Correlation of Neutrophil and Platelet-to-lymphocyte Ratios with Disease Activity in Rheumatoid Arthritis

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INTRODUCTION :

- Rheumatoid arthritis (RA) is a chronic, multisystemic inflammatory disease that is prevalent in 0.75% of the adult population in India.

- It is known to more commonly affect women (female-to-male ratio, 3:1).

- Evaluation of disease activity is essential for managing RA since it might have a significant impact on the choice of treatment.

INTRODUCTION :

- Presently, illness activity evaluation is primarily based on clinical symptomatology, signs, laboratory investigations, and questionnaires.

- It has been widely understood that C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are two valuable indices of inflammation and have been extensively utilized for assessment of disease activity.

- Neither one of those indices has been found to fully capture the disease progression in RA.

- INTRODUCTION :
- Neutrophil-to-lymphocyte ratio (NLR) as well as platelet-to-lymphocyte ratio (PLR) has always been associated with a reaction or response of inflammatory origin.
- Increase in the ratios has been used to identify and indicate poorer prognosis of several inflammatory illnesses such as malignancies, chronic renal parenchymal disease, as well as myocardial and pancreatic abnormalities.

MATERIALS AND METHODS

- Study Subjects Following approval from the Institutional Ethics Committee (IEC), **prospective, analytical** , **hospital-based study** was conducted over a year.
- Seventy-four newly diagnosed and follow-up patients with RA, aged 18 years and above, diagnosed as per the 2010 ACR/EULAR criteria (irrespective of disease duration), were included in the study group through consecutive sampling, informed consent taken.

MATERIALS AND METHODS

- 74 healthy individuals were selected and assigned to the control group. Along with the acquisition of sociodemographic data, relevant haematological investigations (neutrophil count, platelet count, lymphocyte count, ESR, CRP) were performed for patients and controls, whereas disease activity assessment was done only for the patients through the disease activity score 28-ESR (DAS28-ESR).
- The study subjects were further split into two groups based on the DAS28 score, as either being in the state of remission (DAS28 <2.6) or in the state of active disease (DAS28 ≥2.6).

Materials and Methods

Excluded patients :

-smokers

-respiratory diseases (chronic obstructive airway disease, asthma, tuberculosis complicated by pleuropulmonary sequelae, thoracic surgery, irradiation history)

-different autoimmune pathological diagnosis

-malignancy

-haematological pathologies

-history of blood transfusions within a period of 3 months

-acute inflammatory etiology or an acute infection

-chronic hepatic parenchymal disease; chronic renal parenchymal disease; pancreatic insufficiency.

Clinical Sample Collection and Analysis

- The venous blood of all patients was obtained in a fasting state, with routine blood investigations being performed by an automatic blood analyzer (Beckman Coulter cell counter) ;
- (reference values: neutrophils 1.6–8.2 × 109/L, lymphocytes 0.8–4.9 × 109/L, and platelets 150–400 × 109/L).

Data Analysis

- Pearson Chi-squared test, linear regression of bivariate data were performed, and a receiver operating characteristic (ROC) curve was generated to compare and define any correlation between these parameters, respectively.

- Independent *t*-test was utilized to compare the mean values of demographic and hematological parameters between the patient group and control group. Data were tabulated in MS Excel spreadsheets, and SPSS .

