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THE WHITE BLOOD CELL COUNT (WBC) AND NEUTROPHIL-TO-LYMPHOCYTE RATIO (NRL) IN MULTIPLE SCLEROSIS

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Abstract

Introduction. Multiple sclerosis (MS) is one of the main chronic inflammatory diseases of the central nervous system that causes functional disability in people. Assessment of the state of the immune system begins with an analysis of the total number of blood leukocytes and their population composition (the number of neutrophils and lymphocytes). The ratio of neutrophils and lymphocytes (NRL) is a marker of inflammation.

The aim of the study. The aim of this study was to investigate the WBC and neutrophil-to-lymphocyte ratio in patients with different forms of MS.

Results. In patients with MS in 23.5% of cases the WBC is higher than 9×109/L. In 5.9% of MS cases leukopenia is observed, and in the vast majority of cases (70, 6%) the level of blood leukocytes was in the range of 4-9×109/L. Leukopenia and leukocytosis are more common in women than in men ($p<0.05$). Leukocytosis and leukopenia are most often found in RRMS form, while in the SPMS form patients in 93.8 % of cases the normal level of leukocytes found. MS's patients had a significantly higher NLR ($p < 0.05$) than the control group. No significant difference in WBC and NLR was found between groups of MS clinical forms. No association was found between NLR and an age and sex.

Conclusions. NRL is an inexpensive and affordable indicator, which is determined by the automatic determination of the total number of leukocytes in the blood. It can be an additional informative indicator of inflammation against the background of normal leukocyte levels.

Key words: multiple sclerosis; NRL; WBC; neutrophil-to-lymphocyte ratio.

Despite the significant achievements of science in studying the pathogenesis of multiple sclerosis, research remains relevant. Multiple sclerosis (MS) is a common inflammatory neurological disease associated with demyelination of the central nervous system. Now MS is a leader among the causes of disability in the young age. In Ukraine, as in the EU, this pathology most often found in people aged 18 to 34 years.

According to modern notions, MS is a multifactorial chronic progressive disease characterized by central nervous system damage. The process of demyelination based on mechanisms that mutually reinforce each other: inflammatory response, neurodegeneration with abnormal remyelination and axonal damage (primary or secondary) [1]. There are many publications on studies of the ratio of neutrophils to lymphocytes as a marker of inflammation in MS [1, 2, 5]. Serum hematological indices such as the neutrophil-to-lymphocyte ratio (NLR) have been used as biomarkers of pathogenic inflammation and prognostication in multiple areas of medicine. Recent evidence shows correlation of NRL with psychological parameters as well [3]. But insufficiently studied in relation to the severity of the disease.

Objective and tasks: to investigate the WBC and neutrophil-to-lymphocyte ratio (NLR) in patients with different forms of MS.

Materials and methods of the study. Sixty-eight patients with a verified diagnosis of MS on the basis MacDonald et al. [4] criteria (34 patients with relapsing-remitting MS (RRMS), 18 patients with primary progressive MS (PPMS), 16 patients with secondary progressive MS (SPMS)) and 36 healthy controls were examined. The average age of patients was 36.8±2.12 years. All patients agreed to participate in the study. A study of the total number of blood leukocytes, lymphocytes and neutrophils was performed by automated analyzers. The NLRs were calculated for all participants and were compared with among the groups.

Statistical analysis of the data was performed using mathematical methods and STATISTICA 8.0 software package (Statsoft, USA). Each variable was tested for normal distribution using Shapiro-Wilk test. Basic statistics, such as arithmetic mean (M) and

standard error of the mean (m) were calculated. The results in figures and tables have been provided as M±m. The differences between arithmetic means were considered significant at $p < 0.05$.

Results and discussion

In patients with MS in 23.5% of cases the blood level of leukocytes was higher than 9×10^9/L that is, leukocytosis is established (table 1). In 5.9% of MS cases leukopenia is observed, and in the vast majority of cases (70, 6%) the level of blood leukocytes was in the range of $4\text{-}9\times10^9$/L. Leukopenia and leukocytosis are more common in women than in men ($p<0.05$).

