Annals of Medical Research
DOI: 10.5455/annalsmedres.2018.07.132 2018;25(4)719-22

Original Article

Assessment of change in neutrophil-lymphocyte ratio, platelet-lymphocyteratio in patients with acute and chronic urticaria

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Abstract

Aim: Urticaria is a skin disease characterized by erythematous, oedematous, itchy,and spontaneously disappearing urticaria lesions. One of the most common skin diseases, it is the most common reason underlying the presentations to emergency departments. Our objective is to investigate the role of systemic inflammation in urticaria pathogenesis by measuring the indicators of Neutrophil-Lymphocyte ratio (NLR) and Platelet-Lymphocyte ratio (PLR) in routine hemograms in patients with acute and chronic urticaria.

Material and Methods: Of patients visiting the Dermatology Policlinic of İnönü University Medical School Hospital between July 2017 and February 2018, 69 patients diagnosed with acute urticaria and 188 patients diagnosed with chronic urticaria as well as 90 healthy people taken as controls with an age range of 18to 70 were included in our study. Blood values of patients were studied retrospectively. (For the study, a Research Ethics Approval was obtained from Malatya Research Ethics Board.)

Results: No significant difference was detected among the study groups in terms of demographic properties. Whereas a significant difference was noted among the three groups with regard to NLR values, no statistically significant difference was detected among the groups with respect to PLR values. No statistically significant difference was observed between the group of patients with urticaria and the control group in terms of erythrocyte distribution(p:0.01). On the other hand, when the patient group with chronic urticaria was divided into two subgroups as patients with a complaint duration of 90 days and less, and those with a complaint duration of more than 90 days and evaluated, no statistically significant difference was detected between these groups in terms of RDW, lymphocytes, neutrophils, platelets, NLR and PLR values

Conclusion: In our study, we have determined that systemic inflammation has increased in the group of patients with urticaria as compared to the control group. What's more interesting in this study is our conclusion that the pathways involved in continued inflammation do not change by time in chronic urticaria.

Keywords: Urticaria; Neutrophil-Lymphocyteratio; Platelet-Lymphocyteratio; Systemic Inflammation.

INTRODUCTION

Urticaria is a common disease presenting with itchy, erythematous and oedematous plaques on the body, which might be accompanied by angio-oedema and which deteriorates patients' quality of life. As described in EAACI/GA (2) LEN/EDF/WAO Guideline, persistent and intermittent urticarial plaques lasting longer than six weeks are considered chronic urticaria. Chronic urticaria is further classified into two subclasses as spontaneous urticaria and inducible urticaria (1). It has a prevalence from 0. 5% to 5% and is two times more frequent in women than in men. While the disease, particulary the chronic form thereof, affects patients' sleep quality, work performance and day to day activities, persistent itching and rashes appearing on the body might give rise to patients' withdrawal from social life due to stigmatisation (2).

Studies have been going on for 30 years to elucidate the etiopathogenesis of the urticaria. Mechanisms involved in the pathogenesis can be classified as inflammation resulting from release of pro-inflammatory cytokines upon mast cell activation, autoimmunity based on formation of anti-IgE or anti-FcεRI antibodies, changes in coagulation cascade and angiogenesis (3).

Received: 06.07.2018 **Accepted:** 20.09.2018 **Available online:** 25.09.2018
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Neutrophil-lymphocyteratio (NLR), Platelet-lymphocyteratio (PLR), Erythrocyte distribution width (RDW) and number of plateletshave been studied in many dermatological diseases as various parameters indicating inflammation, and found to be associated with disease activity(4), prognosis (5) and spread of disease. However, even though many costly and hard-to-find inflammatory markers have been studied in such a prevalent disease as urticaria, to the best of our knowledge, no studies have been carried out on NLR and PLR ratios so far.

In this study, it is intended to demonstrate the difference in these parameters - which are easily accessible by a routine haemogram testand can be cheaply, easily and rapidly assessed among patients with acute urticaria, chronic urticaria and healthy controls.

MATERIAL and METHODS

For the study, data from patients, presenting to Dermatology Policlinic of İnönü University Medical School Hospital with complaints of redness and raised welts between July 2017 and February 2018 and diagnosed with acute and chronic urticaria based on a detailed clinical examination and anamnesis, were screened. Patients meeting the inclusion and exclusion criteria were included in the study. Inclusion criteria of the study were as follows: Data from patients within an age range of 18-70 years either with a follow-up of chronic urticaria or suffering from acute urticaria attacks was included in the study. Exclusion criteria of the study were as follows: 1) Those with such autoimmune or inflammatory diseases as DM, thyroid, rheumatological diseases 2) Those with coronary diseases 3) patients with active or chronic infection 4) Those with malignity 5) Those using chronic non-steroidal or immunosuppressive drugs 6) pregnancy 7) obesity 8) Those with chronic urticaria and on a omalizumabtreatment.

