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The Prognostic Efficacy of Inflammatory Indicators in Determining the Cause of Multiple Sclerosis Exacerbation

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Abstract

Multiple sclerosis (MS) is the most prevalent immune-mediated inflammatory disease affecting the central nervous system, presenting with diverse clinical symptoms and manifestations. This study investigates the diagnostic potential of the monocyte-to-lymphocyte ratio (MLR), red cell distribution width-to-lymphocyte ratio (RLR), and systemic immune-inflammation index (SII) in detecting MS attacks among relapsing-remitting MS (RRMS) patients seeking care in the emergency department (ED). The research focused on RRMS patients who presented to the ED, analyzing data from 165 individuals. The inflammatory biomarker values were compared between periods of attack and non-attack using paired t-tests to determine the differences between the two groups. Patients who experienced an MS attack had greater mean values for the neutrophil/lymphocyte ratio (NLR), MLR, RLR, and SII than those who did not. The two groups' respective mean differences in NLR, MLR, RLR, and SII were 5.40 ± 7.25,0.37 ± 0.43,7.77 ± 11.61, and 1469.19 ± 1978.88($p < 0.001$). NLR, RLR, MLR, and SII showed superior diagnostic ability in identifying MS relapse in ROC analysis (AUC:0.87,0.81,0.86, and 0.87,respectively).Our results suggest that SII, MLR, NLR, and RLR could be useful in helping patients with RRMS confirm their diagnosis of attack.

Keywords: Inflammatory biomarker, Monocyte-to-Lymphocyte Ratio, Multiple Sclerosis, Neutrophil-to-Lymphocyte Ratio, Systemic Immune Inflammation Index, Red Cell Distribution Width-to-Lymphocyte Ratio

INTRODUCTION

With a wide range of clinical indications and symptoms, multiple sclerosis (MS) is the most common immune-mediated inflammatory demyelinating illness of the central nervous system [1, 2]. MS shows notable variations in histopathological and radiological alterations, clinical manifestation, course of the illness, and reaction to treatment [3]. Its pathophysiology has been proposed to include demyelination, abnormalities of the blood-brain barrier, inflammation of a dynamic interaction between glia and neurons, and neuro-axonal injury to the brain and spinal cord caused by the innate and adaptive immune systems [4, 5]. It is crucial to differentiate between MS patients experiencing an attack (exacerbation, relapse, or episode) and those who are admitted to the emergency department (ED) because of their varied clinical symptoms along with those who do not. Inflammatory markers were required for this procedure, along with cranial imaging and clinical results. The most recent review study suggested that neutrophils and their phenotype may be connected to the course of MS disease. A common marker for systemic inflammation and infection is the differential white blood cell count [6–8].

Early identification and assessment of treatment response may benefit from the observation of

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$CD15^{+}$neutrophil growth in inactive relapsing-remitting multiple sclerosis (RRMS) [6]. Granulocyte counts were also shown to drop in RRMS patients throughout the remission stage [6]. In autoimmune disease, the peripheral blood neutrophil-to-lymphocyte ratio (NLR) has lately been proposed as a viable, affordable, and efficient surrogate biomarker for systemic inflammatory status and, consequently, disease activity [8–12]. It is unknown how well the systemic immune inflammation index (SII), red cell distribution width (RDW)to lymphocyte ratio (RLR), and monocyte-to-lymphocyte ratio (MLR) reflect disease activity in RRMS patients. This study aimed to evaluate the diagnostic value of MLR, RLR, and SII in detecting MS attacks among RRMS patients.

METHODOLOGY

Subjects

223 RRMS patients who were admitted to a hospital's emergency room between January 2022 and August 2023 were investigated in this study. Interferon-beta and sphingosine-1-phosphate inhibitors are first-line treatments for some of the patients evaluated, while others are left untreated. Nevertheless, none of our patients have been treated with second-line medications (anti Cd20, natalizumab, or cladribine). The study included 125 individuals who were 18 years of age or older, diagnosed with RRMS, and experiencing an MS attack [13]. A monophasic clinical episode with objective indicators and patient-reported symptoms that develops abruptly or sub-acutely in the central nervous system, lasts for at least 24 hours, and reflects a focal or multifocal inflammatory demyelinating event without fever or infection was considered an MS attack [13].These included myelopathy, encephalopathy, headache, altered consciousness, meningism us, focal supratentorial syndrome, focal brainstem or cerebellar syndrome, optic neuritis, ophthalmoplegia, and isolated weariness [14]. Ten patients were disqualified for lack of information, twenty for using steroids within 30 days or for having a recent infection (≤1 month), and twenty-eight for other reasons (such as autoimmune comorbidities (such as psoriasis, Sjogren's syndrome, rheumatoid arthritis.), tumor history, pregnancy, or stressful co-occurring events within the previous six months (such as traumatic bone fractures; Figure 1).

