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The Role of Neutrophile-Lymphocyte and Platelet- Lymphocyte Ratios in the Differential Diagnosis of Idiopathic Pulmonary Fibrosis and Chronic Hypersensitivity Pneumonia

İdiopatik Pulmoner Fibroz ve Kronik Hipersensitivite Ayırıcı Tanısında Nötrofil-Lenfosit ve Platelet-Lenfosit Oranının Rolü

Eda Bayramiç[1], Özer Özdemir[2], Ömer Selim Unat[3], Damla Serçe Unat[2], Tarık Şimşek[2], Fatma Demirci Üçsular[2-4], Gülru Polat[2-4]

[1]Corum Hospital of Chest Diseases, Department of Pulmonology, Corum, Turkey
[2]University of Health Sciences, Turkey, Izmir Dr Suat Seren Training and Research Hospital, Department of Chest Diseases and Surgery. Izmir, Turkey
[3]Ege University, Department of Pulmonology, Izmir, Turkey
[4]University of Health Sciences, Turkey, Izmir Faculty of Medicine, Pulmonology, Izmir, Turkey

Abstract

Aim: Idiopathic pulmonary fibrosis (IPF) and chronic hypersensitivity pneumonitis (CHP) are interstitial lung diseases with overlapping clinical and radiological features, making differential diagnosis challenging. Inflammatory biomarkers such as neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have been investigated in various diseases. This study aims to evaluate the role of NLR and PLR in distinguishing IPF from CHP.

Materials and Methods: This multidisciplinary study included patients diagnosed with IPF and CHP. The neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios were calculated from blood samples obtained at the time of diagnosis. Demographic characteristics, laboratory parameters, and comorbidities were extracted from hospital records. Statistical analyses were performed to compare NLR and PLR values between the study groups and a healthy control group.

Results: Our results indicate that NLR values were significantly higher in both IPF and CHP groups compared to the healthy control group. However, there was no statistically significant difference between IPF and CHP groups, suggesting that NLR and PLR are not reliable markers for differentiating these diseases.

Conclusion: It was concluded that the NLR value was increased in both diseases, but it did not have a differential role for the two diseases. There are still no effective biomarkers in the differential diagnosis and studies are needed on this subject.

Keywords: Idiopathic pulmonary fibrosis; chronic hypersensitivity pneumonitis; neutrophil-to-lymphocyte ratio; platelet-to-lymphocyte ratio; inflammatory biomarkers

Öz

Amaç: İdiyopatik pulmoner fibrozis (IPF) ve kronik hipersensitivite pnömonisi (CHP), klinik ve radyolojik olarak benzer özellikler gösteren interstisyel akciğer hastalıklarıdır ve ayırıcı tanıları zorludur. Nötrofil-lenfosit oranı (NLR) ve trombosit-lenfosit oranı (PLR) gibi inflamatuar biyobelirteçler, çeşitli hastalıklarda araştırılmıştır. Bu çalışmanın amacı, NLR ve PLR'nin IPF ile CHP'yi ayırt etmedeki rolünü değerlendirmektir.

Gereç ve Yöntemler: Bu multidisipliner çalışmada, IPF ve CHP tanısı alan hastaların tanı anında alınan kan örneklerinden nötrofil-lenfosit ve trombosit-lenfosit oranları hesaplandı. Hastane kayıtlarından demografik özellikler, laboratuvar parametreleri ve ek hastalıklar analiz edildi. Çalışma grupları ile sağlıklı kontrol grubu arasındaki NLR ve PLR değerlerini karşılaştırmak için istatistiksel analizler yapıldı.

Bulgular: Çalışmamızda hem IPF hem de CHP gruplarında NLR değerlerinin sağlıklı kontrol grubuna kıyasla anlamlı derecede yüksek olduğu gözlemlendi. Ancak, IPF ve CHP grupları arasında istatistiksel olarak anlamlı bir fark bulunamadı. Bu durum, NLR ve PLR'nin bu iki hastalığın ayırıcı tanısında güvenilir biyobelirteçler olmayabileceğini göstermektedir.

