Journal of American Science
Websites:
http://www.jofamericanscience.org
http://www.sciencepub.net
Emails:
editor@sciencepub.net
sciencepub@gmail.com
MARSLAND PRESS
Multidisciplinary Academic Journal Publisher

# Neutrophil/Lymphocyte and Platelet/Lymphocyte ratios and their relation with disease activity in Systemic Lupus Erythematosis patients

Yosri Zaki El-Zohairy[1], Ehab Abdul Aziem Ahmed[2], Amr Ahmed Rezk[1], Osama Hassan Mohmed[1]
[1]Department of Clinical Pathology, Faculty of Medicine, Al-Azhar University, Cairo, Egypt
[2]Department of Physical Medicine, Rheumatology and Rehabilitation, Faculty of Medicine, Al-Azhar University, Cairo, Egypt
drosamahassan1@gmail.com

**Abstract: Background:** Systemic lupus erythematosus (SLE) is a chronic autoimmune disease. Some evidences suggest that neutrophil-lymphocyte ratio (NLR) associated with different inflammatory malignancies, ischemic injury and cardiovascular disease. Few scholars have investigated the relationship between NLR and SLE. **Aim of the study:** This study aimed to evaluate the role of NLR and PLR in SLE activity assessment. **Methods:** A total of 45 subjects were participated in this study. 30 diagnosed with SLE in patients group and 15 healthy age-and sex-matched in control group.NLR and PLR levels between SLE patients in both remission and excerptions (according to SLEDEI score) and healthy controls were compared, and correlations between these indices and clinical characteristics were analyzed. **Results:** increased NLR and PLR were observed in SLE patients. NLR was positively correlated with antinuclear antibodies (ANA) (r = 0.4, p= 0.03), C3(r = -0.56, p= 0.001), C4 (r = -0.49, p= 0.01) and erythrocyte sedimentation rate (ESR) (r=0.63, p<0.001) ,SLEDAI scores(r=0. 0.53, p<0.001). PLR was positively correlated with with antinuclear antibodies (ANA) (r = 0.43, p= 0.02), Anti-d.DNA antibodies(r = 0.36, p= 0.049), C4 (r = -0.45, p= 0.01) and SLEDAI scores(r=0.445, p<0.001).**Conclusion**: NLR and PLR could reflect inflammatory response and disease activity and disease damage in SLE patients.
[Yosri Zaki El-Zohairy, Ehab Abdul Aziem Ahmed, Amr Ahmed Rezk, Osama Hassan Mohmed **Neutrophil/Lymphocyte and Platelet/Lymphocyte ratios and their relation with disease activity in Systemic Lupus Erythematosis patients.** *J Am Sci*2019;15(12):39-45]. ISSN 1545-1003 (print); ISSN 2375-7264 (online). http://www.jofamericanscience.org.4. doi:10.7537/marsjas151219.04.

**Keywords:** Neutrophil/lymphocyte, platelet/lymphocyte, systemic Lupus erythematosus.

## 1. Introduction

Systemic lupus erythematosis (SLE) is an autoimmune disease with features of autoantibody production, immune complex deposition and multiple target organ damage. The disease can affect any part of the body and the course of the disease is diverse and unpredictable. In SLE, organs and cells undergo damage initially mediated by tissue binding auto-antibodies and immune complexes. In most patients, auto-antibodies are present for a few years before the first clinical symptom appeared(1).

The assessment of SLE patients is therefore difficult for the physician in daily practice. On the other hand, treatment could be different according to disease activity. SLE can be categorized as mild or severe and life threatening disease. In severe activity, leucopenia and lymphopenia can be found(2).

Many clinical and laboratory parameters can be used to evaluate disease activity.The most commonly used markers for this aim are the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) in daily practice. However, both of these markers have some limitations, such as reflection of short term inflammatory activity and low discrimination ability with other superimposed inflammatory conditions(3). The problem is how to evaluate disease activity with simple laboratory parameters which is available in almost every health care facility. Systemic inflammation is associated with changes in circulating blood cells quantity and composition. In-fact, normochromic anemia, thrombocytosis, neutrophilia, and lymphopenia usually occur with many inflammatory conditions. So, the features of circulating blood cell components can be used for the assessment of inflammatory activity(4).