Study Layout as Well as Variables

The study design used for this investigation was retrospective qualitative. Following clearance by the Tribhuvan University Teaching Hospital's Ethics Committee in Kathmandu, the study was carried out retrospectively (NP9812). The Declaration of Helsinki was followed in the conduct of this investigation.

Procedures for This Investigation

58 patients excluded according to eligible criteria

1. Missing data (10)
2. Short-term steroid use in the last 30 days or recent infections (⩽1 month) (20)
3. Other reasons (28)
   - Stressful co-occurring events in the past 6 months (for example, traumatic bone fractures)
   - Tumor history
   - Pregnancy
   - Autoimmune comorbidities (rheumatoid arthritis, psoriasis, Sjögren's syndrome, and so on)

When these individuals were admitted to the emergency room during the attack and non-attack periods, their study parameters were compared. A neurologist assessed the severity of the MS attack. Following the assessment, MS attack patients were enrolled in the study one after the other (attack time). Emergency service visits during the non-attack period were compared with those of the same patients. Patients were chosen in accordance with eligibility requirements after the data was examined by two impartial observers. Within one hour of being admitted to the emergency department, laboratory testing of both patients with and without attacks were assessed. The results of the patients' hematological and biochemical testing were documented. The SII, RLR, MLR, and NLR ratios were computed separately. Platelet count is multiplied by NLR to get SII [15].

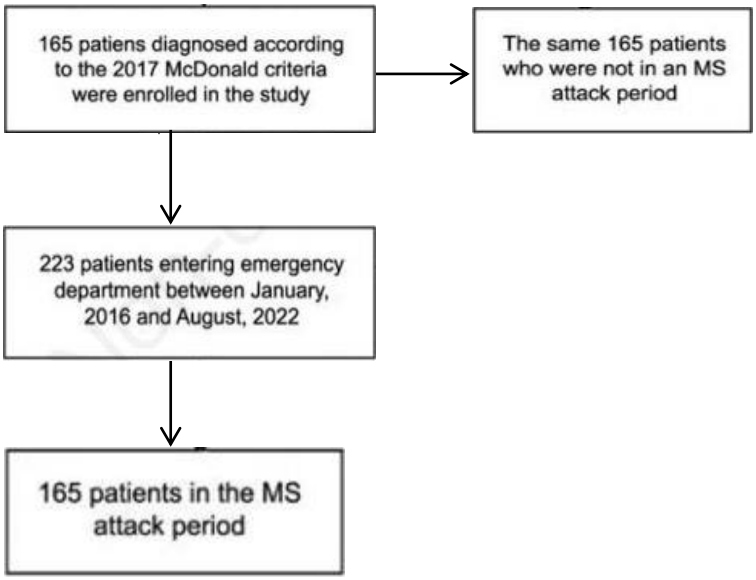

Figure 1. Patients' Selection Flow Chart. MS, Multiple Sclerosis.

Analysis of Power

The study planned to include 165 patients, based on an effect size of 0.2 (the minimum clinically significant difference), a maximum type 1 error of 5%, and a minimum statistical power of 80%. This design aligned with the quasi-experimental approach to assess differences in the mean values of RLR, NLR, MLR, and SII in RRMS patients visiting the emergency department during attack and non-attack periods.