Table 1

White blood cell count (WBC) in patients with Multiple sclerosis with gender comparison

	Whole group No (%)	Male (n=30)	Female (n=38)	P value
WBC > 9×10^9/L (leukocytosis)	16 (23,5)	6 (20)	12 (31,6)	<0,05
WBC $4\text{-}9\times10^9$/L	48 (70,6)	23(76,6)	23 (60,6)	NS
WBC < 4×10^9/L (leukopenia)	4 (5,9)	1 (3,4)	3 (7,9)	<0,05

Leukocytosis and leukopenia are most often found in RRMS form, while in the SPMS form MS patients in 93.8 % of cases the normal level of leukocytes found (table 2).

Table 2

White blood cell count (WBC) in patients with Multiple sclerosis with clinical form comparison

	Whole group No (%)	PPMS (n=18)	SPMS (n=16)	RRMS (n=34)	P value
WBC > 9×10^9/L (leukocytosis)	16 (23,5)	5 (27.8)	1 (6.3)	10 (29.4)	p_1<0,05 p_2<0,05
WBC $4\text{-}9\times10^9$/L	48 (70,6)	12 (66.7)	15 (93.8)	21 (61.8)	NS
WBC < 4×10^9/L (leukopenia)	4 (5,9)	1 (5.6)	-	3 (8.8)	p_1<0,05

Notes: p_1- the difference is significant between RRMS group and PPMS group;

p_2- the difference is probable between RRMS group and SPMS group.

In most patients with multiple sclerosis, there is an increase in the number of neutrophilic granulocytes in the peripheral blood (6,58 ± 0,40 $\times10^9$/L in MS and 4,58 ±

$0,42\times10^9$/L in control). MS patients had a significantly higher NLR ($p < 0.05$) than the control group (table 3).

Table 3

White blood cell count (WBC) and neutrophile to lymphocyte ratio (NLR) in patients with Multiple Sclerosis

	Control (n=36)	MS (n=68)	P value
WBC, $\times10^9$/L	6,25±0,62	8,98±0,65	<0.05
NLR	2,5±0,15	3,76±0,42	<0,05

No significant difference in WBC and NLR was found between groups of MS clinical forms (table 4). No difference in NLR was found between RRMS and progressive MS patients and neither between SPMS and PPMS patients. No association was found between NLR and an age and sex.

Table 4

White blood count (WBC) and neutrophile-to-lymphocyte ratio (NLR) in patients with different forms of Multiple Sclerosis.

Gropes	WBC, $\times10^9$/L	NLR
Control (n=36)	6,25±0,62	2,5±0,15
MS (n=68)	8,98±0,65*	3,76±0,42*
PPMS (n=18)	9,5±0,8*	3,50±0,50*
SPMS (n=16)	9,22±0,8*	4,15±0,37*
RRMS (n=34)	8,37±0,7*	3,67±0,62*

Notes: * - the difference is significant to the control.

The rate of NRL in the scientific literature is considered a marker of inflammation [1]. NLR has also been investigated as a possible marker relating to the depression, anxiety, and stress score in MS patients [5]. Our research has confirmed that this indicator may be inferior to the marker of the inflammatory process in multiple sclerosis [6, 7, 8]. A higher level of multiple sclerosis indicates the predominance of the neutrophilic phase of inflammation. NRL characterizes the functional state of immunity, the ratio of its nonspecific and specific link. An increased NLR is associated with a decreased antioxidant capacity, even in the early stage of neuronal damage [8, 9]. At the present stage of research, neutrophils will be assigned one of the leading roles in neuroinflammation, the pathogenesis of autoimmune processes along with lymphocytes [9, 10]. The authors consider the neutrophils as important pathogenic targets in the development of multiple sclerosis, and their number and functional activity need

to be monitored. NRL is an indicator of an increase in the number of circulating neutrophils. Bisgaard A. K. at al showed that NLR was higher in MS andneuritis patients compared to healthy control, indicating the occurrence of chronic inflammation [11].

The present study has some limitations, many of which are related to small sample size. The NLR contributing to the knowledge of MS immunology.

Conclusion. NRL is an inexpensive and affordable indicator, which is determined by the automatic determination of the total number of leukocytes in the blood. It can be an additional informative indicator of inflammation against the background of normal leukocyte levels.

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