Studying biomarkers in rheumatology intensely appeared from the need to understand the mechanisms underlying some rheumatic diseases. Parameters of hemogram, particularly those including immune system elements are important in the assessment of different diseases and/or signs. Immune system elements involve the neutrophils, lymphocytes and platelets that have a role in the control of inflammation, while also undergoing changes secondary to inflammation(5).

Platelets may play a great role in inflammation and immune-modulation postulated by the presence of

crosstalk between markers of coagulation and the inflammatory system. Upon activation, platelets release pro-inflammatory platelets micro-particles, which interact with leucocytes resulting in joint and systemic inflammation in SLE[6].

Platelet count, mean platelet volume (MPV) and platelet distribution width (PDW) are three useful indices of platelet function reflecting the platelet production rate[7]. White blood cells and its differential count can be done as a part of routine investigations[8].

Also, neutrophil-lymphocyte ratio (NLR), MPV and PDW can be determined from routine complete blood counts (CBC), but are usually neglected by clinicians[9]. Neutrophils are ready in active SLE patients and have a role to increase disease by secreting proteases, prostaglandins, and reactive oxygen intermediates to synovial space and by activating other cells via secretion of Blymphocyte stimulator (BLyS), tumor necrosis factor-a (TNF-a), interleukin-17 (IL-17), and many other mediators[10].

NLR is the proportion of absolute neutrophil to lymphocyte counts while PLRis the proportion of platelet count to lymphocyte count and both are retrieved from the CBC test. It has become widely agreed that NLR is a useful tool for the development of activity in chronic inflammatory diseases like ulcerative colitis (UC) and familial Mediterranean fever (FMF)[11]. However, the relation between NLR and chronic inflammatory arthritis was barely investigated[12]. PLR change may be associated with inflammation and cytokines levels[13].

Neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) came into use as markers of systemic inflammation and were assessed in malignancy researches [14]. However, to our knowledge, the relationship between NLR and PLR in SLE activity has not been well studied so far. NLR and PLR can be calculated easily and less costly as compared with detection of other inflammatory cytokines that could be used as biomarkers for inflammatory response or disease activity in SLE patients[15].

## 2. Patient and Methods

This study was conducted on 30 patients diagnosed with Systemic Lupus Erythematosus as defined by American College of Rheumatology (ACR) 1982 classification criteria for SLE[16] and and the SLICC classification criteria for SLE (2015)[17]and a control group of 15 age- and gender-matched apparently healthy subjects.

The patients were selected from Al-Azhar University Hospitals over a period from 2nd Fab 2019 to 2nd of August 2019. All patients were selected from SLE patients attending the Rheumatology Outpatient Clinic or admitted to physical medicine, Rheumatology and rehabilitation department.

**Inclusion criteria:**

Patients diagnosed with SLEand Patients aged 16 years or more.

**Exclusion Criteria:**

Patients with other autoimmune disease, malignant diseases, with evidence of any concomitant inflammatory disease; acute infection or chronic inflammation status, or Patients with other known blood diseases that may affect the results.

Control group: It included fifteen apparently healthy individuals with matched age and sex.

**Methods:**

The patients were subjected to the following:

Full medical history: with special emphasis on age, sex, disease duration, SLE symptoms, Full clinical examination, Assessment of disease activity by the SLE Disease Activity Index 2000 (SLEDAI) system[18]. Laboratory investigations including: Complete urine analysis with assessment of active urinary sediments (RBCs – WBCs – proteins or cast, 24Hr protein in urine, SGOT,SGPT, S.Albumin, Serum creatinine (mg/dl) Complete blood picture with differential white blood cell cout, Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), ANA, Anti-dsDNA antibody, Serum Complement C3 and C4 and estimation of both Neutrophil to lymphocyte ratio (NLR) and Platelet to lymphocyte ratio (PLR).Informed written consent were taken from all subjects enrolled in the study.***Sampling:*** Four milliliters (4 ml) venous blood were collected under complete aseptic conditions, each blood Sample was distributed into tubes as follows: Two ml of blood were delivered into plastic tube containing 1 .5 ± 0.25 mg dipotassium EDTA per 1 ml blood for performing complete blood picture on Sysmex XP 300 and Cell-Dyn Ruby Hematology Analyzer and two ml of blood were delivered into dry plain plastic tube that will be centrifuged for collection serum for immunological and chemical tests.