Analysis of Statistics

The central limit theorem states that continuous measures, like hematological data, should be used to determine if the means, not the data, are normally distributed [16]. The standard deviations for continuous measurements in this investigation did not exceed the meaning. Consequently, parametric tests were employed after this theory was deemed appropriate. Data analysis included calculating the mean, standard deviation, and range (minimum and maximum values) for continuous variables. Categorical data were analyzed using frequency and percentage distributions. A paired t-test was used to compare mean inflammatory biomarker levels between attack and non-attack groups. Diagnostic cut-off points were identified through receiver operating characteristic (ROC) analysis. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated to assess statistical significance. AUC values were classified as poor if they were between 0.5 and 0.6, good if they were between 0.6 and 0.7, acceptable if they were between 0.7 and 0.8, excellent if they were between 0.8 and 0.9, and outstanding if they were above 0.9. The data's level of statistical significance is defined as $p < 0.05$. The Medals statistical package New York software was used for data evaluation and research power analysis.

RESULTS

Out of the 165 patients in our study, 106 (64.2%) were female. The patients were 39.3 ± 11.7 years old on average (Tables 1 and 2). Patients who experienced an MS attack had an average NLR of 8.22 ± 7.35, while those who did not experience an incident had an average NLR of 2.81 ± 1.65. The two groups' mean NLRs differed by 5.40 ± 7.25, which was statistically significant ($p < 0.001$; Table 3, Figure 2). Patients who experienced an MS attack had an MLR of 0.67 ± 0.43, while those who did not had an attack had an MLR of 0.30 ± 0.17. The two groups' mean MLRs differed by 0.37 ± 0.43, which was statistically significant ($p < 0.001$; Table 3, Figure 2). Patients who experienced an MS attack had an average RLR of 15.45 ± 12.06, while those who did not experience an attack had an average RLR of 7.68 ± 3.88. The statistically significant difference between the two groups' mean RLRs was 7.77 ±

11.61 substantially. (Table 3, Figure 2, $p < 0.001$). Patients who experienced an MS attack had an average SII of 2195.76 ± 2011.06, while those who did not experience an attack had an average SII of 726.57 ± 457.92. The two groups' mean SIIs differed by 1469.19 ± 78.88, which was statistically significant ($p < 0.001$; Table 3, Figure 2).

Table 1. Distribution of Descriptive Characteristics (n = 165).

Characteristics	Groups	Count (n)	Percent (%)
Sex	Male	106	64.2
	Female	59	35.8

Table 2. Evaluation of the Difference in Biochemistry and Hemogram Parameters Between Attack and Non-Attack Periods (n = 165).

Characteristics	Min-Max	Median	Mean ± S.D.
Age	19–69	38	39.3 ± 11.7

Note: Min, minimum; Max, maximum; S.D., standard deviation.

The attack and non-attack groups' means for white blood cells, RDW, platelets, neutrophils, lymphocytes, monocytes, and eosinophils differed statistically significantly (Table 3). The means of glucose, alanine aminotransferase, aspartate aminotransferase, and C-reactive protein showed statistically significant differences between the two groups, whereas the means of urea, creatinine, hemoglobin, and hematocrit did not (Table 3).

