CLINICAL STUDY

What is the neutrophil/lymphocyte ratio in sarcoidosis?

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ABSTRACT

AIM: Information regarding the Neutrophil/Lymphocyte ratio (NLR) in sarcoidosis and the data from studies recommending its use as an indicator of inflammation and in the differential diagnosis and prognosis, are limited. With this study, it was aimed to obtain data regarding the NLR level in the patients at the time of presentation to the hospital and to determine the characteristics of patients in whom the NLR value was > 2.

RESULTS: During the study period, of the 3434 patients with the sub-diagnosis of D86, 1300 cases whose complete blood count values had been recorded at the time of presentation were included in the study. Of the cases, 40 % were pulmonary sarcoidosis, 7 % were pulmonary sarcoidosis with sarcoidosis of the lymph nodes, 8 % were lymph node sarcoidosis, 1 % were sarcoidosis, of other combined areas, and 40 % of the cases were sarcoidosis that were unspecified. The F/M of the cases were 947/353, and the average age of the cases was 44. When the sarcoidosis groups were grouped into NLR < 2 (Group 1) and NLR ≥ 2 (Gorup 2), 27 % were Group 1, 73 % were Group 2, and a significant correlation was found between the two groups. When the inflammatory indicators were compared with NLR, the PLT/MPV was found to be statistically insignificant, and the ACE, ESR and CRP were found to be statistically significant.

CONCLUSION: The Neutrophil/Lymphocyte ratio in the complete blood count, which is an easy and cheap test, can be used as an indicator of inflammation in Sarcoidosis. In clinical practice, wide-based studies comprising the activity and the staging in the prognosis of sarcoidosis are required *(Tab. 2, Fig. 2, Ref. 26)*. Text in PDF *www.elis.sk*.

KEY WORDS: sarcoidosis, neutrophil/lymphocyte ratio, value.

Introductıon

Sarcoidosis is a multi-systemic, inflammatory, and granulomatous disease, the etiology of which is unknown (1). Determination of its activity and severity is important with regard to the prognosis. While the clinical, radiological and the physiological parameters are used in the follow-up of the disease, the use of serum indicators consistent with the afore-mentioned gains importance (1, 2, 3). It is known that there are studies that have demonstrated an increase in various parameters and indicators in active disease, such as angiotensin converting enzyme (ACE), adenosine deaminase (ADA), total IgE, neopterin, and an increase in lymphocytes in bronchoalveloar lavage fluid (4, 5, 6).

The Neutrophil/Lymphocyte Ratio (NLR) in the complete blood count, which is a very cheap and easy-to-perform test, is used as an inflammatory indicator in pulmonary and other malignancies, in acute coronary syndrome and in the determination of the prognosis in critically ill patients at the intensive care unit (7–11). The significance of NLR in the diagnosis, follow-up and activity in sarcoidosis is not precisely known. However, there is a limited number of studies that recommend the utilization of Neutrophil/

Lymphocyte ratio in the differential diagnosis and determination of the prognosis (12, 13).

In this study, it was aimed to find an answer to the question whether the Neutrophil/Lymphocyte ratio, which is an indicator of inflammation in sarcoidosis, is as effective as other indicators in the follow-up of inflammation, and the factors that affect this ratio. The center at which this study was performed, is a hospital of approximately 1000 beds in capacity and is a pulmonology training center, which is a good center in its field.
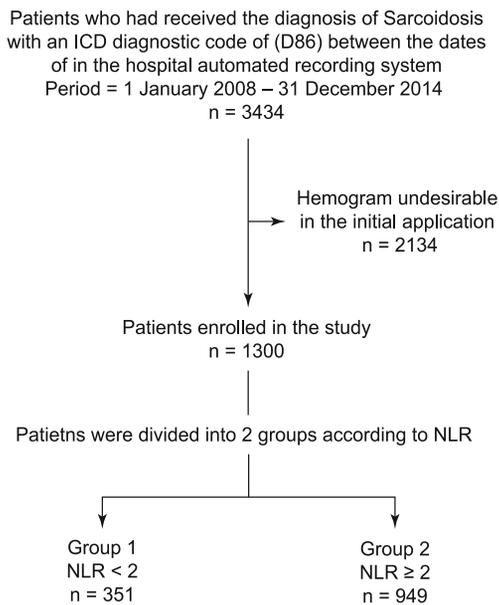
Methods

Patients

Patients who had received the diagnosis of Sarcoidosis with an ICD diagnostic code of D86 between the dates of 1 January 2008 – 31 December 2014 in the hospital automated recording system, and whose data were evaluated and determined to comply with all of the inclusion criteria, were included in the study (Flow chart, Fig. 1).