**Statistical Analysis**

Data were analyzed using Statistical Program for Social Science (SPSS) version 20.0.

Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage. **Mean (average)**: the central value of a discrete set of numbers, specifically the sum of values divided by the number of values. **Standard deviation (SD)**: is the measure of dispersion of a set of values. A low SD indicates that the values tend to be close to the mean of the set, while a high SD indicate that the values are spread out over a wider range. The following tests were done: **Independent-samples t-test of significance**: was used when comparing between two

means. **Chi-square test**: was used when comparing between non-parametric data. **Pearson's correlation coefficient (r)**: test was used for correlating data.

**I.General characteristics of Subjects (SLE patients and control):**

A total of 30 patients with SLE were finally included in this study, all of them are female patients , with an average age of 39.6 ± 6.9; disease duration among them ranges from 0ne year to ten years with the mean 4.6 ± 2.3.Among 15 healthy controls, all of them are females and the average age of them was 39.4 ± 4.1. There was no statistically significant difference between the two groups of sex and age. According to SLEDAI score we found that 13 patients (43.3%) had sever disease activity, while 2 patients(6.6%) had a moderate disease activity and 15 patients (50%) had no disease activity. (**Table1)**

**Table (1): General clinical characteristics of Subjects.**

| Variables | Patients (N =30) | Control (N = 15) |
|---|---|---|
| Age (y) | 39.6 ± 6.9 | 39.4 ± 4.1 |
| Gender (n,%) | | |
| Female | 30(100%) | 15(100%) |
| Male | 0(0%) | 0(0%) |
| Disease onset (y) (min-max) | 4.6±2.3(1-10) | |
| SLEDAI (n,%) | | |
| 0-3 | 15(50%) | |
| 4-12 | 2(6.6) | |
| >12 | 13(43.4) | |

**II.The differences in PLR and NLR, and related laboratory indicators between SLE patients and healthy controls:**

There were no statistical significant difference **(p-value > 0.05)** between patients and control as regard WBCs, Neutrophils, ALT, AST and ALB,while there was a highly statistical significant difference**(p-value < 0.001)**as regard RBCs, Hb level, ESR, CRP, ANA and PLR. Also, There were a statistical significant difference **(p-value < 0.05)** between patients and control as regard PLT, lymphocytes and NLR. The mean RBCs in patients were3.51 ± 0.52million/ml while it was 4.24 ± 0.33million/ml in control group**(p-value < 0.001)**.The mean Hb in patients was 9.71 ± 1.53g/dl while it was 12.15 ± 0.41million/ml in control group**(p-value < 0.001)**. The mean ESR in patients was 69.8 ± 15.33 mm/h while it was 6.33 ± 1.99mm/h in control group **(p-value < 0.001)**. The mean CRP in patients was 14.7 ± 2.8 mg/dl while it was 2.85 ± 0.91 mg/dl in control group **(p-value < 0.001)**. The mean ANA in patients was 5.36 ± 3.32 while it was 0.96 ± 0.26 in control group **(p-value < 0.001)**.Also there was Statistically significant difference **(p-value < 0.05)** between patients and control as regard serum creatinine level . The mean creat in patients was 1.13 ± 0.55 mg/dl while it was 0.75 ± 0.18 mg/dl in control group **(p-value = 0.002)**.(**Table 2**)

**Table (2): com**
**parison between patients and control as regard laboratory data.**

| variable | Patients(N = 30) | Control(N = 15) | P-value |
|---|---|---|---|
| RBCs (million/ml) | 3.51 ± 0.52 | 4.24±0.33 | < 0.001 |
| Hb (g/dl) | 9.71±1.53 | 12.15±0.41 | < 0.001 |
| PLT ($x10^3$/ul) | 256.03±130.1 | 281.1±63.7 | 0.016 |
| WBCs ($x10^3$/ul) | 5.9±2.3 | 10.5±14.3 | 0.241 |
| Neutro. ($x10^3$/ul) | 3.6±1.7 | 3.9±1.3 | 0.961 |
| Lympho. ($x10^3$/ul) | 1.5±0.7 | 1.8±0.5 | 0.001 |
| ALT (U/ml) | 22.72±18.89 | 16.47±3.40 | 0.093 |
| AST(U/L) | 20.1±10.7 | 17.3±3.2 | 0.322 |
| ALB (mg/dl) | 3.8±0.3 | 3.± 0.4 | 0.935 |
| Creat (mg/dl) | 1.13±0.55 | 0.75±0.18 | 0.002 |
| ESR (mm/h) | 69.8±15.33 | 6.33±1.99 | < 0.001 |
| CRP (mg/dl) | 14.7±2.8 | 2.85±0.91 | < 0.001 |
| ANA | 5.36±3.32 | 0.96±0.26 | < 0.001 |
| PLR | 199.78±107.93 | 170.03±78.06 | < 0.001 |
| NLR | 2.92.08± | 2.14±0.28 | 0.022 |

