Original Research Article

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Comparing the frequency of anemia in rheumatoid arthritis and axial spondyloarthritis patients and its relationship with hemogram parameters

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ABSTRACT

Background: To compare the frequency of anemia in rheumatoid arthritis (RA) and radiographic axial spondyloarthritis (r-axSpA) patients and to investigate its relationship with hemogram parameters used as inflammation markers.

Methods: The study included 87 RA patients and 116 r-axSpA patients. Characteristics of the patients, hemogram parameters (neutrophil-lymphocyte ratio 'NLR', platelet-lymphocyte ratio 'PLR', systemic immune-inflammation index 'SII', red blood cell distribution width 'RDW' and mean platelet volume 'MPV'), laboratory parameters (erythrocyte sedimentation rate 'ESR' and C-reactive protein 'CRP') and indices (Disease Activity Score in 28 Joints (DAS-28) for RA and the Bath Ankylosing Spondylitis (AS) Disease Activity Index (BASDAI) and AS Disease Activity Score with CRP (ASDAS-CRP) for axSpA) were recorded.

Results: The mean age for RA and r-axSpA patients was 55.8±12.0 and 43.8±10.1 years. Anemia was present in 47.1% of RA patients and 31.9% of r-axSpA patients and more prominent in RA patients (p=0.030). There was a significant female gender superiority in those with anemia in r-axSpA patients (p<0.001). ESR, PLR, SII and RDW values were significantly higher in patients with anemia in the RA (p=0.002, p=0.048, p=0.035, p<0.001, respectively), whereas only ESR was significantly greater in patients with anemia in the r-axSpA (p=0.012). There was no significant difference between disease activity and anemia in both disease groups.

Conclusions: Although the frequency of anemia was not affected by disease activity, female gender involvement was prominent. The increase in ESR and RDW values may reflect the possibility of developing anemia in rheumatic diseases.

Keywords: Anemia, Axial spondyloarthritis, Rheumatoid arthritis

INTRODUCTION

Anemia of chronic disease (ACD), also known as anemia of inflammation, is a hypoproliferative anemia that develops in response to systemic disease or inflammation, such as infection, cancer and autoimmune conditions. Tumor necrosis factor-alpha (TNF-α) and interleukin (IL)-6, pro-inflammatory cytokines, play an important role in the pathogenesis of ACD through their inhibitory effect on erythropoiesis release and iron from reticuloendothelial system. The effects of cytokines on

erythropoiesis may depend on the acute phase protein hepcidin, which is synthesized by the liver and has been discovered in recent years.^{1,2}

Anemia, which occurs when the oxygen-carrying capacity of the blood cannot meet the oxygen needs of body tissues, generally causes signs and symptoms such as fatigue, impaired cognitive function, loss of appetite, shortness of breath with exertion and loss of libido.3 Anemia and thrombocytosis are the most common hematological findings in rheumatoid arthritis (RA) patients.⁴ In fact, anemia is the most common extra-articular manifestation of RA and its prevalence is estimated to vary between 30% and 70% of patients.^{5,6} Anemia can also occur in patients with axial spondyloarthritis (axSpA) and significantly affects the patient's quality of life¹.

Hemogram parameters have recently been suggested as markers of inflammation in various studies conducted in different parts of the world.⁷ In the realm of medical diagnostics, the quest for reliable biomarkers to assess systemic inflammation and immune response has led to the emergence of several novel indices.

Among them, parameters such as neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) have gained considerable attention due to their simplicity, accessibility and potential prognostic value across various medical conditions. Elevated NLR and PLR has been associated with various conditions including autoimmune and inflammatory disorders, cardiovascular diseases and malignancies.⁸⁻¹⁴

Systemic immune-inflammation index (SII) is a similar inflammatory marker calculated by the formula neutrophil count x platelet count / lymphocyte count and provides valuable information in monitoring rheumatological diseases and response to treatment, as well as in diagnosing or predicting prognosis for many solid organ tumors. ¹⁵ Additionally, red blood cell distribution width (RDW) is a continuous measure that represents the variability (heterogeneity) in the size of circulating erythrocytes and has been independently associated with the risk of cardiovascular events and death.