Sonuç: Nötrofil-lenfosit oranı değerinin her iki hastalıkta da arttığı ancak iki hastalık için ayırıcı bir rolü olmadığı sonucuna varılmıştır. Ayırıcı tanıda hala etkili biyobelirteçler yoktur ve bu konuda çalışmalara ihtiyaç vardır.

Anahtar sözcükler: İdiyopatik pulmoner fibrozis; kronik hipersensitivite pnömonisi; nötrofil-lenfosit oranı; trombosit-lenfosit oranı; inflamatuar biyobelirteçler

Corresponding Author: Damla Serçe Unat
University of Health Sciences, Turkey, Izmir Dr Suat Seren Training and Research Hospital,
Clinic of Chest Diseases and Surgery. Izmir, Turkey
E-mail: sercedamla@gmail.com
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INTRODUCTION

Interstitial lung diseases (ILD) are a group of diseases with similar clinical, radiological and pathological features. Although it develops with diseases such as various drugs, exposure to some inorganic or organic antigens, and collagen vascular disease, they can sometimes be idiopathic (1).

Idiopathic pulmonary fibrosis (IPF) is the most common form of idiopathic interstitial pneumonias with a poor prognosis causing progressive fibrosis of the lungs. (2). This fibrotic process results in characteristic usual interstitial pneumonia (UIP) pattern on computed tomography images and pathological lung biopsies of the patients. However, UIP-like patterns may also be seen in other fibrotic diseases, like chronic hypersensitivity pneumonitis (HP) (3). HP is one of the diseases that can be detected in acute or chronic conditions after exposure in susceptible individuals and may be responsible for lung fibrosis in the chronic stage. Chronic hypersensitivity pneumonitis (CHP) may often be misdiagnosed as IPF due to radiological and histological similarities (3).

Many biomarkers are used to make differential diagnosis of diseases, predict prognosis, and evaluate treatment response is being investigated. Biomarkers that are easily accessible, reliable and cheap and that give fast results are usually preferred. However, there is not any reliable biomarker that may be used in differential diagnosis of chronic HP and IPF.

In this study, the role of neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) in the differential diagnosis of IPF and CHP was investigated. NLR and PLR are markers of inflammation and oxidative stress. We hypothesized that these parameters may be different in IPF where inflammation is less pronounced in the pathogenesis, and chronic HP, in which inflammation plays more role in the pathogenesis of the disease although wanes in late phases of disease.

MATERIALS and METHODS

Ethical approval was obtained from the local ethics committee (28.06.2021/39050). Patients diagnosed with IPF and CHP, according to multidisciplinary discussion in the tertiary level Chest Diseases Hospital between January 2013 and December 2018 were included in the study. Hospital electronic data records and laboratory data of the hospitalized patients were analyzed retrospectively. Neutrophil-to-lymphocyte ratio and Platelet-to-lymphocyte ratio were derived from complete blood counts of the included patients that were calculated from the blood samples taken at the time of diagnosis of patients. The patients were examined together with clinical, imaging methods and histopathological diagnoses.

Patient Selection: Patients diagnosed with IPF and chronic HP with compatible radiological and/or histological findings and multidisciplinary team evaluation were screened for inclusion in the study. These patients were included in the IPF group after reevaluation and verification of diagnosis according to the IPF diagnosis guideline published jointly by ATS/ERS/JRS/ALAT in 2018 (2). Patients with diagnosis of chronic HP were also reevaluated according to the guideline for the diagnosis of hypersensitivity pneumonia in adults, jointly published by ATS/JRS/ALAT in 2020 (3). A control group was formed with 94 healthy individuals who applied to our hospital's outpatient clinic and did not have any lung disease. Patient selection and patient population were schematized in Figure 1 (for IPF group) and Figure 2 (for CHP group). Complete blood count was analyzed by spectrophotometric / impedance (Beckman Coulter LH 780 Analyzer; Beckman Coulter, Inc., CA, USA) method in our hospital laboratory. Data regarding demographic characteristics, laboratory examination, spirometric analyses and comorbidities were derived from hospital records.