**III. The differences in PLR and NLR, and related laboratory indicators between SLE patients:**

There were highly statistical significant relation **(p-value < 0.001)** between ANA, C3 and C4, serum Creat and 24Hr proteinuria in active SLE cases (according to SLEDAI) and Statistically significant relation **(p-value < 0.05)** between ALB, CRP, PLR and NLR as well in active SLE cases. while there were no statistical significant relation **(p-value > 0.05)** between ESR, ALT and AST in active SLE patients. (**Table 3**)

**Table (3): The differences in PLR and NLR, and related laboratory indicators between SLE patients.**

| Variables | SLEDI > 3 (N = 15) | SLEDI < 3 (N = 15) | P-value |
|---|---|---|---|
| NLR | 3.98±2.53 | 1.82±0.19 | 0.005 |
| PLR | 257.63±125.72 | 141.93±33.93 | 0.003 |
| ESR (mm/h) | 76.46±19.83 | 64.0±6.4 | 0.05 |
| CRP (mg/dl) | 17.8±8.2 | 12.0±1.25 | 0.026 |
| ALT (U/ml) | 28.29±26.39 | 17.53±2.72 | 0.153 |
| AST (U/L) | 22.13±14.83 | 18.07±2.69 | 0.313 |
| ALB (mg/dl) | 3.74±0.36 | 4.04±0.33 | 0.025 |
| Creat (mg/dl) | 1.51±0.54 | 0.75±0.18 | < 0.001 |
| Proteinuria | 3.05±1.38 | 0.06±0.02 | < 0.001 |
| ANA | 8.10±2.78 | 2.79±0.55 | < 0.001 |
| Anti-d.DNA | 48.27±57.90 | 12.93±4.45 | 0.033 |
| C3 | 59.64±17.92 | 120.77±11.17 | < 0.001 |
| C4 | 8.04±4.13 | 26.32±5.56 | < 0.001 |

**IV.Correlation between NLR, PLR and other studied parameters in active patients group:**

There were a statistical significant positive correlation between NLR and SLEDAI, ESR, ANA, 24hr protein in urine while there were statistical significant andnegative correlation between NLR and C3 and C4.(Figure 1,2). Also, there were a statistical significant **positive** correlation between PLR and SLEDAI, A.dDNA, ANA, 24hr protein in urine while there were statistical significant andnegative correlation between NLR and C4. (Figure3,4)

