Correlation between neutrophil-to-lymphocyte ratio and disease activity score using SDAI in established rheumatoid arthritis patients

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ABSTRACT

Rheumatoid arthritis (RA) is a multisystem inflammatory disorder predominantly affecting joint structures leading to joint erosions, destruction of cartilage and frank deformities if not treated. However disease not confined to joint but also involves other organ systems.

Objective. To determine the correlation between neutrophil-to-lymphocyte ratio and disease activity score using SDAI in established rheumatoid arthritis patients.

Material and methods. This was an observational cross-sectional study, done at the Rheumatology Clinic/Medicine OPD of DOW University Hospital. Patients with ages between 18 to 70 years old, of any gender, diagnosed with rheumatoid arthritis according to American College of Rheumatology criteria were included. Data of all patients who met the inclusion criteria were recorded in predesigned questionnaire, after informed consent. Data were analyzed by calculating median and mode for quantitative variables, frequency and percentages for qualitative variables. Correlations were tested using Pearson correlation test. P values <0.05 were considered significant throughout the study.

Outcome. The sample included 64 patients, seven males and 57 females. Mean age was 43.22±11.58. Fifty eight patients (90.6%) were sero-positives while six were negative (9.4%). The Pearson r for the correlation between NLR and SDAI was 0.105 and sig (2 tailed) value was 0.409. The Pearson r was close to 0, meaning a weak relationship between NLR and SDAI. Cross tabulation of NLR and SDAI of patients, using Chi Square yield, proved to have statistically insignificant results (p value = 0.181).

Conclusion. The study results revealed a weak correlation between neutrophil-to-lymphocyte ratio and disease activity score using SDAI in established rheumatoid arthritis patients.

Keywords: neutrophil-to-lymphocyte ratio, disease activity score, rheumatoid arthritis, inflammatory disorder, SDAI

Abbreviations (in alphabetical order):

DMARs	– Disease Modifiying Antirheumatic drugs	RA	– Rheumatoid arthritis
NLR	– Neutrophil-to-lymphocyte ratio	SDAI	– Simplified Disease Activity Index

BACKGROUND

Rheumatoid arthritis (RA) is a multisystem inflammatory disorder predominantly affecting joint structures leading to joint erosions, destruction of cartilage and frank deformities, if not treated. However, disease is not confined to joint, but also involves other organ systems. Globally it's about 1% prevalent [1], while local data from Southern Pakistan shows prevalence of 0.14% [2] while from Northern Pakistan it's about 0.55% [3].

The course of disease oscillates in time, aggregated disease status being utmost causal factor of articular and extra articular involvement of RA [4]. ACR (American College of Rheumatology) recommends "treat to target" strategy in management of RA [5], EULAR (European League Against Rheumatism) also accredited same plan of action for physicians. For assessing disease activity to follow recommendations, ACR in 2015 presented different disease activity scores like Clinical Disease Activity Index (CDAI), Disease Activity Score in 28 joints (DAS28), Patient Activity Scale (PAS), Routine Assessment of Patient Index Data 3 (RAPID3), Simplified Disease Activity Index (SDAI). 2019 ACR guidelines still recommend same [6].

SDAI scoring system is both a feasible and a credible tool for assessing disease severity. It's is the numeric value of a composite of swollen and tender joint count, C-reactive protein CRP, and a patient and clinician evaluation of disease activity on a visual analog scale [7].

The complete blood count is an available investigation, certain parameters of peripheral blood cell count ratio being comparatively newer markers for systemic inflammation in multiple diseases [8,9], and it includes also neutrophil-to-lymphocyte ratio (NLR) [10,11]. Literature search shows that NLR were remarkably elevated with RA in comparison to healthy individuals. These parameters have direct correspondence to disease activity and help in optimizing the treatment goal [12,13]. This association of NLR to disease activity are more used in the Western literature, and less applicable to our population because there are differences in topography and environment of our ethnicity compared to the Western world. Thus, we study correlation between neutrophil-to-lymphocyte ratio and disease activity score using SDAI in established rheumatoid arthritis patients [14].

OBJECTIVE

The objective of our study is to determine the correlation between neutrophil--lymphocyte ratio and disease activity score using SDAI in established rheumatoid arthritis patients.

