLR was positively correlated with CRP ($p = 0.233$, $p = 0.013$) and inversely correlated with eosinophils ($p = -0.487$, $p < 0.001$) and basophils ($p = -0.276$, $p = 0.003$). Eosinophils and basophils were moderately positively correlated ($p = 0.430$, $p < 0.001$), while basophils were inversely correlated with CRP ($p = -0.230$, $p = 0.014$) and eosinophils with MPV ($p = -0.1919$, $p = 0.042$). No significant correlations were observed between CRP and eosinophils, MPV, or PDW, or between NLR and MPV or PDW. No significant changes were found between groups of chronic and acute urticaria for studied variables. Hospitalized patients with urticaria demonstrated a distinct hematological profile, particularly increased NLR and MPV and decreased eosinophil, basophil, lymphocyte, and PDW values. The association between NLR and CRP suggests potential relevance as a low-cost marker of systemic inflammation. Further prospective studies are needed to validate these findings in the Albanian population and to determine the potential utility of these hematological indices as markers of urticaria disease activity.

Keywords: Urticaria; Hematological indices; Neutrophil-to-lymphocyte ratio; Systemic inflammation; Biomarkers

Field: Medical Sciences and Health

1. INTRODUCTION

Urticaria is a skin disorder characterized by the presence of wheals, angioedema, or both. It encompasses a broad range of clinical presentations, and different urticaria subtypes may occur co-exist in the same patient. (Zuberbier et al., 2026) It is reported that urticaria affects up to 20% of people worldwide (Kolkhir et al., 2022) and its global burden has increased, reaching 66.48 million cases in 2021, with higher rates among females and younger individuals and a projected continued rise. (Tan et al., 2025)

Urticaria is considered acute when symptoms last ≤ 6 weeks and chronic when they persist for > 6 weeks and may be further categorized as inducible or spontaneous depending on the presence of identifiable triggers. (Zuberbier et al., 2026) Mast cell activation leads to the release of mediators, including histamine and platelet-activating factor (PAF), which contribute to itching, vasodilation, erythema, and recruitment of inflammatory cells. (Zuberbier et al., 2026) However, the inflammatory response in urticaria is not restricted to mast cells. Basophils, eosinophils, platelets, and components of both the innate and adaptive immune systems may contribute to the development and persistence of the disease. Assessment of urticaria severity remains challenging, as clinical evaluation largely depends on subjective patient-reported measures. Therefore, there is growing interest in accessible laboratory biomarkers that may complement clinical assessment. Complete blood count parameters and derived inflammatory indices,

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have gained attention as inexpensive and readily available markers of systemic inflammation.

Eosinopenia and basopenia in CSU(chronic spontaneous urticaria) has been related to CSU subtypes (Su Küçük & Yücel, 2026) According a recent publication, the combination of eosinopenia and basopenia may better predict poor response to second-generation H1-antihistamines than eosinopenia alone (OR 9.5 vs. 4.8). Eosinopenia is associated with type IIb autoimmunity, higher disease activity, and poorer treatment response, supporting its potential role as a biomarker in CSU (Kolkhir et al., 2020).

Recent studies report that CRP(c-reactive protein) may serve as potential biomarkers for distinguishing patients with CSU from healthy controls (Plavsic et al., 2021) with serum CRP concentrations significantly higher in CSU patients as compared with the healthy subjects and significantly correlated with the platelet count in CSU patients. (Kasperska-Zajac et al., 2014). Elevated C-reactive protein (CRP) levels have been associated with greater urticaria activity, impaired quality of life, and poorer response to antihistamine treatment. (Kolkhir et al., 2018)

Increased platelet count and MPV in CSU may reflect the inflammatory state of the disease, suggesting an ongoing but compensated platelet destruction–production process(Di Pino et al., 2022). A positive correlation between CRP and NLR (neutrophil to lymphocyte ratio) was reported in the CSU group. (Temizel et al., 2026) High NLR and low eosinophil and basophil counts have been associated with a poor response to second-generation H1-antihistamines, whereas normal or high eosinophil counts were associated with a better treatment response (Calzari et al., 2025)

However, findings remain inconsistent and sometimes controversial across studies while data on these hematological biomarkers in Albanian patients with urticaria are currently lacking.