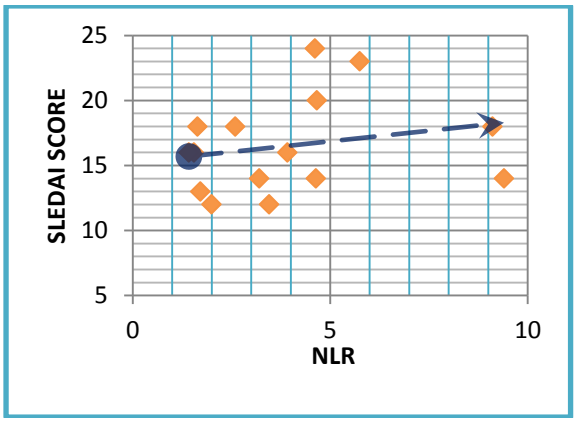


**Figure (1)** Correlation between NLR and SLEDAIin active SLE patients.

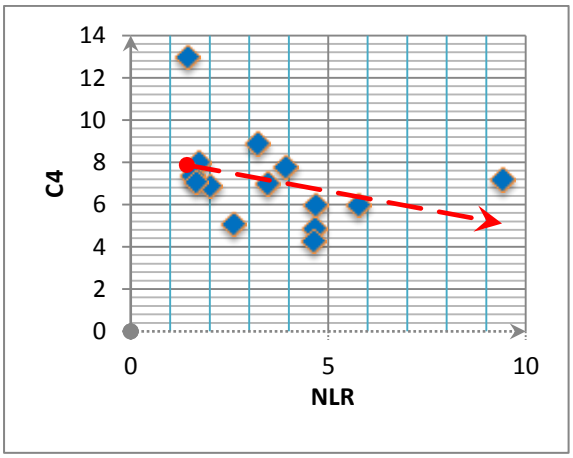


**Figure (2)** Correlation between NLR and C4 in active SLE patients.

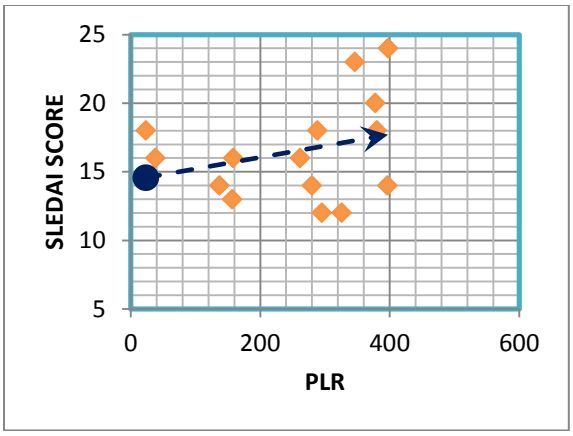


**Figure (3)** Correlation between PLR and SLEDAIin active SLE patients.

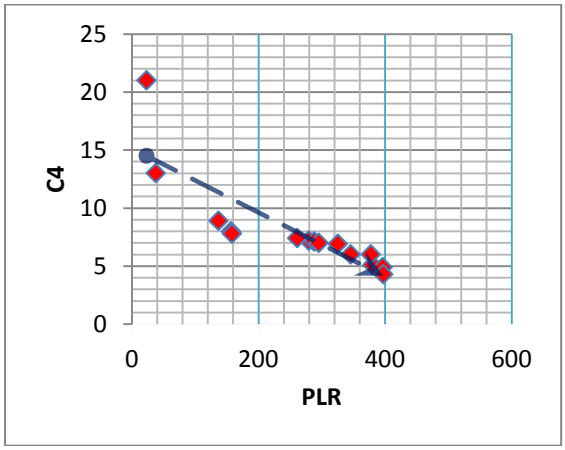


**Figure (4)** Correlation between PLR and C4in active SLE patients.

**4. Discussion:**

The study recruited 30 patients with SLE. They were subjected to careful history taking, thorough clinical and laboratory investigations including urine analysis, CBC, ESR, Liver and Kidney functions and immunological parameters as ANA , Anti-Ds DNA , C3 and C4. All 30 cases are female (100%).Active SLE cases (according to SLEDAI score) are 15 female patients(100%). Remission cases are 15 female patients (100%). All cases age ranged from (20-59) with mean age 39.6±6.9.These Findings were in agreement with *Ginzler et al.,*[19] ,who reported that More than 90% of cases of SLE occur in women frequently starting at childbearing age.

As regard results of complete blood picture (CBC), SLE patients and control cases had no statistically significant difference as regard neutrophil count and total leucocytic count (p=0.961 and p= 0.241 respectively). This was against,*Stojan et al.,*[20] who reported that leukopenia is common and may reflect active disease. while there was statistical significant difference **(p-value<0.016)**as regard platelet count which was in agreement with *Stojan et al.,*[21] who reported that anemia and thrombocytopenia may also be observed with active disease. On the other hand, Lymphocyte count level of active SLE cases, was significantly decreased compared to remission cases, **(p-value =0.001)**. This was in agreement with *Amaylia et al*[22]who reported that lymphopenia is a chief finding in Lupus fluctuations and can reflect case activity. Hemoglobin level and RBCs count of SLE cases, was high significantly decreased compared to control group, **(p-value <0.001)**.This was in agreement withY. *Haitaoet al .,*[23]**.**

Regarding Liver function tests, SGPT, SGOT and serum albumin in SLE patients showed no significant difference compared to control group, they were (p=0.093, p= 0.322, p=0.935) respectively. Meanwhile, Serum Albumin level of active SLE group (according to SLEDAI score) 3.7±0.36 was significantly decreased compared to remission group (according to SLEDAI score) 4.04±0.33 (p<0.005). This was in agreement with *Yip et al.*[24]who reported that serum albumin as a marker for disease activity in patients with systemic lupus erythematosus, with and without nephritis.