A positive relationship has been detected between inflammatory indices such as C-reactive protein (CRP).⁷ It has also been shown that it may reflect disease activity in various rheumatic diseases. ^{14,16,17}

Mean platelet volume (MPV) reflects the platelet production rate in the bone marrow and the platelet size in circulation and can be used as an indicator of platelet function and activation and the severity of inflammation.

Many rheumatological conditions in which cytokines such as IL-1, IL-6 and TNF- α are excessively secreted cause low MPV levels. Therefore, MPV has been studied as an indicator of disease activity in various inflammatory conditions. The aim of this study is to compare the frequency of anemia in RA and radiographic (r) axSpA patients and to investigate its relationship with hemogram parameters used as inflammation markers.

METHODS

Study place

This cross-sectional study was conducted at the Department of Physical Medicine and Rehabilitation in Bezmialem Vakif University.

Study duration

Study was done between 2023 and 2024.

Ethical approval

The work was approved by the Ethical Committee of Bezmialem Vakif University (Trial Registration:2023/363). Written consent was acquired by each patient enrolled.

87 RA patients diagnosed according to 2010 ACR/EULAR (American College Rheumatology/European League Against Rheumatism) RA classification criteria and 116 r-axSpA patients diagnosed according to ASAS (Assessment of SpondyloArthritis International Society) criteria were included in the study. ²⁰⁻²¹ According to the modified New York criteria, radiographic sacroiliitis was defined as bilateral grade≥2 or unilateral grade 3-4 on pelvic radiograph.²²

Inclusion criteria

Inclusion criteria were as the patients diagnosed with RA and r-axSpA for at least 1 year and being over 18 years of age, patients who have not yet received biological DMARD and targeted DMARD treatments.

Exclusion criteria

Exclusion criteria were as being under 18 years of age, patients with a history of pregnancy, alcohol abuse, malignancy, mental retardation, serious emotional disorder, renal or liver failure, hematological disease (such as thalassemia), thyroid disease, gastrointestinal bleeding, patients with a history of an accompanying secondary rheumatic disease (inflammatory bowel disease (Chron's disease, ulcerative colitis), psoriasis or psoriatic arthritis, Reiter's syndrome), patients with iron, vitamin B12 and folate deficiency, patients using drug therapy that will affect erythropoiesis or iron metabolism, patients using biological DMARDs and targeted DMARD treatments.

The socio-demographic data, body mass index (BMI), laboratory parameters (erythrocyte sedimentation rate (ESR) and CRP) and hemogram parameters (NLR, PLR, SII, RDW and MPV) were collected. Moreover, disease activity score in 28 Joints (DAS-28) for RA patients and the Bath Ankylosing Spondylitis (AS) Disease Activity Index (BASDAI) and AS Disease Activity Score with CRP (ASDAS-CRP) for r-axSpA patients were recorded. ²³⁻²⁵ Anemia was defined according to the criteria of World Health Organization (WHO) as a hemoglobin (Hb) level<12 mg/dL for women and<13 mg/dL for men.

Statistical analysis

Descriptive statistics of the qualitative variables in the study are given as numbers and percentages and

descriptive statistics of the quantitative variables are given as mean, median, standard deviation, minimum and maximum. Relationships between qualitative variables were examined with Pearson chi-square and Fisher exact chi-square analyses. The suitability of quantitative variables to normal distribution was examined with the Kolmogorov Smirnov test. Student t-test was used to compare the means of two independent groups and Mann Whitney U test was used to compare the medians of two independent groups. Relationships between quantitative variables were evaluated with Spearman correlation analysis. We calculated the areas under the Receiver Operating Characteristic (ROC) curve (AUC) to assess the discriminatory ability of the different hemogram parameters for anemia. The statistical significance level was taken as 0.05 and SPSS (Version 26.0. Armonk, NY: IBM Corp) package program was used in the calculations.

