

# Correlation of Neutrophil to Lymphocyte Ratio and Disease Activity in Patients of Ankylosing Spondylitis on Etanercept Therapy

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## Abstract

**Background:** Ankylosing spondylitis, a chronic disease, in which spinal inflammation develops which continuously causes backache and inadequacy in the functions of spine. Anti-inflammatory medications are available but along with that, assessment of inflammatory markers is obligatory to assess disease activity.

**Objective:** To determine association between neutrophil to lymphocyte ratio and activity of disease in patients of ankylosing spondylitis on etanercept therapy

**Study type settings & duration:** This quasi experimental trial was conducted at Department of Rheumatology, Mayo Hospital, Lahore from September 2019 to March 2020.

**Methodology:** Patients of aged 41-49 years of both genders diagnosed with ankylosing spondylitis and were taking etanercept as medication for 6 months were enrolled. Blood samples were taken at baseline and after 6 months of therapy and analyzed for assessment of neutrophil lymphocyte ratio (NLR) and ASDAS score. Data was entered, decoded and analyzed using SPSS version 22.

**Results:** The mean age of the participants was 45.03 ( $\pm 2.44$ ) years and majority of them 24 (80%) were males. The mean NLR was 2.9 ( $\pm 1.0$ ) at baseline which reduced significantly to 1.6 ( $\pm 0.5$ ) after six months therapy ( $p < 0.05$ ). Similarly the mean baseline ASDAS was 3.8 ( $\pm 0.9$ ) which significantly reduced to 2.4 ( $\pm 0.6$ ) after six months of therapy ( $p < 0.05$ ). There was statistical significant positive correlation between NLR and ASDAS i.e.  $r = 0.659$  ( $p < 0.05$ ).

**Conclusion:** NLR and activity of disease showed positive correlation in patients with ankylosing spondylitis, which illustrated that NLR can also be used as a key predictor of inflammation that makes it a dependable tool for assessing activity of disease in patients of ankylosing spondylitis on Etanercept therapy.

**Key words:** Neutrophil to lymphocyte ratio, ankylosing spondylitis, disease activity, etanercept therapy.

## Introduction

Ankylosing spondylitis (AS), an insidiously destructive is one of the most familiar forms of spondylo arthritis and is described by inflammation and the new bone development. It is progressive type of arthritis, includes the axial part

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### Authors Contribution

SZ conceptualized the project. SS & YI did the data collection. Literature search and statistical analysis were performed by SS & UM. HMM & SA did the drafting, revision & writing of manuscript.

of skeleton which considerably affect the life quality.<sup>1</sup> In the case of ankylosing spondylitis, it is specifically problematic to describe the disease activity. This is due to variability in the clinical depiction in several patients.<sup>2,3</sup> However the AS pathogenesis is still not clear especially the development of new bone due to issue in collecting tissue from the joints of spinal cord<sup>4</sup> and more work is required to understand the pathogenesis disease.<sup>5,6</sup>

Currently there is no gold standard method or scoring system to determine the disease activity of patients suffering from ankylosing spondylitis. However, various biomarkers and scores are used to determine the systemic inflammation including neutrophil to lymphocyte ratio (NLR), C-reactive protein (CRP), and platelet-to-lymphocyte ratio (PLR).<sup>7</sup> The NLR has also been reported as a good predictor to determine the systemic inflammation in

ankylosing spondylitis along with specifying the Spondylitis Disease Activity Score (ASDAS) has also been reported as predictive markers for evaluating the disease activity among ankylosing spondylitis patients.<sup>9</sup>

Various studies have reported the predictive role of NLR and PLR in systemic inflammation from different countries and populations<sup>10,11</sup> and increased levels of NLR or PLR have been associated with poor disease prognosis and survival rate for several inflammatory syndromes.<sup>12</sup> Recently a study from Pakistan has also reported association of NLR and PLR with more active disease activity.<sup>13</sup> However a little data is available about association AS activity and NLR with Etanercept therapy, therefore we planned this study to determine the association of NLR and disease activity in patient taking Etanercept therapy.

## Methodology

This quasi experimental trial was conducted at Department of Rheumatology, Mayo Hospital, Lahore for a period of six months i.e. September 2019 to March 2020. A total of 30 patients aged between 41-49 years of both gender presenting with ankylosing spondylitis were enrolled using con recruited for the study. Patients who were taking disease-modifying anti-rheumatic medicines from previous 4 weeks before inclusion, intra-articular injections during last 3 months; history of cardiac failure, multiple sclerosis, airway diseases that include chronic obstructive pulmonary disease or asthma, any recurrent infection, lymphoma, any type of malignancy; fibromyalgias or any other rheumatic diseases; pregnancy and lactation; previous history of poor compliance to medicines, psychological or neurological illness, alcohol use or drug addiction were excluded from the study. At baseline, blood sample was taken and sent to the hospital laboratory for assessment of NLR. Meanwhile patients were evaluated for ASDAS score. All patients were given subcutaneous dose of 25 mg Etanercept therapy twice weekly for 6 months. Patients were followed-up in OPD for 6 months. After 6 months, blood sample were taken and sent to the laboratory of the hospital for

disease activity.<sup>8</sup> Similarly, the Ankylosing assessment of NLR. Meanwhile patients were evaluated again for ASDAS score. .

All the gathered data was entered and analyzed using SPSS v.22 Correlation of NLR with ASDAS was evaluated by calculating Pearson's correlation coefficient. The *p*-value of  $\leq 0.05$  was considered as a significant.

The ethical approval was taken from institutional review board of King Edward Medical University, Lahore.