For the study, data from 586 patients was screened. 138 patients were excluded based on unavailability of complete blood values, 33 patients for receiving different diagnoses in the following periods, 8 patients on account of being above 70 years of age, 69 patients due to detection of an additional autoimmune disease, 34 patients due to infection, 10 patients due to malignity, 13 patients based on use of nonsteroidal or immunosuppressive drugs, 13 patients due to coronary arterial disease, 3 patients due to pregnancy and 2 patients on account of morbid obesity. Data from 348 patients were assessed. 243 people were selected by random simple sampling method from among healthy volunteers from the society. Taking the inclusion and exclusion criteria of the study into account, 153 healthy volunteers were excluded from the study. Ninetyhealthy volunteers were included in the study.

Statistical analysis:

Study data were analyzed by SPSS ver. 17.0 for Windows software (SPSS, Inc.; Chicago, IL, USA). Conformity of the data with normal distribution was assessed by Kolmogorov-Smirnov test. As normal distribution hypothesis could not be corroborated, numerical data was summarized as medians, minimum and maximum values. In group comparisons, Kruskal-Wallis test followed by Conover paired comparison method were used. For comparison of two independent groups, Mann-Whitney U testwas used. Categorical data was shown in numbers and percentages, and Pearson's chi-square test was used for comparison. Level of significance for all tests was accepted as 0.05.

RESULTS

A total of 348 patients were included in the study. Whereas 224 of the participants consisted of females, 124 thereof were male patients. There was no statistically significant gender difference between the groups (p>0.05). (See Table 1. Gender distribution in study groups)

Table 1. Gender distribution in study groups

	Gender		
	Female	Male	Total
Acute	48 (69.6%)	21 (30.4%)	69
Chronic	115 (61.2%)	73 (38.8%)	188
Control	61 (67.0%)	30 (33.0%)	91
Total	224 (64.4%)	124 (35.6%)	348

No statistically significant difference was found among the acute urticaria group, the chronic urticariagroup and the control group in comparison thereof with regard to age. When they were evaluated based on duration of the disease, whereas average duration of disease was 10 days in the group with acute urticaria, it was 182.5 days in the group with chronic urticaria. (See Table-2: Average age and duration of disease in study groups.)

Table 2. Average age and duration of disease in study groups

	Acute	Chronic	Control	P
	Median (Min-Max)	Median (Min-Max)	Median (Min-Max)	
Age	37 (20-68)	37 (19-69)	34 (20-63)	0.2363
Duration	10 (1-1000)	182.5 (4-10950)		

When patients with acute urticaria and those with chronic urticaria were compared in terms of RDW values, no difference was noted between the groups (p: 0.01); however, it was found that RDW values of the said patient groups were higher as compared to the control group. As for NLR value, no statistically significant difference was detected among all groups. While the group of patients with acute urticaria had the highest NLR level, this level was lower in control group in comparison with patients with acute and chronic urticaria. In the ROC analysis for NLR, 1.99 was calculated as the value of the catheter between urticaria and control group. As for PLR, platelet and lymphocyte values, no statistically significant difference was determined among the groups (p: 0.53, p: 0.28 p: 0.52). A statistically significant difference was detected among the 3 groups as regards neutrophil value. (See Table 3 Detailed values by group).

On the other hand, when the patient group with chronic urticaria was divided into two subgroups as patients with a complaint duration of 90 days and less, and those with a complaint duration of more than 90 days and evaluated, no statistically significant difference was detected between these groups in terms of RDW, lymphocyte, neutrophil, platelet, NLR and PLR values. (See Table 4. Values of the group of patients with chronic urticaria)

Table 3. RDW, NLR, PLR, Lymphocyte, Neutrophil, and Platelet values by group

	Acute (n=69) Median (Min-Max)	Chronic (n=188) Median (Min-Max)	Control (n=90) Median (Min-Max)	p-value
RDW	13.2 (11.5-19.6)[a]	13.1 (4.15-20.6)[a]	12.7 (11.6-15.8)[b]	0.01
NLR	2.16 (0.83-20.24)[a]	1.93 (0.48-14.66)[b]	1.64 (0.55-4.02)[c]	<0.001
PLR	112.2 (52.17-433.33)	115.28 (11.98-473.97)	106.28 (59.91-226.59)	0.53
Lymphocyte	2.53 (0.66-6.06)	2.37 (0.73-19.2)	2.43 (1.05-4.57)	0.52
Neutrophil	5.67 (2.15-16.8)[a]	4.56 (2.03-29.03)[b]	3.9 (1.9-6.28)[c]	<0.001
Platelet	282 (166-426)	276 (142-572)	265.5 (155-426)	0.28

Table 4. Comparison of RDW, Lymphocyte, Neutrophil, Platelet, NLR, and PLR values of the patient group with chronic urticaria