METHODS

We used an observational cross-sectional study to determine the correlation between neutrophil-to-lymphocyte ratios with simplified disease activity index (SDAI) in established rheumatoid arthritis. The study was conducted in the Rheumatology Clinic/Medicine OPD of a tertiary care hospital. The duration of study was of 3 months. Data collection was done after the approval of institutional review board committee and the allotment of a IRB number. The sample group was formed from patients with ages from 18 to 70 years old, regardless of gender, diagnosed with rheumatoid arthritis according to American College of Rheumatology criteria. Patients with diabetes mellitus, hypertension, chronic liver and kidney disease, obstructive lung disease, ischemic heart disease, hematologic disorders other than anemia were excluded. Pregnant females or with any malignant disease were also excluded.

Random sampling method was used. Sample size was calculated for correlation using a sample size calcultor [15] and it is found to be 64. The expected correlation coefficient from previous studies taken were 0.345 [14]. For the purpose of recruitment, those who fulfiled the selection criteria were included after taking verbal consent. Demographic characteristic including age, sex, marital status, occupations were noted. Venous blood sample were taken under aseptic condition. The sample were investigated for CBC, ESR, and CRP by institutional laboratory using automated analyzer. Neutrophil-to-lymphocyte ratio was calculated manually. These tests were routinely done for rheumatoid arthritis patients during each follow-up visit. Hence, no extra finance or budget were needed. SDAI scores were calculated, and data analyzed with SPSS version 20. Mean, median and mode were calculated for quantitative variable, frequency and percentages were calculated for qualitative variable. Chi square test was applied for comparison of qualitative data and t test was used for quantitative variables. Correlations were tested using Pearson correlation test. P values <0.05 were considered significant throughout the study.

RESULT

Out of 64 patients, 7 were males and 57 females. Mean age was 43.22±11.58. Fifty eight patients (90.6%) were tested sero-positive while six were negative (9.4%). The frequency of NLR ratio is revealed in Figure 1. SDAI scores of patients were displayed in Figure 2.

The Pearson r for the correlation between NLR and SDAI is 0.105 and sig (2 tailed) value is 0.409. The Pearson r was close to 0, meaning a weak relationship between the two variable NLR and SDAI. Table 1 shows the cross tabulation of NLR and SDAI of
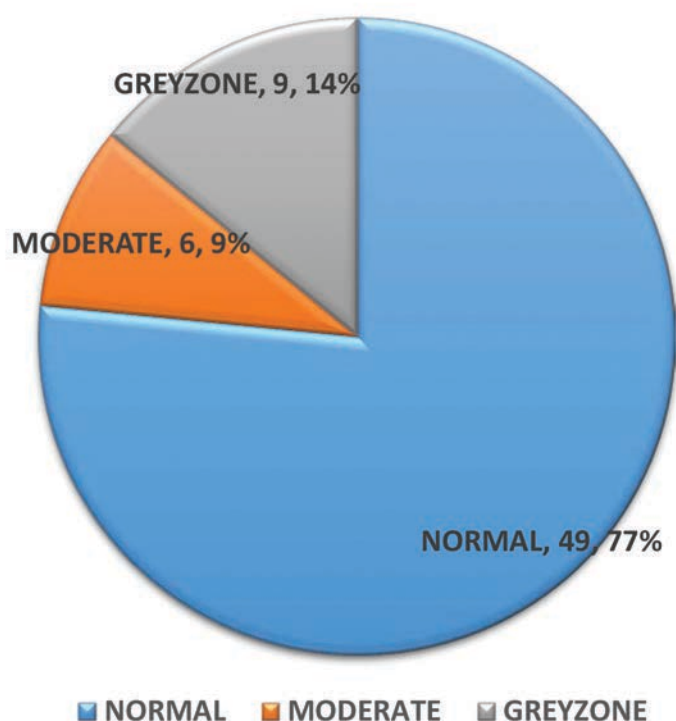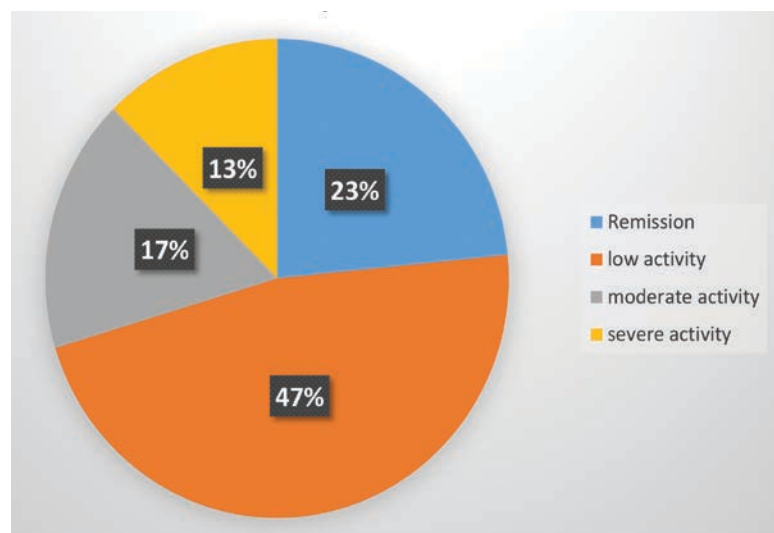
FIGURE 1. Frequency of NLR

FIGURE 2. SDAI scores of patients

patients. Chi Square used to calculate p value 0.181 was statistically not significant.