RESULTS

The demographic and clinical characteristics of the patients are presented in Table 1. The mean age for RA and r-axSpA patients was 55.8±12.0 and 43.8±10.1 years. Anemia was present in 47.1% (n=41) of RA patients and 31.9% (n=37) of r-axSpA patients and more prominent in

RA patients (p=0.030). Moreover, there was a statistically significant difference between the two groups in terms of age, smoking, disease duration, lymphocyte count, CRP, ESR, Hb, WBC, PLR, RDW and MPV values (Table 1).

The comparisons between patients with and without anemia in RA and r-AxSpA patients are presented in table 2. There a significant female gender superiority in patients with anemia in r-axSpA (p<0.001). ESR, PLR, SII and RDW values were found to be significantly higher in patients with anemia in the RA (p=0.002, p=0.048, p=0.035, p<0.001, respectively), whereas only ESR was significantly greater in patients with anemia in the r-axSpA (p=0.012).

There was no significant difference in disease activity and anemia in both groups (Table 2). The correlations between Hb value and other parameters amoung patients are presented in Table 3. There was a negative correlation between Hb value and ESR, platelet count, PLR and RDW values in the RA patients. There was a negative correlation with the Hb value and CRP, ESR and RDW values and the number of WBC and neutrophils while there was a positive correlation with the number of monocytes in the r-axSpA patients (Table 3).

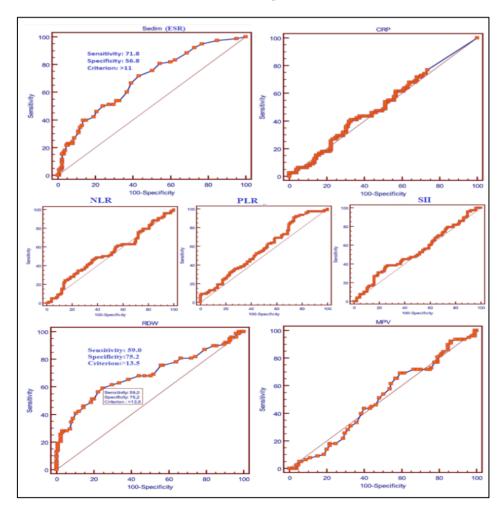


Figure 1: Receiver operating characteristic (ROC) curve and area under the curve (AUC) for CRP, ESR, NLR, PLR, SII, RDW, and MPV in patients with anemia.

The correlations between hemogram parameters and disease activity indices and acute phase reactants are presented in Table 4. In the RA patients, there was a positive correlation between DAS-28 and ESR, CRP, NLR, PLR and SII values.

In the r-axSpA patients, there was a positive correlation between BASDAI and ESR, CRP and NLR values, while

there was a positive correlation between ASDAS-CRP and ESR, CRP, NLR and SII values (Table 4). When ROC analysis was performed, a significant result was obtained in terms of ESR and RDW (AUC:0.691, cut-off>11, 95% confidence interval (CI) 0.623-0.754, 71.8% sensitivity, 51.8% specificity, p<0.001 for ESR; AUC:0.685, cut-off>13.5, 95% CI 0.616-0.748, 59% sensitivity, 75.2% specificity, p<0.001 for RDW) (Figure 1).

Table 1: Characteristics of RA and r-AxSpA patients.