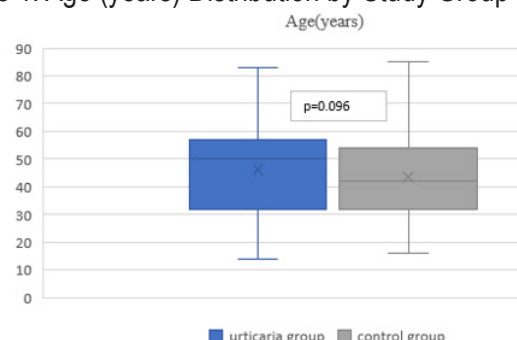
2. MATERIALS AND METHODS

This retrospective, cross-sectional case-control study was conducted at the main tertiary hospital center in Tirana, Albania, and included patients hospitalized with a diagnosis of urticaria and a control group comprising individuals undergoing routine health examinations in private medical practice. Clinical, demographic, and laboratory data were retrospectively extracted from available medical records, with the first complete blood count obtained at hospital admission used for patients with urticaria. The analyzed variables included age, absolute neutrophil, lymphocyte, eosinophil, and basophil counts, mean platelet volume (MPV), platelet distribution width (PDW), and serum C-reactive protein (CRP), expressed in mg/dL. The neutrophil-to-lymphocyte ratio (NLR) was calculated as the absolute neutrophil count divided by the absolute lymphocyte count. The study database and anaysis was performed using Ms Excel 2016 and SPSS. The distribution of continuous variables was assessed using the Shapiro–Wilk test. Differences between the urticaria and control groups were assessed using the Mann–Whitney U test. Associations among hematological parameters, NLR, and CRP were evaluated using Spearman's rank correlation coefficient (ρ). All statistical tests were two-sided, and statistically significance was set 0.05. The study was approved by Ethics Committee of University of Medicine, Tirana.

3. RESULTS

A total of 113 hospitalized patients with urticaria were included in the analysis, comprising 55 (48.7%) patients with acute urticaria and 58 (51.3%) with chronic urticaria. The median age of patients with urticaria was 50 years (IQR, 32–57), and 83 (73.45%) were female. The control group consisted of 398 individuals, with a median age of 42 years (IQR, 32–54), of whom 269 (67.59%) were female.

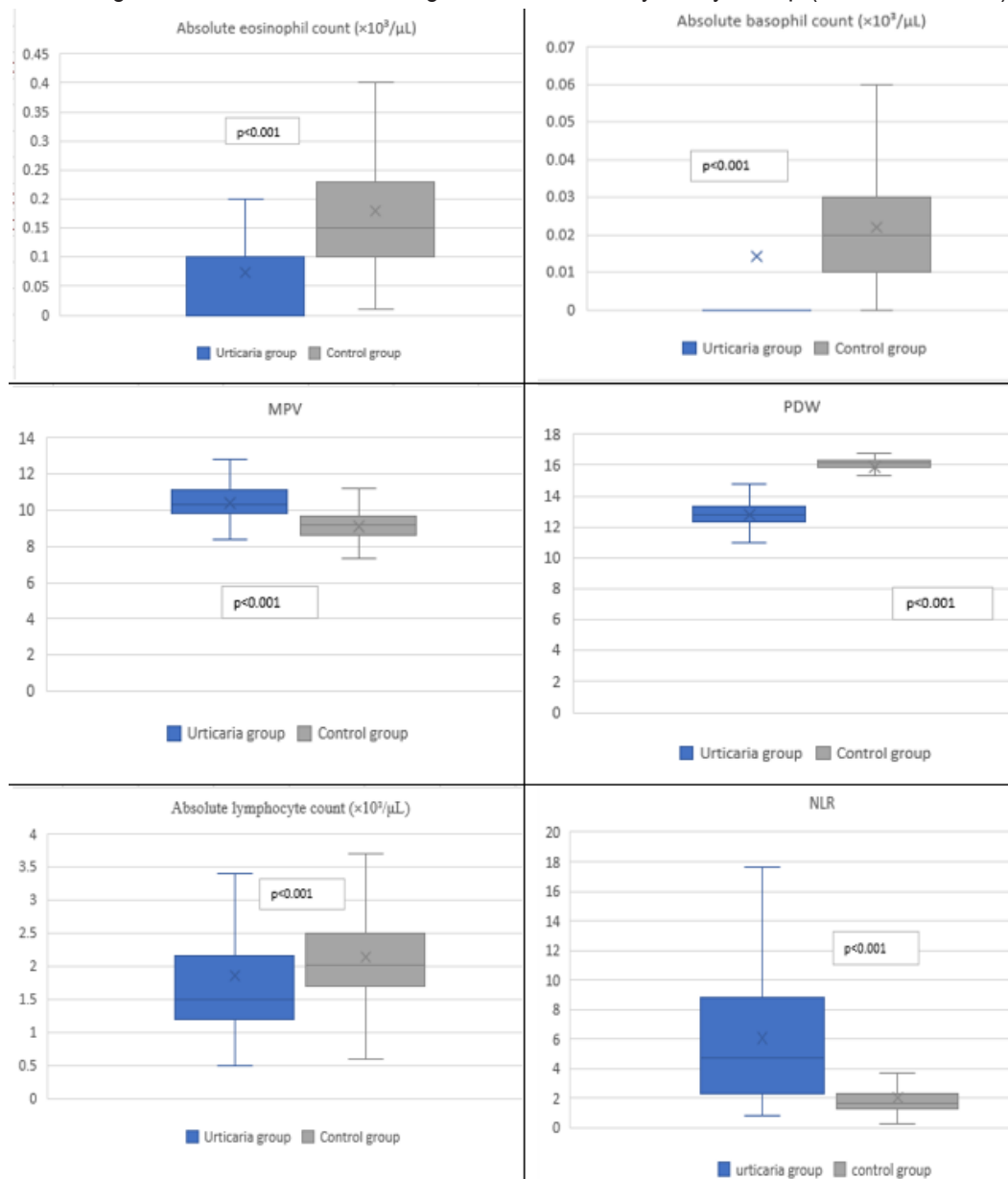
Figure 1. Age (years) Distribution by Study Group Median (IQR).