The study was approved by the local Ethics Committee of the Institution and it was conducted in accordance with the ethical principles stated in the Declaration of Helsinki. Since our study was a retrospective study, and due to the high number of patients in the study, as the patients could not be summoned again, patient consent forms were not obtained. On the condition that the patients' identities would remain confidential the use of the data was agreed by the hospital's academic committee.

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Patients who had received the diagnosis of Sarcoidosis
with an ICD diagnostic code of (D86) between the dates
of in the hospital automated recording system
Period = 1 January 2008 – 31 December 2014
n = 3434

Hemogram undesirable
in the initial application
n = 2134

Patients enrolled in the study
n = 1300

Patietns were divided into 2 groups according to NLR

Group 1
NLR < 2
n = 351

Group 2
NLR ≥ 2
n = 949

Fig. 1. Flow chart of patients enrollment.

Definitions

Clinical definition of D86 in the ICD Codes and its sub-diagnoses in the hospital automation system:

D86.9 Sarcoidosis unspecified: Investigations are performed with the suspicion of sarcoidosis; however, cases that have not been proven histopathologically;

D86.0 Pulmonary Sarcoidosis: Cases in which the diagnosis of sarcoidosis has been proven histopathologically and with involvement of the pulmonary parenchyme;

D86.1 Lymph Nodes Sarcoidosis: Cases in which the diagnosis sarcoidosis has been proven histopathologically and with mediastinal lymphadenoapthy;

D86.2 Pulmonary Sarcoidosis together with Lymph Nodes Sarcoidosis: Cases in which the diagnosis sarcoidosis has been proven histopathologically and with mediastinal lymphadenoapthy and pulmonary parenchymal involvement;

D86.8 Sarcoidosis, in other organs: Cases in which the diagnosis sarcoidosis has been proven histopathologically (eye, skin, neurosarcoidosis, arthritis);

Following the determination of patients with D86 diagnostic codes within the indicated time period in the hospital records, those without complete blood count parameters were excluded from the study.

Data

The age, gender, hematological and the biochemistry parameters of the patients who had been found to comply with the study inclusion criteria, were evaluated and the NLR was calculated. The NLR ratio was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count (12, 13).

Statistical analysis

The descriptive statistical data were given as frequency, percentage, mean and standard deviation (SS). In the study groups (in sarcoidosis cases with NLR of 2 and higher and those without), for the recorded data, the continuous numerical values (age and complete blood count values) were compared using the Student-T test or the Mann–Whitney-U test according to the parametric/non-parametric data, and the binary variants (gender, mortality) were compared using the Ki-Square test. A p-value of < 0.05 was accepted as statistically significant for the statistical analyses. The SPSS-20 portable package program was used to perform the statistical analyses.

Results

During the period of the study, 1300 cases with the diagnosis code of sarcoidosis D86 in the hospital records sytem were included in the study. The majority of our cases were women and over 40 years of age. The demographic features of the cases and the distribution of the sarcoidosis groups have been demonstrated in Table 1.

When the sarcoidosis cases were grouped into NLR < 2 (Group 1) and NLR ≥2 (Group 2), 27 % of the cases constituted the Group 1, and 73 % constituted the Group 2. The distribution according to the subgroups of Sarcoidosis is shown in Table 2.
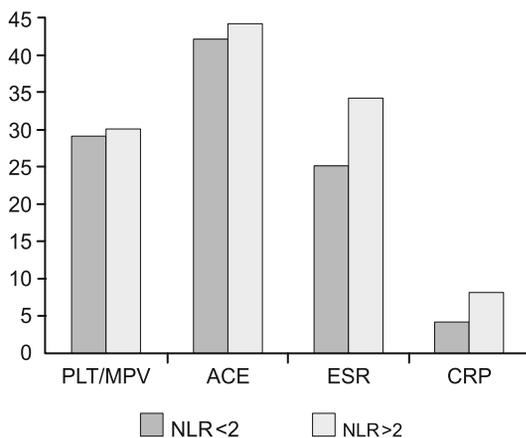
When the inflammatory indicators (PLT/MPV, ACE, ESR, CRP) were compared with the NLR groups, while the PLT/MPV ratio was found to be statistically insignificant, ACE, ESR and CRP were found to be statistically significant (p < 0.01) (Fig. 2).

Tab. 1. Demographic features of the cases and distribution of the Sarcoidosis groups.

	n	%
Female	947	73
Age, mean	1300	44
Pulmonary Sarcoidosis	514	40
Pulmonary Sarcoidosis, together with Sarcoidosis of the Lymph Nodes	90	7
Sarcoidosis of the Lymph Nodes	109	8
Sarcoidosis, other and of combined locations	16	1
Sarcoidosis, unspecified	571	44

Tab. 2. The distribution of Group 1 and Group 2 according to the subgroups of Sarcoidosis.

