

# To Study Neutrophil to Lymphocyte Ratio and Platelet - Lymphocyte Ratio in Patient with Rheumatoid Arthritis

Dr. Tarun Khan<sup>1</sup>, Dr. P. D Meena<sup>2</sup>, Dr. Ziya ul Haq<sup>3</sup>

<sup>1</sup>Postgraduate Resident, Department of General Medicine, S. M. S. Medical College & Attached Group of Hospital, Jaipur, India

<sup>2</sup>Associate Professor, Department of General Medicine, S. M. S. Medical College & Attached Group of Hospital, Jaipur, India

<sup>3</sup>Postgraduate Resident, Department of General Medicine, S. M. S. Medical College & Attached Group of Hospital, Jaipur, India  
(Corresponding Author)

**Abstract:** Introduction: Rheumatoid arthritis (RA) is a chronic and systemic autoimmune diseases with synovial joints inflammation; that culminate into progressive damage of joint, especially with persistent inflammation. Rheumatoid arthritis signs and symptoms may vary in severity and may even come and go. Aim and Objective: To determine any association between NLR, PLR, and RA. Material and Methods: This was a Hospital based, cross-sectional and comparative study. This study was conducted at SMS Medical College and Hospital (Department of Medicine), Jaipur, Rajasthan, India. Data collection was started after approval from institutional research review board to April 2021 and another 2 months were required for the write up. Sample size was calculated to be 30 subjects in each group. Result: Sample size was calculated to be 30 subjects in each group. Mean age of RA cases was  $58.03 \pm 15.69$  years, while that of Controls was  $57.87 \pm 15.59$  years. Most of the RA Cases were females (63.3%), while only 11 cases (36.7%) were males. The mean hemoglobin level was slightly higher among RA cases ( $12.37 \pm 2.48$  g/dl) as compared to controls ( $11.6$  g/dl). The mean TLC count was higher among RA cases ( $7.77 \pm 3.86 \times 10^3$ /cumm) as compared to controls ( $5.7 \pm 1.76 \times 10^3$ /cumm). Conclusion: Neutrophil lymphocyte ratio and platelet lymphocyte ratio were significantly associated with Rheumatoid arthritis. They can be obtained via complete blood count, which is convenient, inexpensive, and fast. Therefore, the NLR and PLR is especially suitable for peripheral centers and can serve as an additional useful marker for the diagnosis of RA.

**Keywords:** Rheumatoid arthritis, Platelet – Lymphocyte Ratio, Neutrophil-lymphocyte ratio.

## 1. Introduction

Rheumatoid arthritis (RA) is a chronic and systemic autoimmune diseases with synovial joints inflammation; that culminate into progressive damage of joint, especially with persistent inflammation.<sup>1,2</sup>

Rheumatoid arthritis signs and symptoms may vary in severity and may even come and go. Periods of increased disease activity, called flares, alternate with periods of relative remission — when the swelling and pain fade or disappear. The traditional stepwise management of RA has evolved in recent times to the currently accepted Treat to Target approach which includes NSAIDS and systemic corticosteroids to control inflammation, biological and non-biological DMARDS to retard disease progression, surgery and physical rehabilitation.

Clinically, the diagnostic indicators and markers that estimate disease activity in patients with RA are presence of C-reactive protein (CRP), the erythrocyte sedimentation rate (ESR), and the rheumatoid factor (RF). CRP & ESR, both of these markers have some limitations, such as reflection of short term inflammatory activity and low discrimination ability with other superimposed inflammatory conditions.<sup>3</sup>

Various factors have been suggested as biomarkers of disease activity in RA patients including cytokines<sup>4</sup>, oxidative stress<sup>5</sup>, vitamin D deficiency<sup>6</sup> and cartilage oligomeric matrix protein<sup>7</sup>.

Platelet count, mean platelet volume (MPV) and platelet distribution width (PDW) are three useful indices of platelet function reflecting the platelet production rate.<sup>8</sup> Also, neutrophil-lymphocyte ratio (NLR), MPV and PDW can be determined from routine complete blood counts (CBC), but are usually neglected by clinicians.<sup>9</sup> NLR is the proportion of absolute neutrophil to lymphocyte counts retrieved from the CBC test. Also, CBC is carried out routinely in RA patients for monitoring drugs side effects and possible disease related changes. However, the relation between NLR and chronic inflammatory arthritis was barely investigated<sup>10</sup> NLR and platelet-lymphocyte ratio (PLR) came into use as markers of systemic inflammation and were assessed in malignancy researches<sup>11</sup>. However, to date, data about NLR, PLR, and their association with inflammation are lacking for patients with RA. Therefore, present study was done to determine any association between NLR, PLR, and RA.