Source: Authors' research

Absolute eosinophil, basophil, and lymphocyte counts, mean platelet volume (MPV), platelet distribution width (PDW), and neutrophil-to-lymphocyte ratio (NLR) were compared using the Mann-Whitney U test. All evaluated hematological parameters differed significantly between patients with urticaria and controls ($p < 0.001$). Median eosinophil count was significantly lower in patients with urticaria than in controls, $0.00 (0.00-0.10) \times 10^3/\mu\text{L}$ versus $0.15 (0.10-0.23) \times 10^3/\mu\text{L}$, respectively ($U = 7760.00$, $p < 0.001$), as was basophil count, $0.00 (0.00-0.00) \times 10^3/\mu\text{L}$ versus $0.02 (0.01-0.03) \times 10^3/\mu\text{L}$ ($U = 9284.50$, $p < 0.001$). Undetectable eosinophil and basophil counts were observed in 79 (69.91%) and 99 (87.61%) patients, respectively.

Figure 2. Distribution of Hemogram Parameters by Study Group (Median and IQR)



Source: Authors' research

MPV was significantly higher in patients with urticaria, $10.30 (9.80-11.10)$ fL versus $9.20 (8.60-9.70)$ fL ($U = 7888.00$, $p < 0.001$), whereas PDW was lower, $7.60 (4.60-11.30)$ fL versus $16.10 (15.90-16.30)$ fL ($U = 2456.00$, $p < 0.001$). The absolute lymphocyte count was also lower, $1.50 (1.20-2.10) \times 10^3/\mu\text{L}$ versus $2.01 (1.69-2.51) \times 10^3/\mu\text{L}$ ($U = 14151.00$, $p < 0.001$), while NLR was substantially higher, $4.75 (2.29-8.62)$ versus $1.66 (1.28-2.28)$ ($U = 8095.00$, $p < 0.001$).

CRP resulted $0.30(0.11-0.97)$ mg/dL and was elevated (> 0.5 mg/dL) in 41(36.28%) of urticaria patients.