Statistics: Statistical analysis was performed using 'SPSS 18.0 for Windows-Chicago, USA'. The results were presented as means ± standard deviation, median, and minimum - maximum. Shapiro-Wilk and Kolmogorov-Smirnov normality tests were used to determine the normality distribution of continuous data. To evaluate whether there was a statistical difference in the parameters examined in the IPF, CHP and control groups, Analysis of Variance (one-way ANOVA) was used for data with normal distribution, and Kruskal-Wallis test was used for data that did not. Student's t-test was used for parametric results and Mann-Whitney U test was used for non-parametric results in pairwise comparisons of groups. Chi-square and Fisher's exact test were used to compare categorical data between groups, and results were given as numbers and percentages (%). Spearman Correlation was used for results showing normal distribution of the relationship between continuous variables, and Pearson Correlation coefficient was used for results not showing normal distribution. Receiver Operating Characteristic (ROC) analysis was performed to evaluate the effectiveness of NLR and PLR in predicting the separation of sick people from healthy individuals, and the most appropriate cut-off value was determined according to Youden index. $P<0.05$ was considered statistically significant in all tests.

Figure 1. Patient selection and patient population were schematized in for IPF group.

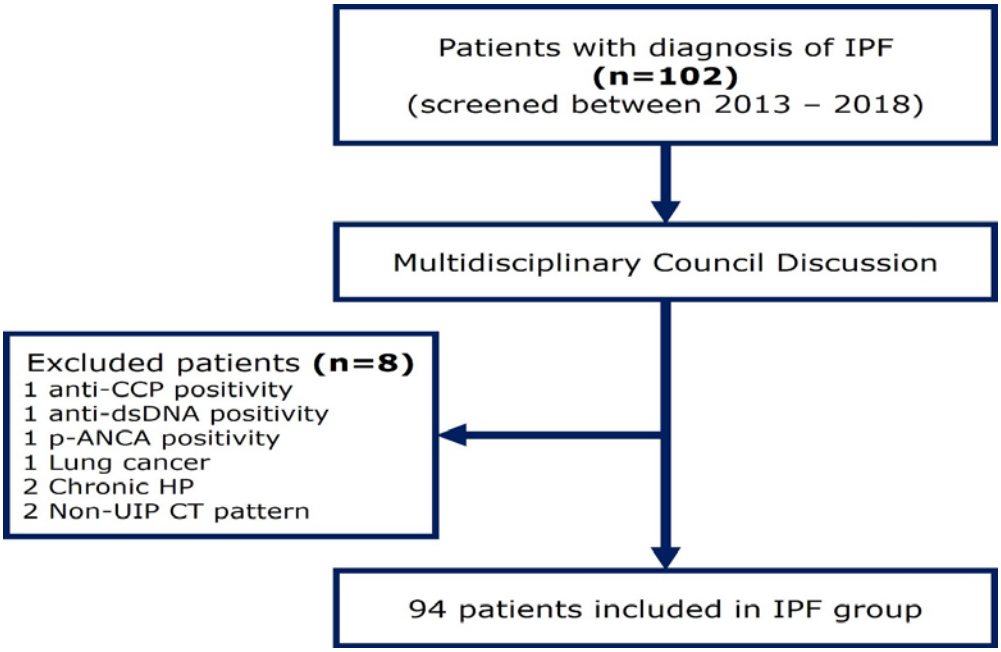
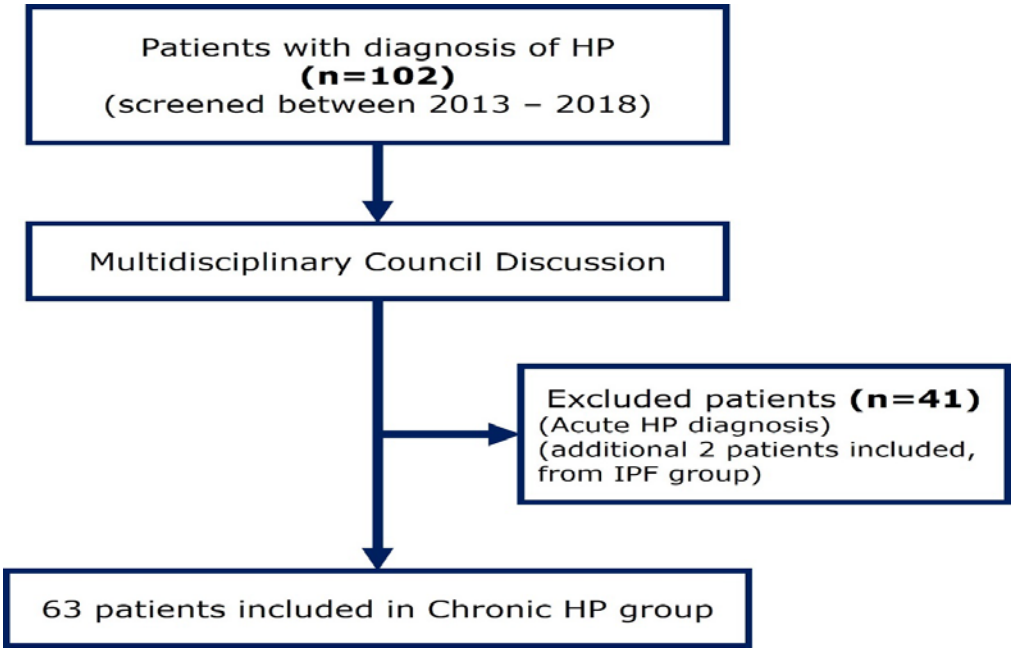