## 2. Material and Methods

This was a Hospital based, cross-sectional and comparative study. This study was conducted at SMS Medical College and Hospital (Department of Medicine), Jaipur, Rajasthan, India. Data collection was started after approval from institutional research review board to April 2021 and another 2 months were required for the write up. Sample size was calculated to be 30 subjects in each group.

### Inclusion Criteria:

- 1) Rheumatoid arthritis patients of any age and either gender diagnosed with proper history, clinical and

Volume 11 Issue 4, April 2022

[www.ijsr.net](http://www.ijsr.net)

Licensed Under Creative Commons Attribution CC BY

laboratory findings, diagnosed on basis of America criteria of rheumatology visiting the Medicine OPD or admitted to IPD during the study period, irrespective of the duration of disease or disease activity.

- 2) Patients who give written and informed consent to be a part of study.

**Exclusion Criteria**

- 1) Patient having systemic disease like diabetes mellitus, hypertension, chronic renal failure, coronary artery disease, chronic respiratory diseases, cancer, haematological abnormalities.
- 2) Patients with acute and chronic infections.
3. Pregnancy, post-partum period.

**3. Observation**

We found that the mean age of RA cases was  $58.03 \pm 15.69$  years, while that of Controls was  $57.87 \pm 15.59$  years. Most of the RA Cases were females (63.3%), while only 11 cases (36.7%) were males.

The mean hemoglobin level was slightly higher among RA cases ( $12.37 \pm 2.48$  g/dl) as compared to controls ( $11.6$  g/dl). The mean TLC count was higher among RA cases ( $7.77 \pm 3.86 \times 10^3$ /cumm) as compared to controls ( $5.7 \pm 1.76 \times 10^3$ /cumm). The mean neutrophil percentage was higher among RA cases ( $66.23 \pm 10.86\%$ ) as compared to controls ( $52.6 \pm 7.23\%$ ). The mean absolute neutrophil count was higher among RA cases ( $5.21 \pm 2.82 \times 10^3$ /cumm) as compared to controls ( $3 \pm 1.03 \times 10^3$ /cumm). The mean absolute lymphocyte count was lower among RA cases ( $1.69 \pm 0.81 \times 10^3$ /cumm) as compared to controls ( $2.05 \pm 0.46 \times 10^3$ /cumm). The mean platelet count was higher among RA cases ( $322.9 \pm 110.98 \times 10^3$ /cumm) as compared to controls ( $234.87 \pm 74.56 \times 10^3$ /cumm). The mean CRP level was much higher among RA cases ( $60.1 \pm 27.3$  mg/dl) as compared to controls ( $1.93 \pm 1.08$  x mg/dl). The mean ESR level was much higher among RA cases ( $46.3 \pm 18.68$  mm) as compared to controls ( $10.23 \pm 3.62$  mm).

The mean Anti CCP level was much higher among RA cases ( $151.1 \pm 59.61$  EU/ml) as compared to controls ( $4.6 \pm 2.88$  EU/ml).

**Table 1:** Comparison of Neutrophil: Lymphocyte ratio among study groups

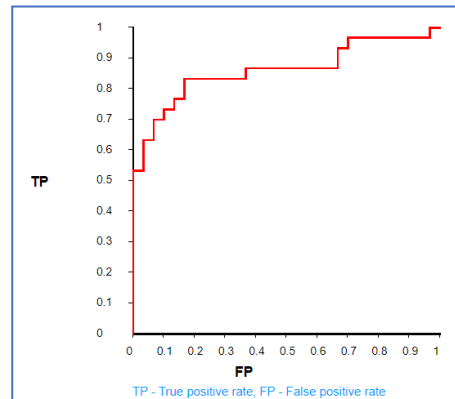
Group	N	Mean $\pm$ SD	t value	P value
RA Cases	30	$2.81 \pm 1.22$	5.507	<0.001 (S)
Controls	30	$1.48 \pm 0.51$		

In above table the mean N: L ratio was higher among RA cases ( $2.81 \pm 1.22$ ) as compared to controls ( $1.48 \pm 0.51$ ). This difference in N: L ratio among RA cases and controls was found to be statistically significant ( $p < 0.001$ ).

The mean P: L ratio was higher among RA cases ( $184.88 \pm 52.31$ ) as compared to controls ( $115.56 \pm 35.67$ ). This difference in P: L ratio among RA cases and controls was found to be statistically significant ( $p < 0.001$ ).