Regarding Kidney function tests, serum creatinine in active SLE group (according to SLEDAI score) show significant difference compared to those in remission group (according to SLEDAI score), they were (p<0.001). This was in agreement *Borchers et al.,*[25]reported that elevated renal function tests is a sign of SLE activity.

Regardin C3and C4, there was a highly statistical significant decrease in both C3 and C4 found in active SLE in comparison to Remission group (p<0.001 for both). This was in agreement with, *Nived et al.,*[26] who observed that low complement concentrations and also high activation of the complement system are characteristic findings in active SLE and had led to the practice of using measurement of complement for the diagnosis

Regarding ANA, there was a high statistically significant increase found in active SLE cases in comparison to remission cases (p<0.001). This was in agreement with, Jennings *et al.,*[27]who reported that ANA test is highly sensitive test and that it is positive in more than 98% of people with SLE

Regarding A.DNA, there was a statistically significant increase found in active SLE cases in comparison to remission cases (p=0.003). This was in agreement with *Abd-Elhafeez et al.,*[28] reported that rising titers of A.DNA can be used to confirm SLE disease activity.

Regarding ESR, there was a highly statistically significant increase in ESR in SLE patients in comparison to control group (p<0.001). while there

no statistically significance increase between active and remission cases (P=0.05). *Stoll et al.,*[29] noted that ESR is used as a marker of inflammation. Inflammation could indicate lupus activity.

Regarding CRP, there was a statistically significant increase in CRP in active SLE cases in comparison to patients in remission) (p=0.026)*Mok et al.,*[30]reported that CRP is elevated with activity of lupus and positively and significantly correlates with lupus disease activity Index.

The neutrophil-to-lymphocyte ratio (NLR) is a simple ratio of the absolute neutrophil and lymphocyte counts obtained on the differential section of the total white blood cell count (WBC) of a complete blood cell (CBC) count. NLR is a marker of inflammatory response and has been shown to be associated with poor outcomes in patients with several types of diseases[31].In addition, *Chua et al.,*[32] observed that Neutrophil Lymphocyte ratio (NLR) has been evaluated and used as inflammatory marker in malignancies, infection and coronary artery diseases. In the present work, there was a statistical significant increase in NLR in active SLE patients in comparison to patients in remission (P=0.005).

Moreover, there was statistical significant increase in NLR in SLE patients and control group(P=0.022).On the same side, *Lixiu et al.,*[33] found that high NLR is independently associated with SLE activity, and showed a significant increase in NLR in Lupus nephritis patients. They stated that NLR could reflect inflammatory response and disease activity in SLE patients. Furthermore, this was in agreement with, *Yunxiu et al.,*[34]who reported that NLR was increased in active group in comparison to remission group. Meanwhile, *Delgado et al.,*[35] showed that NLR is not superior to lymphocyte alone in differentiating disease activity in SLE.

Platelet Lymphocyte Ratio (PLR) is a novel inflammatory biomarker used as prognostic factor in various diseases such as diabetes mellitus, coronary artery disease, ulcerative colitis and inflammatory arthritis and malignancies[36]. In the present study, there was statisticalsignificance increase in PLR in active SLE patients in comparison to cases in remission (P=0.03) Moreover, there was a highly statistical significant increase in PLR in SLE patients in comparison to control group (P<0.001).

Trying to correlate NLR with other known markers of SLE activity, there was a positive correlation of NLR in active SLE patient in relation to (ESR, ANA, 24Hr protein in urine and SLEDAI Score). Also there was a strong negative correlation in NLR in patients of in group I (active SLE) in relation to (C3 and C4) .This was in agreement with, *Baodong et al.,*[37] which observed that NLR was increased in SLE and positivity correlated with other markers of activity.

In addition, there was a positive correlation of PLR in active SLE patients in relation to markers of activity (ANA, AdsDNA, 24Hr protein in urine and SLEDAI). Furthermore, there was a statistically significant negative correlation found between PLR and C4 (P value <0.05) .The present study showed that, PLR was positivity correlated with SLEDAI,(p=0.01).This was in agreement with *Baodong et al.,* which observed that PLR was increased in SLE with lupus nephritis in comparison to SLE without nephritis and positivity correlated with increasing scores of SLEDAI.