Figure 2. Patient selection and patient population were schematized in for CHP group.



RESULTS

Among the patients diagnosed with IPF, 76 (80.9%) were male, 18 (19.1%) were female; 33 (52.4%) patients with CHP were male and 30 (47.6%) were female. There was a statistically significant difference between the two groups in terms of gender and most of the males were in the IPF group ($p<0.001$).

In the control group, 47 (50%) men and 47 (50%) women were equal in number. The median age was 68 (49-80) in the IPF group, 67 (42-88) in CHP, and 53.5 (41-69) in the control group. There was no significant difference between the IPF and CHP groups in terms of age ($p=0.627$). Comparison of laboratory parameters of IPF and CHP groups is presented in Table 1.

Table 1. Comparison of IPF and CHP complete blood count, sedimentation, and CRP parameters

Parameters	IPF (n=94)	CHP (n=63)	*p*
Hemoglobin; gr/dl, mean ± SD	13.97±1.60	13.57±2.05	0.198
Hematocrit; %, mean ± SD	41.83±4.46	40.94±5.74	0.303
MCV fL, mean ± SD	86.71±6.66	84.43±7.60	0.048
RDW, %	14.25 (11.90-20.70)	14.20 (12.20-20.30)	0.534
MPV, fL	8.20 (6.00-12.00)	8.50 (5.90-12.60)	0.374
PDW, %	16.80 (15.90-19.00)	16.90 (11.50-19.00)	0.311
Leukocyte; x10.3/uL, mean ±SD	8.84 ±2.20	8.86 ±2.12	0.837
Neutrophil, x10.3/uL	5.20 (2.50-12.00)	5.10 (2.20 -10.10)	0.645
Neutrophil, %	62.80 ±8.59	63.71 ±9.59	0.536
Lymphocytex,10.3/uL	2.10 (0.80-4.70)	2.20 (0.50-4.50)	0.681
Lymphocyte; %, mean ± SD	25.89 ±7.50	24.94 ±8.89	0.470
Platelet, 10.3/uL	260.000 (91.000-640.000)	266.000 (125.000-567.000)	0.662
Eosinophil, x10.3/uL	200 (0.00-800)	300 (0.00-6000)	0.324
Eosinophil, %	2.80 (0.10-25)	2.90 (0.00-14.80)	0.806
NLR	2.58 (0.89-10)	2.53 (0.93-17.80)	0.513
PLR	118.850 (43.33-432.73)	120.00 (37.88-465.83)	0.355
Sedimentation; mm/h, mean ± SD	9.39 ±5.38	13.88 ±8.91	0.006
CRP, mg/L	0.49 (0.03-8.85)	0.60 (0.05-14.15)	0.126