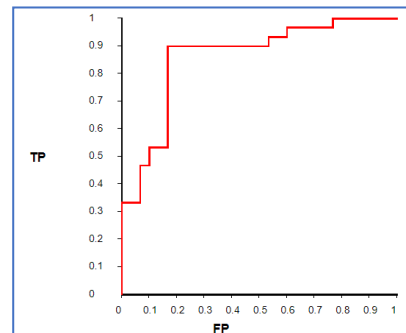
On ROC curve analysis (fig.1), the area under the curve (AUC) for N: L ratio for identifying Rheumatoid arthritis

was 0.861. This high AUC indicates that N: L ratio is a good indicator of Rheumatoid arthritis ( $p < 0.001$ ). Using Youden’s index the critical cutoff value of N: L ratio  $> 1.77$  had a sensitivity of 83.3% and specificity of 86.7% for identifying Rheumatoid arthritis.



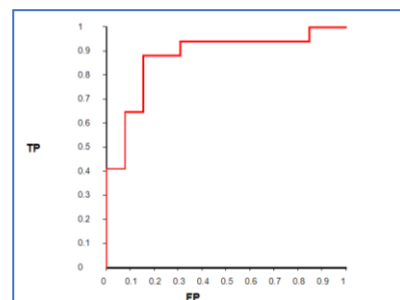
**Figure 1:** ROC Curve for N: L ratio for Rheumatoid arthritis

On ROC curve analysis (fig.2), the area under the curve (AUC) for P: L ratio for identifying Rheumatoid arthritis was 0.860. This high AUC indicates that P: L ratio is a good indicator of Rheumatoid arthritis ( $p < 0.001$ ). Using Youden’s index the critical cutoff value of P: L ratio  $> 117.4$  had a sensitivity of 90% and specificity of 83.3% for identifying Rheumatoid arthritis.



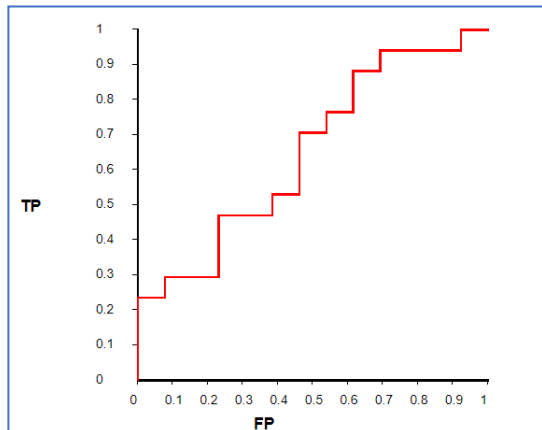
**Figure 2:** ROC Curve for P: L ratio for Rheumatoid arthritis

On ROC curve analysis (fig.3), the area under the curve (AUC) for N: L ratio for identifying active disease in Rheumatoid arthritis was 0.857. This high AUC indicates that N: L ratio is a good indicator for differentiating active disease from remission in Rheumatoid arthritis ( $p < 0.001$ ). Using Youden’s index the critical cutoff value of N: L ratio  $> 2.72$  had a sensitivity of 85.71% and specificity of 76.92% for identifying active disease.



**Figure 3:** ROC Curve for N: L ratio for disease activity in Rheumatoid arthritis

On ROC curve analysis (fig.4), the area under the curve (AUC) for P: L ratio for identifying active disease in Rheumatoid arthritis was 0.651. P: L ratio was not found to be a good indicator for differentiating active disease from remission in Rheumatoid arthritis ( $p>0.05$ ).



**Figure 4:** ROC Curve for P: L ratio for disease activity in Rheumatoid arthritis

#### 4. Discussion

In the present study the mean age of RA cases was observed to be  $50.43 \pm 5.7$  years, while that of Controls was  $48.4 \pm 5.15$  years. This difference was however not found to be statistically significant. Most of the RA Cases were females (63.3%), while only 11 cases (36.7%) were males. **Mini Bhatnagar et al (2017)**<sup>12</sup> found that the mean age of RA patients was 43.32 years (SD $\pm$ 11.67) with a minimum age of 22 years and maximum age of 70 years, majority were females. **Mervat Ismail Abd-Elazeem et al (2018)**<sup>13</sup> found that the mean age of patients was  $40.7 \pm 10.1$  years.

