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Investigation of the relationship between Cobb angle and inflammatory markers in patients with adolescent idiopathic scoliosis

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Abstract

Aim: The role of inflammation and immune system pathologies in Adolescent Idiopathic Scoliosis (AIS) has recently been the focus of research. It has been reported that the neutrophil/lymphocyte (NLR), platelet/lymphocyte (PLR) and monocyte/lymphocyte (MLR) ratios may be markers of inflammation severity. In addition, the systemic immune inflammation index (SII), including peripheral neutrophils, lymphocytes, monocytes and platelets, systemic inflammatory response index (SIRI) and systemic inflammation total index (AISI) are also known as inflammation marker indexes. This study aimed to investigate the relationship between NLR, PLR, MLR, SII, SIRI, AISI and Cobb angle in patients with AIS.

Materials and Methods: Pediatric patients aged 10-18 years who were requested to undergo scoliosis radiography with a preliminary diagnosis of AIS were retrospectively screened. Cobb angles, neutrophils, lymphocytes, platelets, monocytes, neutrophil percentage, white blood cells (WBC) and hemoglobin values were recorded. The NLR, PLR, MLR, SII, SIRI and AISI values were calculated. The patients were divided into four groups according to their Cobb angle. We examined whether there was a difference between the groups in terms of neutrophil, lymphocyte, platelet, monocyte, neutrophil percentage, WBC, Hemoglobin, NLR, PLR, MLR, SII, SIRI, AISI values. It was examined whether there was a correlation between the Cobb angle and NLR, PLR, MLR, SII, SIRI and AISI in patients diagnosed with scoliosis with a Cobb angle greater than 10°.

Results: A significant difference in NLR was observed between groups 2 and 4. A positive correlation was observed between groups 2, 3, and 4 patients with a Cobb angle greater than 0 and NLR; no correlation was observed between PLR, MLR, SII, SIRI and AISI.

Conclusion: NLR, which is associated with the severity of inflammation, is a marker that correlates with the scoliosis angle in patients with AIS. Larger-scale studies are needed to elucidate the relationship between AIS and the NLR.

Introduction

Idiopathic scoliosis is a three-dimensional deformity of the spine and the most common form is adolescent idiopathic scoliosis (AIS) [1, 2]. Various genetic, hormonal, metabolic and environmental factors play role in the development of AIS [3]. It is difficult to predict which child will develop AIS and who is at risk of curve progression, which limits the development of definitive treatments. The role of inflammation and immune system pathologies in individuals with AIS haves recently attracted attention [4,5,6].

Ratios and indices consisting of complete blood count parameters are important for inflammation and are being increasingly used in clinical practice. The inflammatory response can accelerate the production of neutrophils and apoptosis of lymphocytes, resulting in an increase in the number of neutrophils and a decrease in the number of lymphocytes.

Therefore, the neutrophil/lymphocyte ratio (NLR) is thought to be related to the severity of inflammation [7,8]. It has been reported that the platelet/lymphocyte ratio (PLR) and monocyte/lymphocyte (MLR) ratio, which includes platelets and monocytes, may also be indicators of inflammation severity [9,10] . In addition, the systemic immune inflammation index (SII), which includes peripheral neutrophils, lymphocytes, monocytes and platelets, systemic inflammatory response index (SIRI) and systemic inflammation total index (AISI) are also known as inflam-

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mation marker indices [11,12]. Recently, these indices have been investigated in many diseases. Atik et al. [13] observed similar MLR levels in patients and controls in their study of subclinical atherosclerosis in patients with psoriatic arthritis. Aktaş et al. [14] observed higher NLR in patients with Hashimoto's disease than in controls. Atik et al. [15] observed higher NLR and SII levels in rheumatoid arthritis patients with lung involvement than in those without.

There are relatively few studies on the relationship between the immune system and scoliosis. This study aimed to investigate the relationship between NLR, PLR, MLR, SII, SIRI, AISI and Cobb angle in individuals with AIS.

Materials and Methods

This retrospective study was conducted in accordance with the principles of the Declaration of Helsinki and approved by the Ethics Committee of the Faculty of Medicine of Fırat University (date: 02.05.2024 / number: 23903). Informed voluntary consent forms were obtained from all participants. Pediatric patients between the ages of 10 and 18 years; who were referred to Elazığ Fethi Sekin City Hospital Polyclinics for scoliosis radiography with a preliminary diagnosis of Adolescent Idiopathic Scoliosis between 01.01.2023 and 31.12.2023, were retrospectively screened. Patients whose hemogram was performed on the same day as the radiograph request were included in the study. Patients with known comorbidities were excluded from this study. Cobb angles were measured and recorded on the patients' scoliosis radiographs. Neutrophil, lymphocyte, platelet, monocyte, neutrophil percentage, white blood cell (WBC), and hemoglobin (Hgb) values were recorded. The NLR, PLR, MLR, SII, SIRI, and AISI values were calculated. The patients were divided into four groups according to their Cobb angle. Those whose angle is 0° are in the 1st group, those with 0°-10° are in the 2nd group, those with 10°-20° are in the 3rd group, and those whose temperature was above 20° are recorded as group 4.