Table 1: Demographic characteristics and hematologic parameters

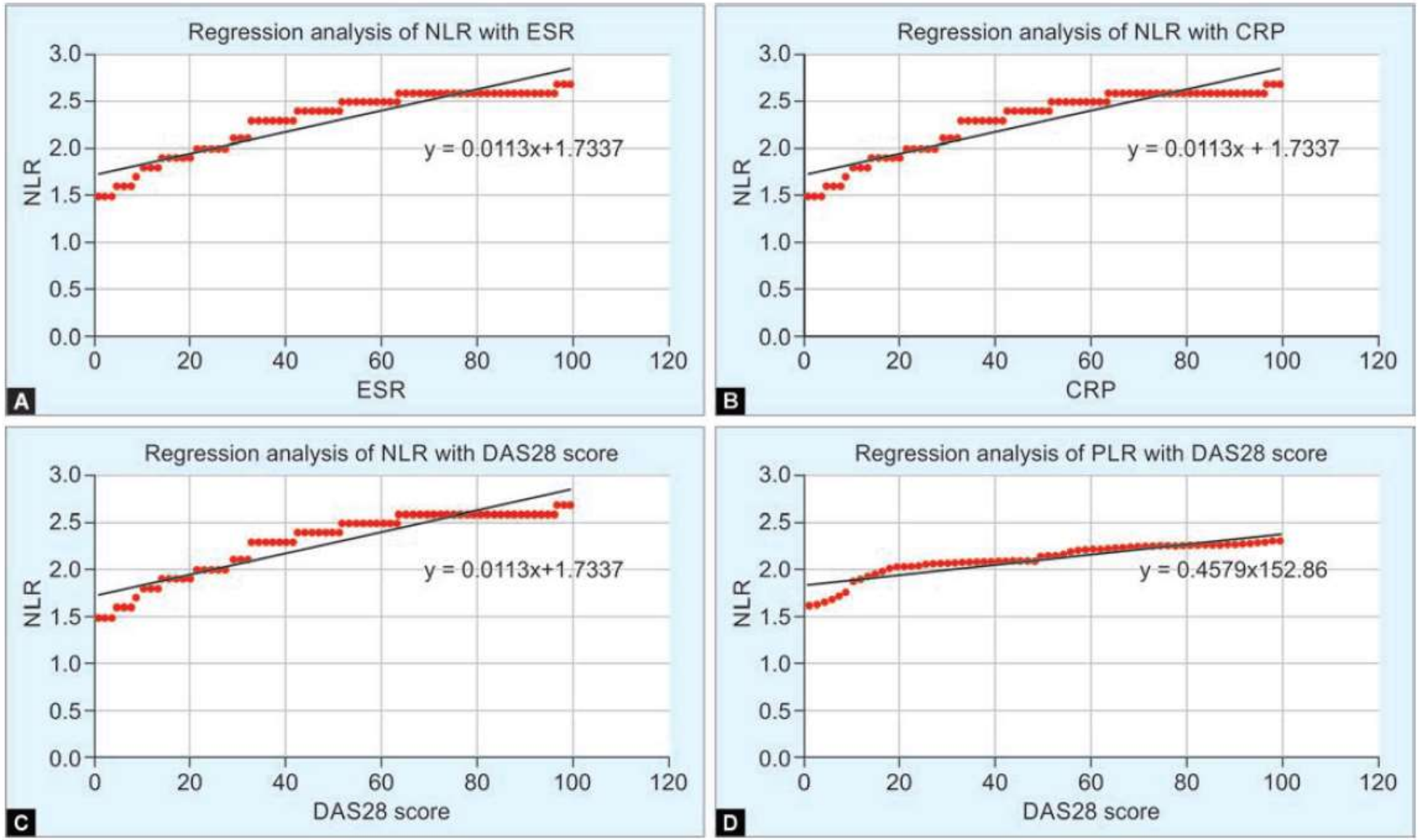
Parameters	*Patients (n = 74)*	*Controls (n = 74)*	*p-value*
Gender (M/F)	21/53	17/57	0.171
Mean age (years)	46.90 ± 11.20	44.70 ± 10.90	0.411
Mean DAS28 score	3.41 ± 1.66	–	–
Mean neutrophil count (10^9/L)	4.56 ± 1.63	3.26 ± 0.83	0.007
Mean lymphocyte count (10^9/L)	1.53 ± 0.71	2.01 ± 0.48	0.009
Mean platelet count (10^9/L)	259.18 ± 77.51	230.32 ± 58.51	0.037
Mean NLR	2.35 ± 0.34	1.41 ± 1.12	0.007
Mean PLR	175.75 ± 14.6	94.62 ± 13.74	0.011
CRP (mg/L)	18.56 ± 23.60	7.24 ± 1.61	0.003
ESR (mm/L)	109.53 ± 40.43	13.28 ± 4.57	0.001

CRP, C-reactive protein; DAS28, disease activity score 28; ESR, erythrocyte sedimentation rate; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio

Table 2: Chi-square correlation of hematologic parameters

Parameters	*Pearson Chi-square value*	*Degree of freedom (df)*	*p-value*
NLR × ESR	665.10	539	0.001
NLR × CRP	800.43	704	0.007
NLR × DAS	814.00	517	0.001
PLR × ESR	3422.50	3332	0.134
PLR × CRP	4458.50	4352	0.127
PLR × DAS	3354.67	3196	0.025

CRP, C-reactive protein; DAS, disease activity score; ESR, erythrocyte sedimentation rate; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio



Figs 1A to D: (A) Regression analysis of NLR with ESR; (B) Regression analysis of NLR with CRP; (C) Regression analysis of NLR with DAS28 score; (D) Regression analysis of PLR with DAS28 score