The mean N: L ratio was higher among RA cases ( $2.81 \pm 1.22$ ) as compared to controls ( $1.48 \pm 0.51$ ). This difference in N: L ratio among RA cases and controls was found to be statistically significant. On ROC curve analysis, the area under the curve (AUC) for N: L ratio for identifying Rheumatoid arthritis was 0.861. Similarly **You-Fan Peng et al (2015)**<sup>14</sup> found that NLR were significantly higher in RA patients compared with healthy controls ( $3.20 \pm 2.06$  vs.  $1.56 \pm 0.47$ ,  $P<0.01$ ). **Ali Uğur Uslu et al (2015)**<sup>15</sup> in a study found that NLR was  $2.12 \pm 0.83$  in the patient group and  $1.58 \pm 0.57$  in the control group and the difference was found to be statistically significant. **Fu H et al (2015)**<sup>16</sup> found that NLR increased significantly in RA patients. **Yingying Zhang et al (2016)**<sup>17</sup> observed that RA patients have high levels of NLR compared to healthy individuals.

The mean P: L ratio was higher among RA cases ( $184.88 \pm 52.31$ ) as compared to controls ( $115.56 \pm 35.67$ ). This difference in P: L ratio among RA cases and controls was found to be statistically significant. The mechanism to explain the increased levels of PLR in RA is the presence of a chronic inflammatory state that affects the progressive damage of joint. On ROC curve analysis, the area under the curve (AUC) for P: L ratio for identifying Rheumatoid arthritis was 0.860. **You-Fan Peng et al (2015)**<sup>14</sup> found that PLR were significantly higher in RA patients compared with healthy controls ( $192.85 \pm 101.78$  vs.  $103.49 \pm 28.68$ ,  $P<0.01$ ).

Receiver operating characteristic (ROC) curves analysis showed that PLR values higher than  $>115.7$  evaluated RA with a sensitivity of 82.5%, a specificity of 74.8% and area under the curve (AUC) of 0.847. **Fu H et al (2015)**<sup>16</sup> found that PLR increased significantly in RA patients. **Yingying Zhang et al (2016)**<sup>17</sup> observed that RA patients have high levels of PLR compared to healthy individuals.

The N: L ratio was higher among RA cases with active disease ( $3.31 \pm 1.29$ ) as compared to RA cases with remission ( $2.15 \pm 0.74$ ). This difference in N: L ratio in relation to disease activity among RA cases was found to be statistically significant. On ROC curve analysis, the area under the curve (AUC) for N: L ratio for identifying active disease in Rheumatoid arthritis was 0.857. **Yingying Zhang et al (2016)**<sup>17</sup> observed that RA patients in active stage have high levels of NLR compared to healthy individuals. **Mervat Ismail Abd-Elazeem et al (2018)**<sup>13</sup> also observed similarly that there was a significant difference regarding NLR between active patients and control. **O Zengin et al (2018)**<sup>18</sup> in a study observed that there was a significant difference in NLR ( $p = 0.001$ ) between active disease and remission in ERA. **S. Chandrashekara et al (2020)**<sup>19</sup> found that increased likelihood for achieving sustained remission was noted in RA patients with baseline NLR  $\leq 2$ .

The P: L ratio was higher among RA cases with active disease ( $196.70 \pm 50.93$ ) as compared to RA cases with remission ( $169.5 \pm 51.97$ ). This difference in P: L ratio in relation to disease activity among RA cases was however not found to be statistically significant. On ROC curve analysis, the area under the curve (AUC) for P: L ratio for identifying active disease in Rheumatoid arthritis was 0.651. **Mervat Ismail Abd-Elazeem et al (2018)**<sup>13</sup> also observed similarly that there was a significant difference regarding PLR between active patients and control. **O Zengin et al (2018)**<sup>18</sup> in a study however observed that there was no significant difference in PLR ( $p = 0.051$ ) between active disease and remission in ERA.

#### 5. Conclusion

Neutrophil lymphocyte ratio and platelet lymphocyte ratio were significantly associated with Rheumatoid arthritis. They can be obtained via complete blood count, which is convenient, inexpensive, and fast. Therefore, the NLR and PLR is especially suitable for peripheral centers and can serve as an additional useful marker for the diagnosis of RA.

#### References

- [1] Scott D. L., Wolfe F., Huizinga T. W., Rheumatoid arthritis, *Lancet.*, 2010, 376, 1094-1108.
- [2] Firestein G. S., Evolving concepts of rheumatoid arthritis, *Nature.*, 2003, 423, 356-361.
- [3] Colglazier CL, Sutej PG. Laboratory testing in the rheumatic diseases: a practical review. *South Med J* 2005; 98 (2): 185-91.
- [4] Al-Saadany HM, Hussein MS, Gaber RA, Zaytoun HA. Th-17 cells and serum IL-17 in rheumatoid arthritis patients: correlation with disease activity and severity. *Egypt Rheumatol* 2016; 38 (1): 1-7.