Data are presented as median (min-max) if otherwise is not stated. IPF: İdiopathic pulmonary fibrosis, CHP: Chronic hypersensitivity pneumonia, MCV: Mean corpuscular volume, RDW: Erythrocyte distribution width, MPV: Mean platelet volume, PDW: Platelet distribution width, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte ratio, CRP: C-reactive protein.

Both groups had a similar rate of comorbidities. At least one comorbidity was present in 49 (52.1%) of IPF patients, and 29 (46%) of chronic HP patients (p=0.52). However, cardiovascular diseases seen more among IPF patients (n=22 (23.4%) vs. n=5 (7.9%), p= 0.02). The median NLR value was 2.58 (min:0.89 - max:10) in the IPF group, and 1.67 (min: 0.69 - max: 3.83) in the control group (p<0.001). When the ROC analysis was performed between the two groups, the NLR cut-off value was 2.41 and the sensitivity was found to be 54.26%, the specificity 87.23%, AUC 0.756, p<0.001. Results are given in Table 2.

The median NLR value was 2.23 (min:0.93-max:17.83) in the CHP group, and 1.67 (min:0.69-max:3.83) in the control group. (p<0.001). When the ROC analysis was performed between the two groups, the NLR cut-off value was 2.27, and the sensitivity was 61.9%, the specificity was 80.9%, AUC: 0.766, p<0.001.

Although NLR values showed statistically significant differences between patient and control groups, the PLR values did not demonstrate significant discriminatory power in our cohort. Therefore, ROC analysis was not performed for PLR. Results are given in Table 3.

Table 2. Comparison of hemogram parameters of IPF and control groups.

Parameters	IPF (n=94)	Control (n=94)	*P*
Hemoglobin, gr/dl, mean ± SD	13.97±1.60	13.83 ±0.85	0.464
Hematocrit, %, mean ± SD	41.83±4.46	41.96 ±2.66	0.810
MCV, fL, mean ± SD	86.71±6.66	87.47 ±4.19	0.352
RDW, %	14.25 (11.90-20.70)	13.20 (11.20-16.10)	< 0.001
MPV, fL	8.20 (6.00-12.00)	8.60 (6.60-10.50)	0.005
PDW, %	16.80 (15.90-19.00)	16.80 (14.30-22.00)	0.268
Leukocyte; x10.3/uL, mean ± SD	8.84 ±2.20	7.10 (3.90-9.60)	< 0.001
Neutrophil x10.3/uL,	5.20 (2.50-12.00)	3.90 (1.90-6.90)	< 0.001
Neutrophil, %, mean ± SD	62.80 ±8.59	56.08 ±7.61	< 0.001
Lymphocyte x10.3/uL	2.10 (0.80-4.70)	2.40 (1.20-3.60)	0.036
Lymphocyte, %, mean ± SD	25.89 ±7.50	33.27 ±6.71	< 0.001
Plateletx10.3/uL	260.000 (91.000-640.000)	262.00 (167.00-445.00	0.401
Eosinophil x10.3/uL	200 (0.00-800)	0.20 (0.00-0.50)	< 0.001
Eosinophil, %	2.80 (0.10-25)	2.20 (0.20-6.30)	0.017
NLR	2.58 (0.89-10)	1.67 (0.69-3.83)	< 0.001
PLR	118.850 (43.33-432.73)	115 (51-233)	0.657

Data are presented as median (min-max) if otherwise is not stated. IPF: Idiopathic pulmonary fibrosis, CHP: Chronic hypersensitivity pneumonia, MCV: Mean corpuscular volume, RDW: Erythrocyte distribution width, MPV: Mean platelet volume, PDW: Platelet distribution width, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet lymphocyte ratio.