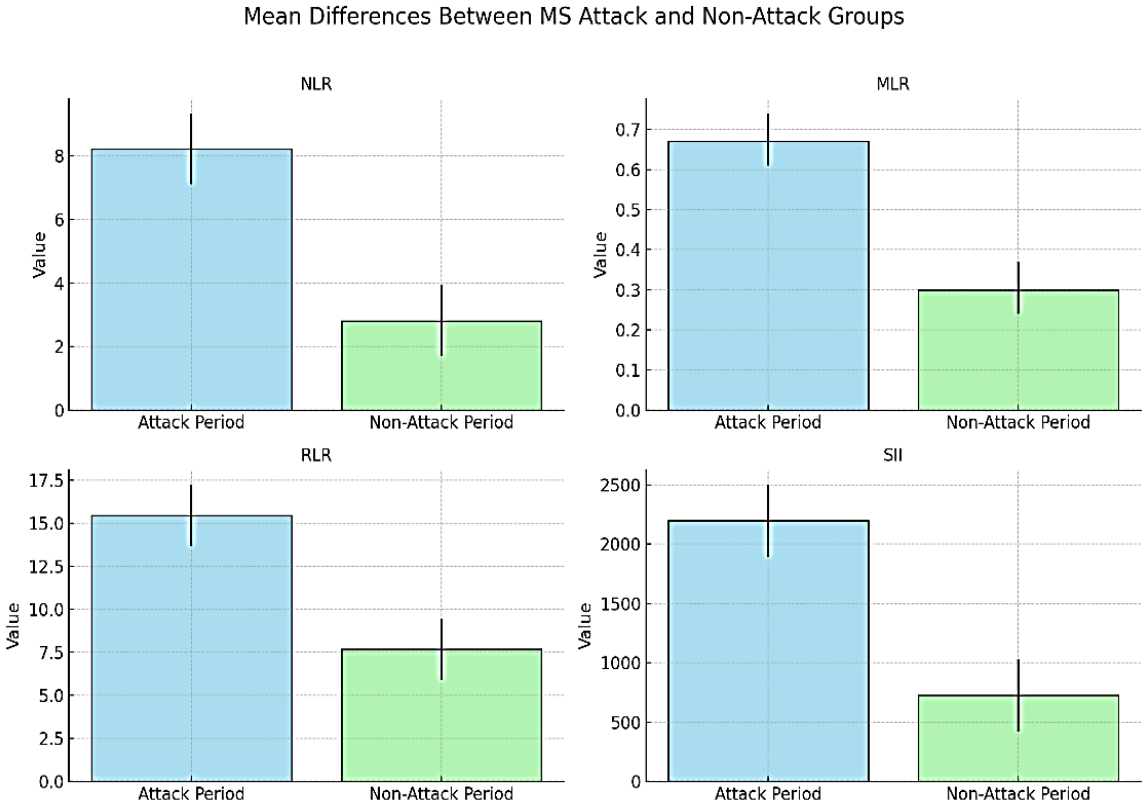

Figure 2. The Mean Difference Between NLR, MLR, RLR and SII Between MS Attack and Non-Attack Groups.

CI, confidence interval; MS, multiple sclerosis; RLR, red blood cell distribution width to lymphocyte ratio; MLR, monocyte to lymphocyte ratio; NLR, neutrophil to lymphocyte ratio; SII, systemic immune inflammation index.

Whereas the means of urea, creatinine, hemoglobin, and hematocrit did not differ statistically significantly between the two groups, the means of glucose, alanine aminotransferase, aspartate aminotransferase, and C-reactive protein did (Table 3). Excellent diagnostic power in identifying MS relapse was demonstrated by NLR, RLR, MLR, and SII in ROC analysis (AUC: 0.87, 0.81, 0.86, and 0.87, respectively; Table 4).

Table 3. Evaluation of the Difference in Biochemistry and Hemogram Parameters Between Attack and Non-Attack Periods.

	Attack Period (Mean ± S.D.)	**Non-Attack Period (Mean ± S.D.)**	**Mean Difference (Mean ± S.D.)**	**95% Confidence Interval of the Difference**	**p**
Glucose	108.55 ± 27.99	100.37 ± 23,51	8.17 ± 28.74	3.76–12.59	<0.001
Urea	29.47 ± 10.16	27.83 ± 7.64	1.64 ± 10.15	0.75–3.19	0.4
Creatinine	0.96 ± 3.30	0.70 ± 0.23	0.25 ± 3.33	–0.26–0.76	0.33
ALT	28.87 ± 30.63	19.37 ± 14.02	9.46 ± 30.83	4.76–14.24	<0.001
AST	28.38 ± 22.29	20.95 ± 10.17	7.42 ± 20.74	4.2–10.61	<0.001
CRP	6.84 ± 8.46	4.88 ± 7.78	1.97 ± 10.38	0.3–3.56	0.02
WBC	9.76 ± 3.32	7.79 ± 2.03	1.97 ± 3.31	1.46–2.47	<0.001
HGB	12.98 ± 1.73	13.08 ± 1.71	–0.11 ± 1.72	–0.37–1.62	0.45
HCT	39.09 ± 4.78	39.34 ± 4.65	–0.25 ± 4.76	–0.98–0.48	0.5
PLT	270.25 ± 57.66	258.88 ± 56.08	11.37 ± 57.29	2.5–20.18	0.01
RDW	14.06 ± 1.51	13.47 ± 1.01	0.58 ± 1.26	0.39–0.78	<0.001
NEU	7.52 ± 3.11	4.99 ± 1.76	2.52 ± 3.31	2.01–3.03	<0.001
LYM	1.26 ± 0.61	2.11 ± 0.85	–0.85 ± 0.76	–0.96– (–0.72)	<0.001
MON	0.67 ± 0.26	0.54 ± 0.16	0.13 ± .025	0.09–0.17	<0.001
EOS	0.18 ± 0.14	0.15 ± 0.11	0.03 ± 0.14	0.01–0.05	<0.001
RLR	15.45 ± 12.06	7.68 ± 3.88	7.77 ± 11.61	5.98–9.55	<0.001
MLR	0.67 ± 0.43	0.30 ± 0.17	0.37 ± 0.43	0.31–0.44	<0.001
NLR	8.22 ± 7.35	2.81 ± 1.65	5.40 ± 7.25	4.29–6.52	<0.001
SII	2195.76 ± 2011.06	726.57 ± 457.92	1469.19 ± 1978.88	1165.01–1773.38	<0.001