The Hgb, WBC, neutrophil, lymphocyte, platelet, monocyte, and neutrophil percentage of all patients were recorded. The NLR, PLR, MLR, SII, SIRI and AISI values were calculated. NLR was calculated by dividing the neutrophil number by lymphocyte count, PLR by dividing the platelet number by lymphocyte count, and MLR by dividing the monocyte number by lymphocyte count. SII = [(platelet × neutrophil)/lymphocyte], SIRI = [(neutrophil × monocyte)/lymphocyte], and AISI = [(neutrophil x platelet x monocyte/lymphocyte)]. We examined whether there were a differences between groups in terms of neutrophil, lymphocyte, platelet, monocyte, neutrophil percentage, WBC, Hgb, NLR, PLR, MLR, SII, SIRI, and AISI values. In patients in groups 2, 3, and 4 whose Cobb angle was greater than 0°, we examined whether there was a correlation between the Cobb angle and NLR, PLR, MLR, SII, SIRI, and AISI.

Statistical analysis

All analyzes were conducted with the Statistical Package for Social Sciences software version 22 (SPSS, Inc., USA). Normal distribution of the data was tested with Kolmogorov-Smirnov test. Independent samples t-test was employed to compare the pairs. Repeated measures ANOVA was employed to compare more than two independent variables, and paired samples t-Test was employed to compare the dependent variables. Continuous variables are presented in means ± standard deviations, and categorical data are presented in percentages. $P<0.05$ was accepted statistically significant.

Results

Age, Hgb, WBC, neutrophil, lymphocyte, platelet, monocyte, neutrophil percentage, NLR, PLR, MLR, SII, SIRI, AISI values of all participants were examined. Age, Hgb and Neutrophil percentage showed normal distribution, while other values did not show normal distribution (Table 1, Table 2).

There were 24, 21, 31, and 24 patients in the 1st, 2nd, 3rd and 4th groups, respectively. No difference was observed between the groups in terms of age, Hgb, WBC, Neutrophil, Neutrophil percentage, PLT, Lymphocyte, Monocyte levels (Table 3).

The NLR, PLR, MLR, SII, SIRI, and AISI values were compared among the four groups. While a statistically significant difference was observed in the NLR, no significant difference was observed in other values (Table 4).

The correlation of Cobb angles of 76 patients in Groups 2, 3, and 4 with NLR, PLR, MLR, SII, SIRI, and AISI was analyzed. A correlation was observed between NLR and Cobb angle, but no correlation was observed between the others and Cobb angle (Table 5).

Discussion

Our study showed that NLR was correlated with the Cobb angle and that NLR reached statistical significance between the groups.

Although the etiology of scoliosis has not yet been elucidated, it is believed to be multifactorial. In recent years, molecular studies have been conducted for early diagnosis and treatment of scoliosis. Zhu et al. [13] suggested that vitamin D deficiency may disrupt calcium phosphate metabolism in the bones leading to AIS. Gallant et al. [14] reported a correlation between ghrelin and abnormal cartilage development in patients with AIS. Lowe et al. [15] emphasized in their study that platelet calmodulin levels are particularly related to paraspinous muscle activity and may be associated with the etiology and prognosis of scoliosis. Bertele et al. [16] showed a significant correlation between the Cobb angle and percentage values of beta-2 globulin and gamma globulin.

The relationship between inflammatory markers and scoliosis remains unclear. It is thought that degeneration of the vertebrae due to scoliosis may slightly increase inflammatory mediators in the blood. Hematological ratios (MLR, NLR, PLR, SII, SIRI and AISI) are measurements of chronic, lymphocyte-driven immune system responses reflected by lymphocyte counts. An increased hematological ratio may reflect an immunological imbalance between potential ongoing clinical or subclinical acute inflammation and compromised immune defense. The levels of these ratios may provide information regarding the Cobb angle.

Table 1. Analysis of data that does not show a normal distribution.

	n	Mean	Std. Deviation	Interquartile range	Median	95% Confidence Interval for Mean
Cobb	100	15.14	14.78	6.28	12.42	12.20-18.07
Neutrophil	99	4.38	2.14	2.77	3.81	3.96-4.81
Lymphocyte	100	2.54	1.084	1.90	2.35	2.32-2.75
Platelet	100	293.05	77.62	247.75	282	277.64-308.45
Monocite	100	0.75	0.90	0.45	0.60	0.57-0.93
WBC	100	7.64	2.56	5.80	7.15	7.13-8.15
NLR	100	1.97	3.62	0.78	1.19	1.255-2.69
PLR	100	142.47	106.06	91.84	111.26	121.42-163.51
MLR	100	0.40	0.98	0.18	0.24	0.20-0.60
SII	100	706.10	1131.79	295.72	414.21	481.52-930.67
SIRI	100	1.94	4.55	0.57	0.83	1.03-2.84
AISI	100	537.31	1063.71	161.15	241.65	326.24-748.37

WBC: White Blood Cell, NLR: Neutrophil/Lymphocyte PLR: Platelet/Lymphocyte MLR: Monocite/Lymphocyte SII: Systemic Immune Inflammation Index SIRI: Systemic Inflammatory Response Index and Systemic Inflammation Total Index (AISI).