Variables mean±SD or n (%)	RA (n=87)	r-AxSpA (n=116)	P value	
Gender				
Female	73 (83.9)	58 (50)	رم مرم درم مرم	
Male	14 (16.1)	58 (50)	<0.001	
Age (in years)	55.8±12.0	43.8±10.1	< 0.001	
Body mass index (BMI)	29.1±4.8	28.5±4.7	0.218	
Smoking	9 (10.3)	29 (25)	0.010	
Disease duration (years)	7.38±6.83	3.76±3.14	< 0.001	
RF (+)				
Seropositive	%75.9 (66)	-		
Seronegative	%24.1 (21)		-	
HLA-B27				
(+)	-	% 71.6 (83)		
(-)		% 28.4 (33)	-	
CRP	9.9±16.9	6.9±11.6	0.039	
ESR	22.9±19.7	12.2±9.3	< 0.001	
Hemoglobin (Hb)	12.2±1.5	13.2±1.7	< 0.001	
Anemia frequency	41 (47.1)	37 (31.9)	0.030	
WBC	7178.2±1859.0	8374.4±7784.2	0.048	
Neutrophil count	4.2±1.6	4.4±1.5	0.283	
Lymphocyte count	2.1±0.7	2.4±0.8	0.005	
Platelet count	273.4±69.5	262.1±65.7	0.161	
NLR	2.2±1.2	1.99±0.89	0.451	
PLR	139.7±57.0	120.3±52.0	0.002	
SII	592.6±327.0	528.4±307.1	0.227	
RDW	14.2±2.0	12.9±1.2	< 0.001	
MPV	9.9±1.7	9.0±1.7	< 0.001	

RA: Rheumatoid artritis; r-AxSpA: Radiographic axial spondyloarthritis; RF: Rheumatoid factor; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; WBC: White blood cell count; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; SII: Systemic inflammatory immune index. Bold values are significant at p<0.05.

Table 2: The comparisons between patients with and without anemia in RA and r-AxSpA patients.

Variables mean±SD or N (%)	RA (n=87)	P value	r-AxSpA (n=116)	P value
Gender (female/male)				
Without anemia (F/M)	37 (42.5)/9 (10.3)	0.395	25 (21.6)/54 (46.6)	<0.001
With anemia (F/M)	36 (41.4)/5 (5.8)		33 (28.4)/4 (3.4)	- <0.001
Age (in years)				
Without anemia	56.4±10.4	0.737	43.5±10.6	0.756
With anemia	55.2±13.7		44.6±9.2	0.750
Body mass index (BMI)				
Without anemia	29.7±4.8	0.286	28.0±4.4	0.144
With anemia	28.4±4.8	28.4±4.8		0.144
Smoking (No/Yes)				
Without anemia (N/Y)	41 (47.1)/5 (5.8)	1.000	57 (49.1)/22 (19)	0.362
With anemia (N/Y)	37 (42.5)/4 (4.6)		22 (25.9)/7 (6)	- 0.302

Continued.