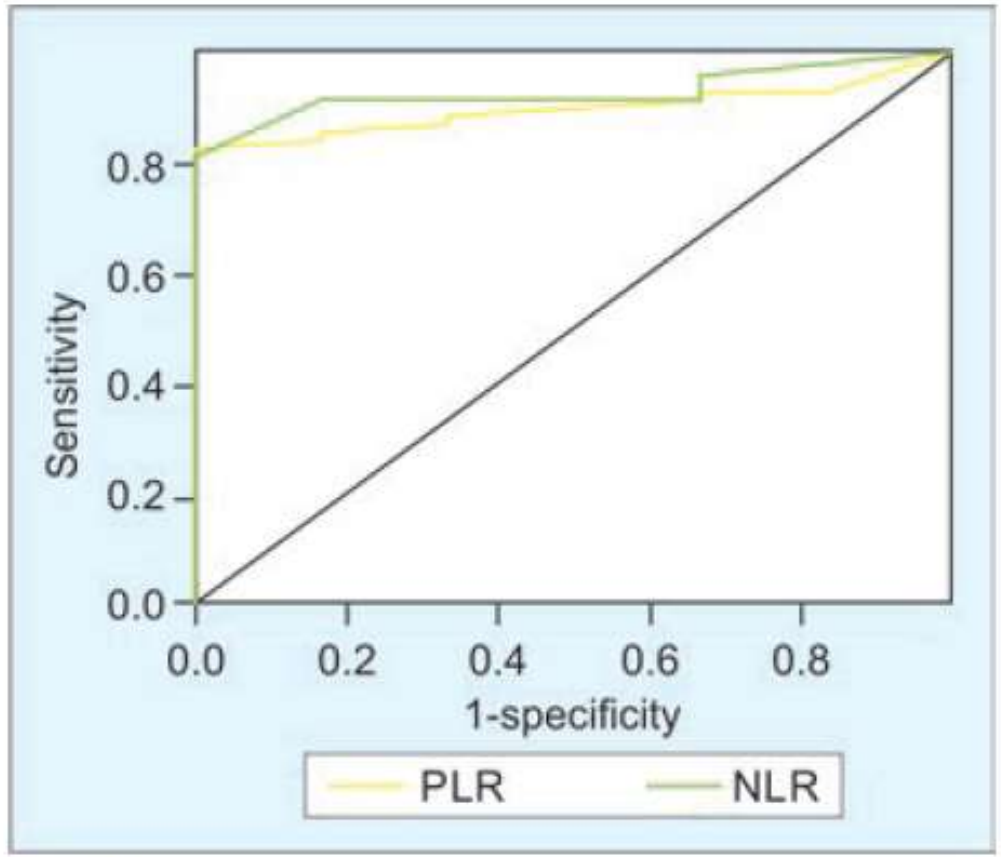


Fig. 2: ROC curve for determination of predictive value of NLR (green) and PLR (yellow)

RESULTS AND OSERVSTION :

- About 42% of the study population were newly detected to have RA, which was also the most common, followed by those with a duration of disease of 1–5 years (39%) and 6–10 years (19%), respectively.

The most extensively used technique for assessing RA disease activity at present is the DAS28 score. There are four categories that make up this assessment:

(1) a count of tender joints when touched (28 in total),

(2) a count of visibaly swollen joints (28 in total),

(3) ESR or CRP , and

(4) the VAS (visual analogue scale) (0-100) (patient's global assessment of health).

- The mean DAS28-ESR of the study population was 3.41 ± 1.66. The maximum number of patients belonged to the category of moderate disease activity (56.65%), and the minimum were in remission (19.54%), with no patient found to have high disease activity.
- The mean neutrophil, platelet, and lymphocyte counts among the patients were 4.56 ± 1.63, 259.18 ± 77.51, and 1.53 ± 0.71 109/L, respectively, and had a difference of statistical significance when compared to the control group .
- About 34% of the patients had an ESR value of ≥100, which was also the most common, followed by those with an ESR value of 25–59 (29.56%). The mean ESR value was 109.53 ± 40.43 mm/L .

DISCUSSION :

- We found that cases suffering from RA had significantly higher values of PLR and NLR when compared to healthy controls, similar to other studies. Our data additionally demonstrated a positive association between NLR and DAS28, CRP, and ESR.
- This agreed with a study by Targońska-Stępniak et al. in which the authors described significant associations of NLR with DAS28 ($p = 0.04$), CRP ($p = 0.001$), PLR ($p = 0.04$), and ESR ($p = 0.02$) that was verified *via* multiple regression testing.
- The NLR has not only been associated with ongoing RA pathology but also with disease remission.

DISCUSSION :

A study found that RA patients with an NLR <2 were considerably more likely to have maintained remission than those who had relapsed, indicating that the ratio may be used to categorize patients into prolonged remission, as demonstrated by a prior study as well . Put together, NLR appears to represent a reliable disease-associated marker.

- We discovered a correlation between PLR and DAS28 but not ESR and CRP.

DISCUSSION :

- NLR and PLR are superior to DAS28 in two ways. Firstly, platelet, neutrophil, and lymphocyte counts are standard lab evaluations for individuals with RA, and it is simple and cost-effective to obtain the NLR as well as PLR.
- Furthermore, NLR as well as PLR being objective indicators, the interobserver variability is less likely to have an impact on the test outcomes.
- NLR as well as PLR are now the recommended options in clinical practice and may be considered as efficient alternative parameters to compete with and possibly replace DAS28 in the assessment of disease activity.

LIMITATION :

The presence of certain limitations was noted in the current study. The study was conducted over a short duration and included a small sample size, for which the results obtained may fail to fully represent the general population.

Following initial assessment at the point of contact with the study participants, the possible variations in the NLR as well as PLR values and their respective correlation with the DAS28 score were not performed, as the cross-sectional study design and short study period could not incorporate long-term follow-up of the study population.

CONCLUSION :

- A positively significant correlation of both the ratios with disease activity was obtained, which indicates that these are potentially simple, reliable, economical, and time-saving bio-indices to assess disease severity in addition to, or independent of, DAS28 score, and can facilitate early initiation of appropriate management in patients suffering from RA.

THANK YOU