Table 3. Comparison of hemogram parameters of CHP and control groups

Parameters	CHP (n=63)	Control (n=94)	*P*
Hemoglobin, gr/dl, mean ± SD	13.57±2.05	13.83 ±0.85	0.343
Hematocrit, %, mean ± SD	40.94±5.74	41.96 ±2.66	0.193
MCV, fL, mean ± SD	84.43±7.60	87.47 ±4.19	0.005
RDW, %	14.20 (12.20-20.30)	13.20 (11.20-16.10)	< 0.001
MPV, fL	8.50 (5.90-12.60)	8.60 (6.60-10.50)	0.187
PDW, %	16.90 (11.50-19.00)	16.80 (14.30-22.00)	0.058
Leukocyte x10.3/uL, mean SD	8.86 ±2.12	7.10 (3.90-9.60)	< 0.001
Neutrophil x10.3/uL	5.10 (2.20 -10.10)	3.90 (1.90-6.90)	< 0.001
Neutrophil, %, mean ± SD	63.71 ±9.59	56.08 ±7.61	< 0.001
Lymphocyte x10.3/uL	2.20 (0.50-4.50)	2.40 (1.20-3.60)	0.066
Lymphocyte, %, mean ± SD	24.94 ±8.89	33.27 ±6.71	< 0.001
Platelet x10.3/uL	266.000 (125.000-567.000)	262.00 (167.00-445.00	0.791
Eosinophil x10.3/uL	300 (0.00-6000)	0.20 (0.00-0.50)	0.000
Eosinophil, %	2.90 (0.00-14.80)	2.20 (0.20-6.30)	0.042
NLR	2.53 (0.93-17.80)	1.67 (0.69-3.83)	< 0.001
PLR	120.00 (37.88-465.83)	115 (51-233)	0.250

Data are presented as median (min-max) if otherwise is not stated. IPF: Idiopathic pulmonary fibrosis, CHP: Chronic hypersensitivity pneumonia, MCV: Mean corpuscular volume, RDW: Erythrocyte distribution width, MPV: Mean platelet volume, PDW: Platelet distribution width, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet lymphocyte ratio.

DISCUSSION

Idiopathic pulmonary fibrosis and CHP are diffuse parenchymal lung diseases with similar clinical, radiological, and pathological features. It is of immense importance to make the differential diagnosis of both diseases because of the differences in their treatment. In our study, the value of NLR and PLR was investigated, but we didn't find any significant difference in differential diagnosis of the two diseases. NLR values were higher in both IPF, and chronic HP patients compared with healthy controls.

Our findings revealed a marked male predominance in the IPF group, while the gender distribution in the CHP group was more balanced. This aligns with previous epidemiological data suggesting a higher prevalence of IPF among males. Although the median ages of the IPF and CHP groups were similar, the control group included relatively younger individuals, which should be considered when interpreting inflammatory markers. Comorbidities were observed at a comparable rate in both disease groups; however, cardiovascular conditions were more frequently encountered in the IPF group.

NLR and PLR are parameters that can be simply calculated from the complete blood count and reflect the inflammatory status. It has been studied in the evaluation of morbidity and mortality in cardiovascular, rheumatological diseases, infections, and many malignancies (5-11). Many studies have also been conducted in respiratory system diseases. In small cell and non-small cell lung cancer, increased NLR and PLR were associated with poor survival, and high values in pulmonary thromboembolism were associated with increased mortality (12-14). It has been shown that NLR and PLR are higher in COPD (Chronic obstructive pulmonary disease) patients than in healthy individuals, and that increased values are associated with acute exacerbations (15). In addition, there are studies in the differential diagnosis and prognosis evaluation of pulmonary sarcoidosis and tuberculosis, non-tuberculosis infections and covid-19-related lung diseases (16-18).