Paired t test ($p < 0.05$ significance); S.D, standard deviation; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; WBC, white blood cells; HGB, hemoglobin; HCT, hematocrit; PLT, platelets; RDW, red cell distribution width; NEU, neutrophil; LYM, lymphocyte; MON, monocyte; EOS, eosinophil; RLR, RDW to lymphocyte ratio; MLR, monocyte to lymphocyte ratio; NLR, neutrophil to lymphocyte ratio; SII, systemic immune inflammation index.

Table 4. Diagnostic Accuracy of Inflammatory Parameters for Differentiation of Multiple Sclerosis (MS) Attack.

MS Attack :169 MS Non-Attack :169	**AUC**	**Cut-off**	**Sensitivity %**	**Specificity %**	**AUC 95% CI**	**p**	**PPV %**	**NPV%**
NLR	0.87	>3.33	84.6	76.9	0.83–0.90	<0.001	78.6	83.3
RLR	0.81	>8.56	75.1	72.8	0.76–0.85	<0.001	73.4	74.5
MLR	0.86	>0.36	82.25	77.51	0.82–0.89	<0.001	78.5	81.84
SII	0.87	>807.92	87.6	70.4	0.83–0.90	<0.001	74.7	85.1

AUC, Area under curve; SE, Standard error; PPV, positive predictive value; NPV, negative predictive value; CI, confidence interval; NLR, neutrophil to lymphocyte ratio; RDW, red cell distribution width; RLR, RDW to lymphocyte ratio; MLR, monocyte to lymphocyte ratio; SII, systemic immune inflammation index.

DISCUSSION

Determining whether people with RRMS who applied to the emergency room are experiencing an attack is important. The hunt for the ideal biomarker is still ongoing, even though numerous biomarkers have been employed for differential diagnosis. Despite the low cost of laboratory parameters derived from peripheral blood. In terms of diagnosis, biomarkers derived from cerebrospinal fluid (CSF) are more useful and readily available. CSF analysis is more expensive and necessitates greater technical expertise. Furthermore, there is a chance that issues will arise throughout process [17]. Thus, hematological inflammatory biomarkers that are inexpensive and simple to compute have become more popular. Recently, NLR – which stands for the ratio of neutrophils to lymphocytes – has been suggested as a useful and non-invasive peripheral biomarker to assess the systemic inflammatory status of several chronic inflammatory illnesses [18, 19]. Patients with MS attacks had greater NLR rates, according to our study. This might be because MS has an inflammatory mechanism that speeds up during attacks. In contrast to the health control group, Bisgaard et al. found that patients with optic neuritis and multiple sclerosis had greater NLR. Additionally, patients in relapse reported higher NLR than those in remission, which is consistent with our study [20].

According to Demirci et al., NLR has a 0.68 AUC, 67% sensitivity, and 97% specificity in predicting disease activity in MS.11.A high NLR was linked to disease activity in a retrospective analysis of RRMS patients at an MS clinic in Italy.10**.** In this study, NLR supported the literature by accurately predicting the MS active period. Peripherally activated T-cells in MS pathogenesis enlist a wide range of myeloid cells, including monocytes and macrophages, to stimulate and propel an inflammatory response, which frequently results in axonal transection and irreparable localized central nervous system (CNS) damage 2. LMR has been shown to be a possible prognostic factor for certain malignancies and a measure of the systemic inflammatory response [21]. The MLR was higher during attack periods in this study than during attack-free times, which could reflect the peripheral immunological status and the inflammatory condition in the central nervous system of multiple sclerosis. According to Hemond et al. High MLR was substantially linked to both brain atrophy and the physical disability status score (EDSS) in MS patients. In other words, when clinical and neuroimaging were subpar, MLR was high in MS [22]. Likewise, during the MS attack phase of this trial, when the clinic was worsened, MLR was elevated. SII is a novel inflammatory index that fully illustrates the equilibrium between the host's inflammatory and immunological states [23].