**Conclusion:**

In conclusion, each of NLR and PLR is independently associated with SLE activity (SLEDAI score) and renal involvement in SLE patients. Because compared to other traditional indicators of activity and LN as 24h proteinuria, C3, C4 and Anti-ds DNA, both NLR and PLR are cheap, quick and easily measurable. These ratios could be promising cheap markers to follow up disease activity, reflects renal involvement and predict disease damage in SLE patients.

**References**


1. **KuoC ,Grainge M , Valdes A et al.(2015):** Familial aggregation of systemic lupus erythematosus and coaggregation of autoimmune diseases in affected families. JAMA Intern.Med .,175(9):1518-1526.
2. **Perhimpunan Reumatologi Indonesia (2011):** Rekomendasidiagnostikdanpengelolaan lupus eritematosussistemik,
3. **Colglazier CL and Sutej PG (2005):** Laboratory testing in the rheumatic diseases: a practical review. South Med J., 98(2):185–91
4. **Kisacik B, Tufan A, Kalyoncu U, Karadag O, Akdogan A, Ozturk MA, et al. (2008):** Mean platelet volume (MPV) as an inflammatory marker in ankylosing spondylitis and rheumatoid arthritis. Joint Bone Spine, 75(3):291–4.
5. **Scapini P and Cassatella MA (2014)**: Social networking of human neutrophils within the immune system. Blood, 124 (5):710–9.
6. **Harifi G and Sibilia J. (2016):** Pathogenic role of platelets in rheumatoid arthritis and systemic autoimmune diseases: Perspectives and therapeutic aspects. Saudi Med J.,37(4):354–60.
7. **Briggs C. Quality counts (2009):** new parameters in blood cell counting. Int J Lab Hematol, 31(3):277–97.
8. **Chua W, Charles K and BaracosVetal.(2011):** Neutrophil/lymphocyte ratio predicts chemotherapy outcomes in patients with advanced colorectal cancer.British Journal of Cancer,104(8):1288-1295.
9. **Sandhaus LM and Meyer P.( 2014):** How useful are CBC and reticulocyte reports to clinicians Am J

ClinPathol x., 118(5):787–93.Am CollCardiol 2007;49(18):1841–50.