In our study, the NLR value of healthy individuals was 1.67 (0.69-3.83), PLR was 115.23 (50.83-233.33), and in a meta-analysis investigating the normal NLR value in the population, NLR was 1.65 (0.78- 3, 53) and in 543 healthy people aged 50-59 years in Iran, NLR was 1.65 (-/+ 0.62) and PLR was 117.76 (-/+ 71.63), which was similar to our study (19,20). In the comparison of IPF and the control group, it was found that NLR was significantly higher in the disease group, while the PLR value was not statistically significant. The high absolute neutrophil count, low lymphocyte count and similar platelet count in the IPF group caused this statistical situation. In a study examining the combined inflammatory markers derived from whole blood parameters of patients diagnosed with IPF, the NLR value was 2.67 (1.89 – 2.67) and higher than the control group, and the PLR value was 132 (± 74), which was like the control group as in our study. In addition, in that study, it was revealed that increased systemic inflammatory markers were correlated with a decreased forced vital capacity (FVC) value (21).

In another study examining the 12-month prognosis of IPF, NLR was found to be 2.5 (1.8-3.3) and PLR was 119 (93.7-150). Although the initial values obtained at the beginning of the study were not associated with prognosis, it was observed that patients with the greatest change in NLR in the recalculated values after one year of follow-up had the highest mortality and worse prognosis. In our study, follow-up NLR and PLR values were not evaluated, but the initial NLR value of the patients in the IPF group was 2.58 (0.89-10.00), and the PLR value was 118 (43.3-432.73), which were similar results (22).

In another retrospective study examining the biomarkers of systemic inflammation in interstitial lung diseases, patients were evaluated according to imaging findings by dividing them into two groups as UIP and NSIP. NLR was 2.84 in the IPF group and 2.80 in the connective tissue disease (CTD) group. Systemic inflammatory markers were expected to be low in the IPF group and higher in the CTD group, but this study also revealed no significant difference between the two groups. Similarly, the NLR in the IPF patients was higher than the control group and similar in the CHP patients support this result (23).

The reasons for the similar increase in NLR in IPF and CHP have also been explained in other studies. For example, in two studies, it has been reported that while mediators released due to repetitive micro-traumas cause fibroblast and myofibroblast proliferation, extracellular matrix increase and alveolar wall thickening and IPF background occur, the role of inflammation in these processes cannot be ignored (24,25). In particular, neutrophils have a significant role in the pathogenesis. There are studies showing the relationship between increased neutrophil count and neutrophil elastase enzyme in BAL and disease severity (26,27). It has been suggested that IPF cases with increased white blood cells compared to the normal population have a poor prognosis and this is a potential biomarker for the disease (25).

Th1 and Th17 cells engage in the pathogenesis with pro-fibrotic roles and the anti-fibrotic roles of Th2 and Th22 during the development of the disease (26). In the calculations made with the enhanced systemic inflammation index (AISI), which includes neutrophils, lymphocytes, platelets, and monocytes, it was observed that patients with poor lung functions, low 6MWT, and short lifespan also had high systemic inflammation values (27).

In our study, NLR and absolute neutrophil counts were significantly higher in CHP patients; PLR, absolute lymphocyte and platelet counts were like healthy individuals. In a study examining 70 HP and 70 healthy people, both NLR and PLR values were found to be higher in the disease group, and a significant difference was found between both parameters when HP patients were divided into acute and chronic. In this study, while the systemic inflammation values of acute patients were higher, the values of chronic patients were also higher than the healthy individuals. It has been suggested that the reason the two parameters were lower in the CHP group than in the acute patients may be due to the development of granulomas in the chronic process, the presence of fibrosis, and the decrease in inflammation in the chronic patient group. As a matter of fact, NLR values in CHP cases were significantly higher than the control group in our study. It supports the view that although inflammation is reduced in CHP cases compared to the acute form, it will still remain (28).