## Results

A total of 30 patients were enrolled and the mean age was 45 ( $\pm 2.44$ ) years. Among them, 24 were males (80%) and 6 females (20%). The mean NLR at baseline was  $2.9 \pm 1.0$  reduced to  $1.6 \pm 0.5$  after 6 months of Etanercept therapy. The reduction in NLR was significant (*p*-value  $< 0.05$ ).

The mean ASDAS score at baseline was  $3.8 \pm 0.9$ , which was reduced to  $2.4 \pm 0.6$  after 6 months of Etanercept therapy. The reduction in ASDAS score was significant (*p*-value  $< 0.05$ ). The correlation analysis was done between NLR and ASDAS at base line and after six months of therapy and positive association was seen (Table & Figure). A positive correlation is seen between NLR and ASDAS after six month treatment with Etanercept therapy.

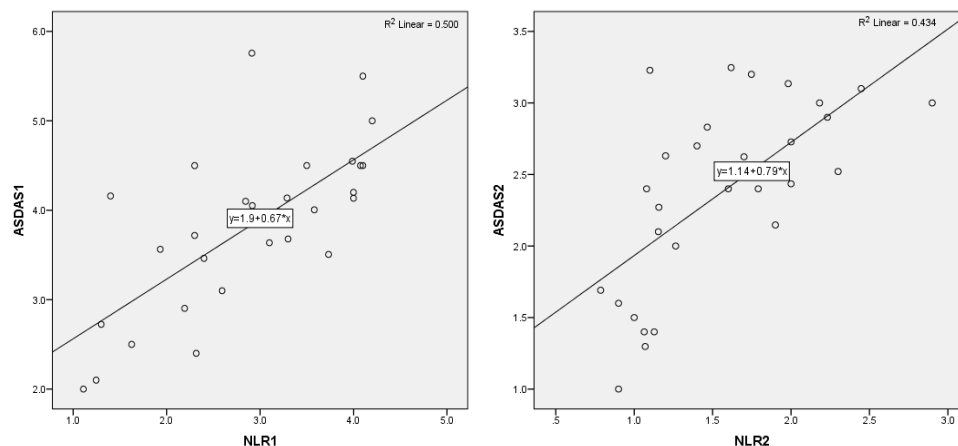
## Discussion

Inflammation is the main element and main fundamental process which leads to the disability as well as high mortality rate in candidates of rheumatoid arthritis and also for ankylosing spondylitis.<sup>14</sup>

Ankylosing Spondylitis with non-steroidal anti-inflammatory drug therapeutic failure is treated with biologics.<sup>15</sup> Etanercept is the first anti-TNF agent. It has been recommended for use in the treatment of patients with diagnosis of rheumatoid arthritis. During last decade, numerous studies showed that Etanercept is effective and safe in treatment of patients with rheumatoid arthritis.

**Table: Correlation between NLR and ASDAS.**

NLR		ASDAS	
		At baseline	After 6 months
At baseline	Pearson Correlation (r)	0.707	
	<i>p</i> -value	0.000	
After 6 months	Pearson Correlation (r)		0.659
	<i>p</i> -value		0.000



**Figure-1: Correlation between NLR and ASDAS at baseline (left) and after 6 months (right).**

It can be given as mono therapy as well as in combination with methotrexate. The safety profile of Etanercept was predictable since its application in the first clinical trials without any new major safety concerns.<sup>16</sup> This anti – TNF agent has modernized the better management of rheumatoid arthritis and significantly controlled the disease severity and activity whereas improving the functionality and life quality of patients. This agent is structurally different from that of other anti TNF agents and thus has necessary features for drug survival, immunogenicity and infection proportion.<sup>17</sup> Increased neutrophil counts are highly related to the poor prognosis as well as it increases the death rate in many circumstances. NLR appeared to be a significant marker for detection of inflammation in several neoplastic & cardiovascular diseases.<sup>14</sup> NLR is the cost - effective and easily available marker to assess the presence of disease activity in some rheumatoid syndromes.<sup>18</sup> Our study showed a significant reduction in NLR and ASDAS after 6 months of treatment with Etanercept therapy. A recent study from Islamabad has also reported NLR as good markers of inflammation in AS patients and showed association of high NLR values with more active disease activity.<sup>13</sup> Kucuk et al have also described that patients with Ankylosing Spondylitis had higher NLR in comparison with the control group. Patients with severe ankylosing spondylitis disease activity were observed to have considerably higher values of NLR in comparison with the patients having mild ankylosing spondylitis disease activity. But Al-Osami et al., found that there is very weak and insignificant relationship exist between NLR and disease activity score i.e.  $r = 0.170$ ,  $p = 0.051$ .<sup>19</sup> Similarly, the NLR had positive correspondence with BASDAI. Our study showed a positive

correlation between NLR and BASDAI. Similar finding has been reported by Inal et al., who found a positive correlation of NLR with disease activity score<sup>20,21</sup> But this correlation was reported to be very weak as compared to the value observed in our study. But in that study, effect of anti-TNF was not undertaken.

In our study, male predominance has been observed which is consistent to previous reports.<sup>22</sup> Similarly in other study male to female ratio was 10:1<sup>19</sup> while in a Iraqi male to female ratio was 11:1, which also showed male predominance for the disease<sup>23</sup> But, this male predominance in above quoted studies were unpredictable to that of studies conducted in other regions of the world.<sup>24-26</sup> This contradiction may be because of the following factors: smaller sample sizes as well as the fact that the number of females identified of having Ankylosing Spondylitis is fewer as compared to males, subsequently, for reasons it is imprecise, females seem to progress the chronic changes in later life and usually less frequent.<sup>19</sup>

This study showed that NLR can be used a predictive marker for the prognosis of Ankylosing Spondylitis in patients taking Etanercept therapy.

**Conflict of interest:** None declared.

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