10. **Kouri VP, Olkkonen J, Ainola M, Li TF, Björkman L, Konttinen YT, et al. (2014):** Neutrophils produce interleukin-17B in rheumatoid synovial tissue.Rheumatology., 53(1):39–47.
11. **Ahsen A, UluMs, Yuksel S et al. (2013):** As a new inflammatory marker for familial Mediterranean fever: neutrophil-to-lymphocyte ratio. Inflammation, 36: 1357-1362.
12. **Mercan R, Bitik B, Tufan A, Bozbulut UB, Atas N, Ozturk MA, et al.( 2016):** The association between neutrophil/lymphocyte ratio and disease activity in rheumatoid arthritis and ankylosing spondylitis. J Clin Lab Anal., 30(5):597–601.
13. **Koutsokeras T and Healy T (2014):** Systemic lupus erythematosus and lupus nephritis. Nat. Rev. Drug Discov., 13: 173-174.
14. **Templeton AJ, McNamara MG, Šeruga B, Vera-Badillo FE, Aneja P, Ocaña A, et al.( 2014):** Prognostic role of neutrophil-to lymphocyte ratio in solid tumors: a systematic review and meta-analysis. J Natl Cancer Inst., 106(6). dju124.
15. **Qin B , Ma N , Tang Q et al.(2016):** Neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) were useful markers in assessment of inflammatory response and disease activity in SLE patients. Modern Rheumatology, 26(3): 372-376.
16. ***Tan EM, Cohen AS, Fries JF, Masi AT, McShane DJ, Rothfield NF, Schaller JG, Talal N, Winchester RJ (1982)*:** The 1982 revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 25:1271–1277
17. ***Petri M, Orbai AM, Alarcón GS, et al.* (2012)**: Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. Arthritis Rheum a; 64:2677–86.
18. ***Johnson S.*** (2017); European League Against Rheumatism and American College of Rheumatology present new SLE classification criteria at the 2017 ACR/ARHP annual meeting. Presentation at: ACR/ARHP 2017 Annual Meeting; November 3-8, San Diego, CA
19. ***Ginzler E, Tayar J. (2015):*** Fast Facts of Lupus. American College of Rheumatology Committee on Communications and Marketing.
20. Erythrocyte sedimentation disease activity Lupus; 22:827.
21. ***Stojan G, Fang H, Magder L, et al (2013):*** Erythrocytesedimentation rate is a predictor of renal and overall SL Edisease activity Lupus; 22:827.
22. ***Amaylia OE, Hendarsyah S, Sumartini D, et al. (2013):*** TheRole of Neutrophil Lymphocyte Count Ratio as an Inflammatory Marker in Systemic Lupus Erythematosus, Acta Medica Indonesiana. The Indonesian Journal of Internal Medicine.170-174.
23. ***Yu Haitao, Jiang L, Yao L, et al. (2018)*** ;Predictive value of the neutrophil-to-lymphocyte ratio and hemoglobin insystemic lupus erythematosus. *ExpTher Med*. 2018;16(2): 1547–1553. doi:10.3892/etm.2018.6309
24. **[1]*Yip J, Aghdassi E, Su J, Lou W et al (2010):*** Serum albumin asa marker for disease activity in patients with systemic lupus erythematosus J Rheumatol. ; 37(8):1667-72.
25. ***Borchers A, Leibushor N, Naguwa S, et al (2012):*** Lupus nephritis: a critical review. Autoimmun Rev; 12:174–194.
26. ***Nived O, Sturfelt G. (2004):*** ACR classification criteria for systemic lupus erythematosus: complement components. Lupus.13: 1-3.
27. ***Jennings I, Kitchen S, Woods TA, et al. (1997):*** Potentiallyclinically important inaccuracies in testing for the lupus anticoagulant: an analysis of results from three surveys of the UK national external quality assessment scheme (NEQAS) for blood coagulation. ThrombHaemost. 77: 934-937.
28. ***Abd-Elhafeez HA, El-Meghawry ES, Omran TM, et al (2017):*** Study of Neutrophil Lymphocyte Ratio and Platelet Lymphocyte Ratio as Inflammatory Markers in Systemic Lupus Erythematosus Egyptian Patients. Electronic J Biol, 13:3.
29. **[1]*Stoll T, Seifert B, Isenberg DA (1996):*** SLICC/ACR damageindex is valid, and renal and pulmonary organ scores are predictors of severe outcome in patients with SLE. Br J Rheumatol. 32: 248-254.
30. ***Mok CC, Lau CS. (2003):*** Pathogenesis of systemic lupus erythematosus. J Clin Pathol. 56: 481-490.
31. ***Grivennikov SI, Greten FR, KarinM (2010):*** Immunity, Inflammation, and cancer. Cell; 140:883–899.
32. ***Chua W, Charles KA, Baracos VE, et al. (2011):*** Neutrophil-lymphocyte ratio predicts chemotherapy outcomes in patients with advanced colorectal cancer. Br J Cancer. 104. 1288-1295.
33. ***Lixiu L, Yuncheng X, Chunmei C, et al. (2015):***Neutrophil-lymphocyte ratio in systemic lupus erythematosus disease: A retrospective study. Int J Clin Exp Med. 8. 11026-11031.
34. ***Yunxiu W, Yanjuan C, Yihua Y, et al. (2016):*** Neutrophil-lymphocyte ratio and platelet-lymphocyte ratio were associated with disease activity in patients with SLE. International Immunopharmacology. 36: 94-33
35. ***Delgado G, Galarza D, Colunga P, et al. (2015) :***Neutrophillymphocyte ratio is not superior to lymphocyte count alone in SLE. Eur J Gastroenterol Hepatol. 27. 108.
36. ***Akkaya E, Gul M, Ugur M, et al. (2014):*** Platelet tolymphocyte ratio: A simple and valuable prognostic marker for acute coronary syndrome. Int J Cardiol 28:13-15.
37. ***Baodong Q, Ning M, Qingqin T, et al (2016) :***Neutrophil-lymphocyte ratio and platelet -lymphocyte ratio were useful markers in assessment of inflammatory response and disease activity in SLE patients: Modern Rheumatology. 6: 372-376