Heart failure, coronary artery disease, and poor outcomes for cancer patients have all been associated with high SII scores.15. But the partnership is unknown how SII and MS attacks differ. SII was found to be closely related to disease activity in this investigation. The peak of inflammatory activity during an MS attack may be linked to an all-encompassing inflammatory biomarker, such as SII, that is higher throughout this period. Inflammatory markers such homocysteine, parathormone, interleukin 4, and interleukin 17 were linked to MS disease activity and disability in a recent study [24]. One of the recently developed inflammatory indices is RLR. Wu et al. found that RLR predicts hepatic impairment in hepatitis E virus patients with excellent sensitivity and specificity [25]. According to Meng et al., RLR may forecast the intensity because of its great diagnostic specificity for primary biliary cirrhosis [26]. No prior research has examined the connection between RLR and MS attacks. The outcomes of this investigation showed that RLR was greater during the MS attack period.

LIMITATIONS

The minimal number of patients is our study's most significant shortcoming. The low incidence of MS disease in the general population and, consequently, the low number of emergency admittance to the department. One limitation of our study is its retrospective nature. However, we anticipate that long-term prospective studies will validate our findings.

Additionally, the study focused exclusively on patients with RRMS, excluding other forms of MS. As a result, our findings are solely applicable to RRMS. Furthermore, the association between the EDSS score and inflammatory markers could not be ascertained because it was not computed in the study.

Furthermore, it's unclear how long the MS attack started at the time of admission to the emergency room. Therefore, it's unclear when the hematological markers were collected throughout the attack time. The state of the relapses of the MRI lesions were excluded from the study, and the patient's history and clinical evaluation were assessed. The patients' treatment kind was not taken into consideration while evaluating their attack period status. Future research may look into this matter.

CONCLUSIONS

Finding RRMS patients who are experiencing an attack is critical in the emergency room. Inflammatory markers play a role in this process. Our results suggest that SII, MLR, NLR, and RLR could be useful in verifying the diagnosis of an attack in RRMS patients who arrive at the emergency room division. Large-scale research is necessary for more definitive findings, though.

Conflict of Interest

The authors declare no potential conflict of interest, and all authors confirm accuracy.

Informed Consent

All patients participating in this study signed a written informed consent form for participating in this study.

Patient Consent for Publication

Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

Ethics Approval and Consent to Participate

The study was performed after approval by the Ethics Committee of the Tribhuvan University Teaching Hospitals, Kathmandu. This study was carried out retrospectively under no (NP9812). The present study was conducted in line with the Declaration of Helsinki.

REFERENCES

1. Reich DS, Lucchinetti CF, Calabresi PA. Multiple sclerosis. Longo DL, editor. N Engl J Med. 2018;378(2):169–80.
2. Hemmer B, Kerschensteiner M, Korn T. Role of the innate and adaptive immune responses in the course of multiple sclerosis. Lancet Neurol. 2015;14(4):406–19.
3. Inojosa H, Schriefer D, Ziemssen T. Clinical outcome measures in multiple sclerosis: A Review. Autoimmune Rev. 2020;19(5):102512.
4. Olsson T, Barcellos LF, Alfredsson L. Interactions between genetic, lifestyle and environmental risk factors for multiple sclerosis. Nat Rev Neurol. 2017;13(1):26–36.
5. D'Amico E, Zanghì A, Gastaldi M, Patti F, Zivadinov R. Placing CD20–targeted B cell depletion in multiple sclerosis therapeutic scenario: Present and future perspectives. Autoimmune Rev. 2019;18(7):665–72.
6. De Bondt M, Hellings N, Opdenakker G, Struyf S. Neutrophils: Underestimated players in the pathogenesis of multiple sclerosis (MS). Int J Mol Sci. 2020;21(12):1–25.
7. Olsson A, Gustavsen S, Lauridsen KG. Neutrophil-to-lymphocyte ratio and CRP as biomarkers in multiple sclerosis: A systematic Review. Acta Neurol Scand. 2021;143(6):577–86.
8. Hasselbalch IC, Søndergaard HB, Koch-Henriksen N. The neutrophil-to-lymphocyte ratio is associated with multiple sclerosis. Mult Scler J Exp Transl Clin. 2018;4(3):2055217318813183.
9. Wang X, Qiu L, Li Z. Understanding the multifaceted role of neutrophils in cancer and autoimmune diseases. Front Immunol. 2018;9:2456.
10. D'Amico E, Zanghì A, Romano A, Patti F, Zivadinov R. The neutrophil-to-lymphocyte ratio is related to disease activity in relapsing-remitting multiple sclerosis. Cells. 2019;8(10):1114.
11. Demirci S, Demirci S, Kutluhan S. The clinical significance of the neutrophil-to-lymphocyte ratio in multiple sclerosis. Int J Neurosci. 2016;126(8):700–6.