Spearman's rank correlation analysis demonstrated a weak inverse correlation between basophils and CRP ($\rho = -0.230$, $p = 0.014$), whereas eosinophils were not significantly correlated with CRP ($\rho = -0.1286$, $p = 0.175$). Eosinophils and basophils demonstrated a positive correlation ($\rho = 0.430$, $p < 0.001$). Neither PDW nor MPV was significantly correlated with CRP ($\rho = -0.009$, $p = 0.925$ and $\rho = -0.076$, $p = 0.427$, respectively). Eosinophils showed a weak inverse correlation with MPV ($\rho = -0.1919$, $p = 0.042$), while basophils were not correlated with MPV ($\rho = -0.007$, $p = 0.944$). NLR demonstrated a weak positive correlation with CRP ($\rho = 0.233$, $p = 0.013$), but no significant correlations with MPV ($\rho = 0.017$, $p = 0.859$) or PDW ($\rho = -0.029$, $p = 0.756$). NLR demonstrated an inverse correlation with eosinophils ($\rho = -0.487$, $p < 0.001$) and an inverse correlation with basophils ($\rho = -0.276$, $p = 0.003$).

No statistically significant changes were found between groups of chronic and acute urticaria for hemogram parameters and CRP levels.

4. DISCUSSION

Our finding of increased MPV is consistent with previous study, which suggested that these changes may reflect increased platelet turnover and an ongoing, compensated platelet destruction-production process associated with inflammation in CSU (Di Pino et al., 2022). Results are controversial with other studies reports where MPV was significantly lower in CU patients compared with the controls (7.45 ± 0.69 vs. 7.96 ± 0.58 fl, $p = 0.000$) in adults (Yim et al., 2019) and also in children with CU, MPV (fL) levels were significantly lower when compared to healthy children (7.42 ± 0.77 and 7.89 ± 0.65 , respectively; $p = 0.004$) (Akelma et al., 2015). Another study found no significant differences in MPV and PDW between CSU group and the healthy subjects. (Kasperska-Zajac et al., 2014)

Disease activity and disease duration may influence MPV and PDW values and could partly explain differences between our findings and those of previous studies. Notably, our study included patients with both acute and chronic urticaria, whereas most previous studies have focused predominantly on chronic spontaneous urticaria, which may contribute to differences in platelet indices. However, no significant differences in MPV or PDW were observed between the acute and chronic urticaria groups in our study.

Kolkhir et al. reported eosinopenia in 10% of patients with CSU, which was associated with higher disease activity, type IIb autoimmunity, elevated CRP levels, and poorer response to antihistamines and omalizumab. Eosinophil counts also correlated positively with basophil counts, and 81% of patients with CSU with undetectable eosinophils had basopenia. (Kolkhir et al., 2020) In our study of hospitalized patients with urticaria, who may represent a subgroup with higher disease activity, eosinopenia and basopenia were frequently observed. Undetectable eosinophil and basophil counts were present in 69.91% and 87.61% of patients, respectively. Serum CRP concentrations were significantly higher in CSU patients as compared with the healthy subjects in adults (Kasperska-Zajac et al., 2014) and children. (Akelma et al., 2015) Elevated CRP levels were reported in approximately one-third of patients with CSU and were associated with ASST (Autologous Serum Skin Test) positivity and arterial hypertension (Kolkhir et al., 2018) and not correlated with disease activity. (Plavsic et al., 2021) In our study CRP was elevated in 36.28% of patients without significant differences between acute and chronic urticaria group.

5. CONCLUSIONS

Hospitalized patients with urticaria demonstrated a distinct peripheral hematological profile, characterized by increased NLR and MPV and reduced eosinophil, basophil, lymphocyte, and PDW values compared with controls. The positive association between NLR and CRP supports its relationship with systemic inflammatory activity, while the inverse association between NLR and eosinophil count may reflect coordinated alterations in circulating leukocyte profiles. The concomitant increase in MPV and reduction in PDW may indicate altered platelet size distribution, activation, and turnover, supporting a potential contribution of platelet-mediated mechanisms to the inflammatory processes underlying urticaria. These findings suggest that routinely available hemogram-derived parameters, particularly NLR, MPV, and PDW, may provide accessible and cost-effective complementary markers of systemic inflammatory alterations. Nevertheless, their clinical and prognostic significance requires further investigation in larger, prospective, and well-characterized cohorts, with appropriate adjustment for potential confounders, including comorbidities, concomitant medications, and other clinical factors, particularly in the Albanian population.

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