	Chronic urticaria group	N	Median	Minimum	Maximum	p
RDW	<=90	69	13.00	11.50	20.60	0.66
	=>91	119	13.10	4.15	19.40	
Lymphocyte	<=90	69	2.35	.73	19.20	0.51
	=>91	119	2.38	.80	12.70	
Neutrophil	<=90	69	4.67	2.45	16.25	0.27
	=>91	119	4.56	2.03	29.03	
Platelet	<=90	69	284.00	152.00	572.00	0.29
	=>91	119	272.00	142.00	494.00	
NLR	<=90	69	1.98	.52	10.39	0.24
	=>91	119	1.84	.48	14.66	
PLR	<=90	69	114.69	11.98	473.97	0.47
	=>91	119	115.36	24.65	352.31	

DISCUSSION

Urticaria is a disease consisting in erythematous, oedematous papules, and the major responsible factors of which are mast cells, basophils and histamine released therefrom. Urticarial lesions occur due to nerve stimulationcaused by release of other mediators other than histamine such as platelet activating factors and cytokines from activated mast cells, vasodilatation and capillary leakage of plasma. Although not all pathways stimulating the mast cells are entirely known in urticaria, it may occur by IgE-mediation or through different pathways (6). However, over the past years, there have been studies showing that coagulation system is activated and expression of coagulation tissue factor in eosinophils is increased by thrombin production in patients with chronic urticaria (7).

NLR ratio obtained by dividing the number of neutrophils by the number of lymphocytes, and PLR ratio obtained by dividing the number of platelets by the number of lymphocytes have been assessed and concluded to be a cheap, easily accessible and reliable parameter available and convenient for in inflammatory diseases. Both of these ratios have been studied in rheumatic diseases, inflammatory diseases, malignity and coronary diseases and in almost all cases they have been observed to be high (8,9). Thrombocytes - the primary role of which is maintenance of hemostasis - also contribute to the migration of inflammatory cells to lesion areas of inflammatory cells by interacting with endothelial cells, leukocytes and progenitor cells, the release of inflammatory cytokines in large quantitiesand the formation of an inflammatory environment (10). It has been shown that number of platelets has increased in patients with urticaria. However, we did not detect any difference among acute urticaria group, chronic urticaria group and control group with regard to number of platelets. Red cell distribution (RDW) is a parameter describing the difference in size of red blood cells. RDW has been considered an inflammatory parameter in many diseases. Moreover, it has been suggested that increase in RDW might be particularly associated with poor prognosis in cardiovascular diseases (11). Whereas a significant difference as regards RDW value existed between our patient group and the control group, no difference was observed between the acute urticaria group and the chronic urticaria group. We intended to determine the variation of these inflammatory parameters in acute

and chronic urticaria groups as compared to healthy controls. We believe that variation in these parameters will contribute to elucidation of these two diseases whose pathogeneses still remain to be clearly understood.

We have determined in our study on acute urticaria group, chronic urticaria group and healthy controls that,of these parameters indicating inflammation in blood, the ratio of NLR was significantly higher in acute urticaria group as compared to chronic urticaria group and the control group. We have determinedNLR value to be higher in the group of patients with chronic urticariabased on a comparison thereof with the control group. Whereas RDW value was higher in group of patients with urticaria as compared to the controls, we observed that there was no difference between the acute urticaria group and the chronic urticaria group. As for other indicators also increasing in inflammation such as the number of platelets, the number of lymphocytes and the PLR ratio, we could not detect any difference between the group of patients with urticaria and the control group.

Just as the chronic urticaria may spontaneously regress within 3 months, so too may it last for years. Pathways responsible for continuation of the disease are not exactly known. We assessed the inflammatory parameters by dividing the group of patients with chronic urticaria into two subgroups. Patients with chronic urticaria were divided into groups of patients with complaints lasting 90 days and less and patients with complaints lasting more than 90 days. No statistically significant difference was detected between duration of disease and such values as PLR NLR, RDW, lymphocytes, neutrophils and platelets. Absence of this difference suggests that the pathways activating the disease do not change in patients suffering from long-lasting chronic urticaria. We did not find a study that evaluated the ratio of NLR and PLR in urticaria patients in the literature. For this reason, we can not compare our results with the literature.

Ünalet al. determined the NLR ratio, PLR ratio and average thrombosis volume to be higher in patients with psoriasis as compared to the healthy controls. However, they did not detect any correlation between these inflammatory parameters and disease severity, joint involvement, and nail involvement. Thus they concluded that these parameters were not adequately convenient for assessment of psoriasis (10). On the other hand, in a study conducted on patients with alopecia areata, no significant difference was detected between the patients with alopecia areata and the healthy controls as regards NLR value and it was concluded that there were no indicators available for use in alopecia areata (11).

It has been noted that in the literature, there is not a consensus in publications on these inflammatory parameters either. Much as these inflammatory parameters increased in many inflammatory diseases, diseases where these inflammatory parameters did not increase were also reported. In our study, we have determined that systematic inflammation has increased in the group of patients with urticaria in comparison with the control group.

CONCLUSIONS

What's more interesting is our conclusion that the pathways involved in continued inflammation do not change by time in chronic urticaria.

Competing interests: The authors declare that they have no competing interest.
Financial Disclosure: There are no financial supports
Ethical approval: Inonu university scientific research and publishing board, 2017/21-2

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