12. Guzel I, Mungan S, Oztekin ZN, Ak F. Is there an association between the Expanded Disability Status Scale and inflammatory markers in multiple sclerosis? J Chin Med Assoc. 2016;79(1):54–7.
13. Thompson AJ, Banwell BL, Barkhof F, et al. Diagnosis of multiple sclerosis: 2017 revisions of the Mc Donald criteria. Lancet Neurol. 2018;17(2):162–73.
14. Brownlee WJ, Hardy TA, Fazekas F, Miller DH. Diagnosis of multiple sclerosis: Progress and challenges. Lancet. 2017;389(10076):1336–46.
15. Yaşar E, Bayramoğlu A. Systemic immune-inflammation index as a predictor of microvascular dysfunction in patients with cardiac syndrome X. Angiology. 2022;73(7):615–21.
16. Norman G. Likert scales, levels of measurement and the "laws" of statistics. Adv Health Sci Educ Theory Pract. 2010;15(5):625–32.
17. Ziemssen T, Akgün K, Brück W. Molecular biomarkers in multiple sclerosis. J Neuroinflammation. 2019;16(1):1–11.
18. Dirican N, Anar C, Kaya S. The clinical significance of hematologic parameters in patients with sarcoidosis. Clin Respir J. 2016;10(1):32–9.
19. Sen BB, Rifaioglu EN, Ekiz O. Neutrophil-to-lymphocyte ratio as a measure of systemic inflammation in psoriasis. Cutan Ocul Toxicol. 2014;33(3):223–7.
20. Bisgaard AK, Pihl-Jensen G, Frederiksen JL. The neutrophil-to-lymphocyte ratio as a disease activity marker in multiple sclerosis and optic neuritis. Mult Scler Relat Disord. 2017;18:213–7.
21. Hutterer GC, Sobolev N, Ehrlich GC. Pre-treatment lymphocyte-monocyte ratio as a potential prognostic factor in a cohort of patients with upper tract urothelial carcinoma. J Clin Pathol. 2015;68(4):351–5.
22. Hemond CC, Glanz BI, Bakshi R. The neutrophil-to-lymphocyte and monocyte-to-lymphocyte ratios are independently associated with neurological disability and brain atrophy in multiple sclerosis. BMC Neurol. 2019;19(1):23.
23. Li S, Liu K, Gao Y. Prognostic value of systemic immune-inflammation index in acute/subacute patients with cerebral venous sinus thrombosis. Stroke Vasc Neurol. 2020;5(4):368.
24. De Carvalho Jennings Pereira WL, Flauzino T, Alfieri DF. Immune-inflammatory, metabolic and hormonal biomarkers are associated with the clinical forms and disability progression in patients with multiple sclerosis: A follow-up study. J Neurol Sci. 2020;410:116630.
25. Wu J, Zhang X, Liu H. RDW, NLR, and RLR in predicting liver failure and prognosis in patients with hepatitis E virus infection. Clin Biochem. 2019;63:24–31.
26. Meng J, Xu H, Liu X. Increased red cell width distribution to lymphocyte ratio is a predictor of histologic severity in primary biliary cholangitis. Medicine (Baltimore). 2018;97(48):13403.