Table 2. Analysis of data that does not show a normal distribution.

	N	Mean	Std. Deviation	95% Confidence Interval for Mean
Age	100	12.46	2.143	12.03-12.88
Neutrophil percentage	100	54.91	13.27	52.28-57.54
Hgb	100	13.80	1.33	13.53-14.06

Table 3. Demographic characteristics and hemogram values of the groups.

	1.Group (n=24)	2.Group (n=21)	3.Group (n=31)	4.Group (n=24)	P*
Age (mean±SD)	11.70±1.94	13.14±1.98	12.16±2.11	13.04±2.25	0.05
Cobb (mean±SD)	0	8.15±0.99	15.59±2.79	35.08±14.15	**0.00**
Hgb (mean±SD)	14.07±1.18	14.01±1.32 7	13.64±1.60	13.52±1.08	0.40
WBC (mean±SD)	8.48±3.40	.23±1.81	7.35±2.19	7.55±2.57	0.32
Neutrophil (mean±SD)	4.48±1.87	4.21±2.06	4.36±2.11	4.48±2.55	0.97
Neutrophil percentage (mean±SD)	55.64±11.14	52.31±15.26	55.73±11.74	55.39±15.62	0.79
Platelet (mean±SD)	290.75±91.97	272.80±44.56	293.61±59.83	312.33±101.53	0.40
Lymphocyte (mean±SD)	2.87±1.36	2.36±0.63	2.42±1.02	2.50±1.15	0.35
Monocite (mean±SD)	0.69±0.32	0.61±0.19	0.66±0.24	1.06±1.79	0.30

WBC: White Blood Cell *:Repeated Measures ANOVA. p<0.05 was considered statistically significant.

Few studies have investigated the relationship between scoliosis and inflammatory marker levels. In contrast to our study, Çelik et al. [17] did not observe a difference in NLR between the groups in their study. The results of our study show that NLR is associated with the Cobb angle in patients with AIS. The NLR is a parameter that can be easily measured in clinical practice and provides cheap and rapid results. Demonstrating the correlation between NLR and Cobb angle in patients with AIS may provide a new perspective on the relationship between inflammation and disease progression in AIS. Because the progression of AIS can be aggressive, it needs to be monitored. Noninva-

Table 4. Comparison of NLR, PLR, MLR, SII, SIRI, AISI values of the groups.

	1.group	2.group	3.group	4.group	P*
NLR	2.10±2.37	0.00±0.00*	2.15±1.49	3.33±6.52*	**0.02**
PLR	127.23±106.77	123.93±39.95	143.98±75.42	171.96±163.54	0.39
MLR	0.30±0.30	0.28±0.14	0.31±0.18	0.71±1.97	0.37
SII	615.79±702.36	529.78±325.50	638.74±484.21	1037.67±2112.9	0.42
SIRI	1.51±1.94	1.32±1.12	1.37±0.95	3.63±8.90	0.22
AISI	448.77±567.00	362.28±298.64	400.75±274.88	955.37±2032.01	0.17

*:When NLR was compared in the 2nd and 4th groups, p=0.011) *:Repeated Measures ANOVA. p<0.05 was considered statistically significant.
NLR: Neutrophil/Lymphocyte PLR: Platelet/Lymphocyte MLR: Monocite/Lymphocyte SII: Systemic Immune Inflammation Index.
SIRI: Systemic Inflammatory Response Index and Systemic Inflammation Total Index (AISI).

Table 5. Correlation analysis between Cobb angle and NLR, PLR, MLR, SII, SIRI, AISI.

		NLR	PLR	MLR	SII	SIRI	AISI
Cobb	r	0.576	0.093	-0.029	0.050	0.023	0.073
	P*	**0.000**	0.423	0.805	0.669	0.843	0.528

NLR: Neutrophil/Lymphocyte PLR: Platelet/Lymphocyte MLR: Monocite/Lymphocyte SII: Systemic Immune Inflammation Index
SIRI: Systemic Inflammatory Response Index and Systemic Inflammation Total Index (AISI). *:Spearman-rho test. p<0.05 was considered statistically significant.

sive methods such as 3D ultrasound have been suggested to prevent repeated X-ray exposure during follow-up [18]. Undoubtedly, important molecular, genetic, and inflammatory biomarkers are needed for scoliosis monitoring or for the early period before scoliosis development. In our study, the high NLR observed in the group with the highest Cobb angle suggests that the NLR can be used as a marker to predict progression. However, in our study, it was not known whether the difference in NLR between the groups is due to an inflammatory mechanism that causes scoliosis or develops as a result of scoliosis.

Conclusion

NLR, which is known to be associated with the severity of inflammation, is a marker that correlates with the scoliosis angle in patients with AIS. Larger-scale studies are needed to elucidate the relationship between AIS and the NLR.

Ethical approval

Approval was received from the Fırat University Faculty of Medicine Ethics Committee for this retrospective study (date: 02.05.2024/number: 23903).

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