In hypersensitivity pneumonia, macrophages and CD8+ T lymphocyte chemotaxis develop first, followed by neutrophil infiltration after agent exposure. Many chemokines and cytokines have been demonstrated in the BAL fluids of patients with HP. The most well-known of these is IL-8, which is produced from alveolar macrophages, fibroblasts, lymphocytes, and endothelium and is a chemoattractant for neutrophils. In addition, MCP-1 (monocyte chemoattractant protein 1) produced from these cells is effective in monocyte-macrophage transformation and has been shown in BAL fluids of patients with HP (29). IFN-alpha (interferon alpha) and CXCL10 (C-X-C motif ligand 10), which are responsible for granuloma formation and alveolitis, are Th1 cytochemokines and play a role in the pathogenesis of the disease. It has been shown that Th2-related immune response is dominant in the pathogenesis of HP with fibrosis, and CCL17 (club cell protein 17) released from this cell is secreted in the lungs in fibrosis due to avian lung (30,31). In patients with farmer's lung, IL-8 and neutrophils increased in BAL and serum after IPT, and a Th1 reaction like the acute phase was induced. Since exposure to low-dose antigen stimulates memory T cells, it has been suggested that it causes progression without acute exacerbation (32). This situation also explains the increase in NLR in CHP.

When the other hematological blood parameters of our study were examined for all three groups, MCV was lower in disease groups than healthy subjects (p=0.009) and RDW was higher than healthy subjects (p=0.000). Leukocyte count (p=0.000), neutrophil count, eosinophil count (p=0.000) was also statistically significantly higher in disease groups than the healthy subjects.

RDW, which is indicative of change in erythrocyte size, indicates increased cell size and decreased homogeneity at higher values. Erythropoiesis, reduction in erythrocyte lifespan, inflammation that will cause membrane deformations can increase RDW. Its normal range is 11.6%-16.5% in our laboratory, and in our study, the median value was 14.25 in the IPF group and 14.20 in the CHP group, which is higher than the control group. There are few studies evaluating RDW, but in a newly published study, the median value was found to be 14.1% in IPF, like our study. In addition, it has been shown that values of 15% and above are correlated with increased mortality, low FVC and DLCO values, hypoxemia, and high incidence of pulmonary hypertension (33). Again, in a recent study supporting these findings, the median RDW was 15.2%, which was higher than our study. However, patients with both IPF and combined pulmonary fibrosis and emphysema syndrome (CPFE) were included in that study, and especially the CPFE group had high values, and this may differ from our study (34). There is no study investigating RDW in CHP.

Although chronic hypersensitivity pneumonitis (CHP) is generally considered an inflammation-dominant interstitial lung disease, recent evidence suggests that idiopathic pulmonary fibrosis (IPF), particularly in progressive forms, may also exhibit marked neutrophilic inflammation. Achaiah et al. (2021) demonstrated that IPF patients can present with systemic inflammation and elevated neutrophil counts, potentially overlapping with the inflammatory profiles observed in CHP patients. This convergence in inflammatory patterns may explain why NLR and PLR did not show significant discriminatory power between IPF and CHP in our cohort. The shared fibrotic and immunologic pathways, involving both innate and adaptive immune responses, complicate the use of simple peripheral blood indices as differential diagnostic tools. Therefore, although both NLR and PLR were elevated compared to healthy controls, their overlap

between the two disease groups limits their utility in clinical distinction (35).

There are some limitations in our study. First, although a considerable number of patients were included in all study groups, it is a single-center study. Also, NLR and PLR values may be affected by the comorbidities and gender of the patients, and these may influence our study results. One of the limitations of this study is the absence of disease severity assessment in the IPF and CHP groups, which limits the evaluation of NLR and PLR in relation to clinical progression. The healthy control group in our study was different from the disease groups in terms of age and sex distribution, these may have an effect on our study results.

CONCLUSION

IPF and CHP are two separate interstitial lung diseases that cause similar clinical and radiological manifestations, and many cases have difficulties in differential diagnosis. In our study, the value of NLR and PLR values obtained from complete blood count, which is a simple, applicable and inexpensive method in most centers, was investigated in the differential diagnosis of the two diseases. It was concluded that the NLR value was increased in both diseases, but it did not have a differential role for the two diseases. There are still no effective biomarkers in the differential diagnosis and studies are needed on this subject.

Author's Contribution

The authors declare no conflict of interest.

All authors declared their contribution to the study at all stages and approved the final version of the manuscript.

All authors declared that this manuscript has not been published before and is not currently being considered for publication elsewhere.

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