TABLE 1. NLR crosstab with SDAI of patients

NLR ratio	SDAI of patient				
	Remission	Low activity	Moderate activity	Severe activity	Total
Normal	14	19	10	6	49
Moderate	1	5	0	0	6
Grey zone	0	6	1	2	9
Total	15	30	11	8	64
Pearson Chi Square	P value >0.05				

DISCUSSION

As we earlier emphasized, among all the rheumatologic groups "treat to target" (T2T) is an established plan for managing RA, and targets are usually estimated by the disease activity scores. SDAI is one way of estimating disease activity in patients visiting outpatient clinics. In the recent years, multiple researchers concluded a direct relation between disease activity and neutrophil-to-lymphocyte ratio (NLR) [16,17]. Another observational study performed by Uslu et al. revealed that patients with remission or low disease activity have noticeably decrease in NLR, although in their study DAS28 was used as predictor of disease severity [13]. Mercan et al. reinforced the findings of Uslu with same DAS28 that with increasing disease activity NLR rises [18].

We used SDAI to assess disease severity in relation to NLR and we found that correlation between NLR and SDAI was 0.105. As Pearson r is close to zero, it means there is a weak relationship between these two variables. Secondly, a Pearson r value of 0.105, positive, was meaning that if NLR increases in value, the SDAI also increases. This changes in NLR are positive, but weakly correlated with SDAI score. Sig (2 tailed) value in our study is 0.409, and since it is >0.05 we come to the conclusion that our results are statistically not significant. It was close to one of the meta-analysis involving 16 studies which revealed a correlation coefficient of 0.277 bringing to an end result of positive and weak correlation [14]. In contrast to our study, their results show statistically significant positive correlation both in Asian and Turkish population. This difference was probably due to the presence of clinical diversities, and difference in tools used for disease activity score, as most of the studies used DAS28. Additionally, most of the studies in this meta-analysis didn't assess the correlation coefficient. However a recent study, published in 2022, by Choe JY shows a significant correlation between NLR and DAS28-ESR [20]. While Yolbas et al. disclosed monotonous NLR in both dormant as well as vigorous disease [20].

While doing cross tabulation of NLR with SDAI of rheumatoid arthritis, we found out some interesting results. 28% of patients having normal NLR were in remission, 39% showed low activity, concluded lower NLR with severe disease activity unlike to patients with recovered state (mean difference, −0.01 to −0.95)

[21]. Another study by Taha SI found similar results, but with crucial difference [23], while 20% showed moderate activity. 12% showed severe activity on SDAI. From patients with moderate elevated NLR, none of them was found in moderate to severe activity score of SDAI. This could have been probably because of low sample size or maybe alone SDAI was not enough to judge the severity index of RA. The majority (83%) recorded a low activity with moderate elevation of NLR. Coming to the grey zone, which is in between normal to moderate, 67% of patients had low activity on SDAI and 22% had severe activity. The greatest percentage recorded the severe group leading to the same impression as Abd-Elazeem MI et al.'s study, while Remalante et al. supported them showing that NLR had low sensitivity and specificity (AUC: 0.629) for establishing RA activity [22]. Thus, our results revealed a weak correlation of NLR and disease activity.

Although our study had a few limitations - being a single center study it used a small sample size and cross-sectional study design. The results could not be generalized because the study subjects may not be truly representative of all rheumatoid arthritis patients in the community. Secondly, numerous features affect NLR like age, gender, BMI [24], and disease modifying anti-rheumatic drugs (DMARDS). Since our study didn't assess BMI or effects of different drugs, the additional researches with larger sample sizes, involving multiple regional centers, are needed to assess the worth of NLR with disease activity.

CONCLUSION

We conclude that neutrophil-to-lymphocyte ratio and SDAI have weak correlation in established rheumatoid arthritis patients. No statistically significant association was found between NLR and SDAI.

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