	NLR<2 Group 1 n=351	NLR>2 Group 2 n=949	p
Pulmonary Sarcoidosis	145 (28)	369 (72)	
Pulmonary Sarcoidosis, together with Lymph Nodes Sarcoidosis	24 (27)	66 (73)	
Lymph Nodes Sarcoidosis	34 (31)	75 (69)	0.27
Sarcoidosis, other and of combined locations	7 (44)	9 (56)	
Sarcoidosis, unspecified	141 (25)	430 (75)	

Fig. 2. Comparison between the NLR groups and the inflammatory indicators (PLT/MPV, ACE, ESR, CRP).

Discussion

In this study, the NLR in Sarcoidosis cases has demonstrated a correlation with ACE, ESR and CRP. It was determined in this study that like other indicators of inflammation, NLR can be used to demonstrate inflammation. NLR was found not to demonstrate a significant difference with regard to gender in sarcoidosis and sarcoidosis subgroups.

Gender and sarcoidosis

Sarcoidosis is observed more frequently in women than in men (1, 14). In series reported with regard to sarcoidosis, as in this study, the numbers of female cases have been higher (15, 16, 17).

Age and sarcoidosis

In spite of the fact that sarcoidosis is observed in all age groups, it is seen more frequently under the age of 40. In particular, the disease peaks between the ages of 20 and 29 (1). There are studies reporting that the disease makes a second peak between the ages of 50 and 65 (14, 18). The mean age of the cases in this study was found to be 44.

Inflammatory markers and sarcoidosis

In the follow-up of sarcoidosis, along with the easy and cheap inflammatory marker tests used routinely, such as ESR, CRP and ACE, there is a limited number of studies recommending the use of Interleukin 18 (IL-18), serum Amyloid A (SAA) and serum soluble Interleukin 2 receptor (sIL2R), which are expensive and for which a difficult technique is required. (2, 6, 19, 20).

In the study carried out in 56 cases in stage 0–1, 60 cases in stage 2–3, making a total of 116 sarcoidosis cases, by Dirican et al which demonstrated the importance of hematological parameters in sarcoidosis, they found the NLR in sarcoidosis cases to be higher than that in the control group, and as in this study, NLR was determined to be correlated with ESR (13). Again, in the same study, in 20 of the 32 cases that had extrapulmonary involvement,

NLR was determined to be ≥2, and this ratio was found to be statistically significant (p = 0.031). In our study, no statistically significant difference was determined in the Sarcoidosis subgroups with regard to the NLR.

In studies carried out with regard to the contribution of inflammatory markers to the diagnosis and prognosis, a positive correlation has been reported between NLR and CRP in malignancy, pneumonia and COPD. In the study of Iliaz et al, NLR was determined to be significantly high in the sarcoidosis and tuberculosis groups compared to the control group (21–24, 12). In our study, a significant correlation was found between NLR and CRP.

The serum ACE value has been used for many years in the follow-up of Sarcoidosis activity, but its specificity is relatively low. The increased serum ACE levels can also be observed in granulomatous diseases other than Sarcoidosis (25, 26). In the study of Dirican et al, they determined that as the stage of the disease increased, the serum ACE level also increased, and they found this situation to be statistically significant. Furthermore, they found no correlation between ACE and NLR, and they attributed this situation to the low number of cases (13). Furthermore, in another study demonstrating the relationship between Sarcoidosis and NLR, a correlation was determined between ACE and NLR (12). In our study, a correlation has been found between ACE and NLR in Sarcoidosis, and this condition may be related to the high number of our cases.

There are a few limitations in our study. The first, due to the study being a retrospective study, there are missing data. However, due to the high number of our cases and the data having been obtained from an electronic environment, and since there was no "entering mistake", it can be said that our study provides beneficial information to clinical applications. The second limitation is that there were no records of the staging and severity of the disease in sarcoidosis patients. Due to the fact that the cases were integrated into the study automatically from the hospital data record system, the stage and the activities were not determined. However, since the NLR value was not researched in the sarcoidosis activity, we do not think that our results have been affected. Together with this, the NLR values of patients having received the diagnosis of sarcoidosis have been recorded at the time of presentation to the hospital. The patients having presented due to primary sarcoidosis rather than an elective or another acute disease, has been deduced from the fact that there were no records of active pneumonia and other acute disorders in the secondary and tertiary diagnoses.

The strength of the study is that it provided information regarding the NLR in a high number of patients with sarcoidosis. Despite a limited number of studies regarding the NLR values in sarcoidosis patients, there is an insufficient number of studies carried out in a wide sarcoidosis group of patients. (12,13).

As a result, NLR can be used as an easily and cheaply measurable marker that demonstrates inflammation in Sarcoidsosis. In clinical practice, wide-based studies including the activity and the staging are required in order to secure its place in determining the prognosis of sarcoidosis. We think that the data in our study will shed light onto future studies with regard to data and methods. Studies demonstrating the relationship of NLR staging and activity will extend the use of NLR in clinical practice.

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