- [5] Hassan SZ, Gheita TA, Kenawy SA, Fahim AT, El-Sorougy IM, Abdou MS. Oxidative stress in systemic lupus erythematosus and rheumatoid arthritis patients: relationship to disease manifestations and activity. *Int J Rheum Dis* 2011; 14 (4): 325–31.
- [6] Gheita TA, Sayed S, Gheita HA, Kenawy SA. Vitamin D status in rheumatoid arthritis patients: relation to clinical manifestations, disease activity, quality of life and fibromyalgia syndrome. *Int J Rheum Dis* 2016; 19 (3): 294–9.
- [7] El Defrawy AO, Gheita TA, Raslan HM, El Ansary MM, El Awar AH. Serum and synovial cartilage oligomeric matrix protein levels in early and established rheumatoid arthritis. *Z Rheumatol* 2016; 75 (9): 917–23.
- [8] Briggs C. Quality counts: new parameters in blood cell counting. *Int J LabHematol* 2009; 31 (3): 277–97.
- [9] Sandhaus LM, Meyer P. How useful are CBC and reticulocyte reports to clinicians? *Am J Clin Pathol* 2002; 118 (5): 787–93.
- [10] Mercan R, Bitik B, Tufan A, Bozbulut UB, Atas N, Ozturk MA, et al. The association between neutrophil/lymphocyte ratio and disease activity in rheumatoid arthritis and ankylosing spondylitis. *J Clin Lab Anal* 2016; 30 (5): 597–601.
- [11] Templeton AJ, McNamara MG, Šeruga B, Vera-Badillo FE, Aneja P, Ocaña A, et al. Prognostic role of neutrophil-to lymphocyte ratio in solid tumors: a systematic review and meta-analysis. *J Natl Cancer Inst* 2014; 106 (6). dju124.
- [12] Mini Bhatnagar, Bimal K Agrawal, Aruna Bhagat Dubey, Gaurav Aggarwal. Rheumatoid Arthritis Disease Activity Assessment Using Neutrophil-To-Lymphocyte Ratio and Platelet-To-Lymphocyte Ratio. *JMSCR* 2017; 5 (10): 28888-28893.
- [13] Mervat Ismail Abd-Elazeem, Rabab Afify Mohamed. Neutrophil-lymphocyte and platelet-lymphocyte ratios in rheumatoid arthritis patients: Relation to disease activity. *The Egyptian Rheumatologist* (2018); 40: 227–231.
- [14] You-Fan Peng, Ling Cao, Yan-Hua Zeng, Zhao-Xia Zhang, Dan Chen, Qiong Zhang, You-Sen Zhu. Platelet to lymphocyte ratio and neutrophil to lymphocyte ratio in patients with rheumatoid arthritis. *DE GRUYTER Open Med.*2015; 10: 249-253.
- [15] Ali Uğur Uslu, Adem Küçük, Ali Şahin, Yunus Ugan, Ramazan Yılmaz, Tayfun Güngör et al. Two new inflammatory markers associated with Disease Activity Score-28 in patients with rheumatoid arthritis: neutrophil-lymphocyte ratio and platelet-lymphocyte ratio. *Int J Rheum Dis.*2015 Sep; 18 (7): 731-5.
- [16] Haitao Fu, Baodong Qin, Zhide Hu, Ning Ma, Min Yang, Tingting Wei et al. Neutrophil-and platelet-to-lymphocyte ratios are correlated with disease activity in rheumatoid arthritis. *Clin Lab.*2015; 61 (3-4): 269-73.
- [17] Yingying Zhang, Yongmei Yin, Shougang Kuai, Zhongbao Shan, Hao Pei, Jun Wang. Combination of neutrophil to lymphocyte ratio and platelet to lymphocyte ratio as diagnostic biomarker for rheumatoid arthritis. *Int J Clin Exp Med* 2016; 9 (11): 22076-22081.
- [18] O Zengin, M E Onder, A Kalem, M Bilici, I H Türkbeyler, Z A Ozturk. New inflammatory markers in early rheumatoid arthritis. *Z Rheumatol.*2018 Mar; 77 (2): 144-150.
- [19] S. Chandrashekara<sup>1</sup>, Deepak Chikkulikere Lingaraju<sup>1</sup>, P. Renuka<sup>3</sup> & K. R. Anupama. Potential of neutrophil to lymphocyte ratio in predicting sustained remission in rheumatoid arthritis compared to other immune activation markers. *Indian J Med Res* 152, September 2020, pp 234-243.