Nich out anemia 7.1±7.1 0.377 4.0±3.5 0.225 RF (+/) Without anemia (+/-) 35 (40.2)/11 (12.7) 1.000 - - Without anemia (+/-) 35 (40.2)/11 (12.7) 1.000 - - Without anemia (+/-) 31 (35.6)/10 (11.5) - <t< th=""><th>Variables mean±SD or N (%)</th><th>RA (n=87)</th><th>P value</th><th>r-AxSpA (n=116)</th><th>P value</th></t<>	Variables mean±SD or N (%)	RA (n=87)	P value	r-AxSpA (n=116)	P value
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Without anemia 19.2±21.7 0.002 10.5±7.9 0.012 With anemia 27.0±16.5 15.6±11.1 NLR Without anemia 2.1±1.4 0.117 2.0±0.9 0.415 Have anemia 2.3±1.0 1.9±0.9 0.415 PLR Without anemia 127.2±46.1 0.048 118.3±42.6 0.827 With anemia 153.7±64.9 124.7±68.4 0.201 SII Without anemia 538.1±321.6 0.035 549.6±332.8 0.201 With anemia 653.8±326.1 483.3±241.4 0.129 Without anemia 13.3±0.9 <0.001 12.8±1.1 0.129 With anemia 15.2±2.4 13.1±1.3 MPV Without anemia 10.1±1.7 0.441 9.0±1.7 0.838	With anemia	12.1±19.6		4.6±6.5	
With anemia 27.0±16.5 15.6±11.1 NLR Without anemia 2.1±1.4 0.117 2.0±0.9 0.415 Have anemia 2.3±1.0 1.9±0.9 PLR Without anemia 127.2±46.1 0.048 118.3±42.6 0.827 With anemia 153.7±64.9 124.7±68.4 SII Without anemia 538.1±321.6 0.035 549.6±332.8 0.201 With anemia 653.8±326.1 483.3±241.4 RDW Without anemia 13.3±0.9 <0.001	ESR				
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Without anemia 2.1±1.4 0.117 2.0±0.9 0.415 Have anemia 2.3±1.0 1.9±0.9 PLR Without anemia 127.2±46.1 0.048 118.3±42.6 0.827 With anemia 153.7±64.9 124.7±68.4 124.7±68.4 SII Without anemia 538.1±321.6 0.035 549.6±332.8 0.201 With anemia 653.8±326.1 483.3±241.4 0.201 RDW Without anemia 13.3±0.9 <0.001 12.8±1.1 0.129 With anemia 15.2±2.4 13.1±1.3 MPV Without anemia 10.1±1.7 0.441 9.0±1.7 0.838	With anemia	27.0±16.5		15.6±11.1	
Have anemia 2.3±1.0 1.9±0.9 PLR Without anemia 127.2±46.1 0.048 118.3±42.6 0.827 With anemia 153.7±64.9 124.7±68.4 SII Without anemia 538.1±321.6 0.035 549.6±332.8 0.201 With anemia 653.8±326.1 483.3±241.4 0.201 RDW Without anemia 13.3±0.9 <0.001 12.8±1.1 0.129 With anemia 15.2±2.4 13.1±1.3 MPV Without anemia 10.1±1.7 0.441 9.0±1.7 0.838	NLR				
PLR Without anemia 127.2±46.1 0.048 118.3±42.6 0.827 With anemia 153.7±64.9 124.7±68.4 SII Without anemia 538.1±321.6 0.035 549.6±332.8 0.201 With anemia 653.8±326.1 483.3±241.4 RDW Without anemia 13.3±0.9 <0.001	Without anemia	2.1±1.4	0.117	2.0±0.9	0.415
Without anemia 127.2±46.1 0.048 118.3±42.6 0.827 With anemia 153.7±64.9 124.7±68.4 SII Without anemia 538.1±321.6 0.035 549.6±332.8 0.201 With anemia 653.8±326.1 483.3±241.4 0.201 RDW Without anemia 13.3±0.9 <0.001 12.8±1.1 0.129 With anemia 15.2±2.4 13.1±1.3 13.1±1.3 MPV Without anemia 10.1±1.7 0.441 9.0±1.7 0.838	Have anemia	2.3±1.0		1.9±0.9	
With anemia 153.7±64.9 124.7±68.4 SII Without anemia 538.1±321.6 0.035 549.6±332.8 0.201 With anemia 653.8±326.1 483.3±241.4 RDW Without anemia 13.3±0.9 <0.001 12.8±1.1 0.129 With anemia 15.2±2.4 13.1±1.3 MPV Without anemia 10.1±1.7 0.441 9.0±1.7 0.838	PLR				
SII Without anemia 538.1±321.6 0.035 549.6±332.8 0.201 With anemia 653.8±326.1 483.3±241.4 RDW Without anemia 13.3±0.9 <0.001	Without anemia	127.2±46.1	0.048	118.3±42.6	0.827
Without anemia 538.1±321.6 0.035 549.6±332.8 0.201 With anemia 653.8±326.1 483.3±241.4 RDW Without anemia 13.3±0.9 <0.001 12.8±1.1 0.129 With anemia 15.2±2.4 13.1±1.3 MPV Without anemia 10.1±1.7 0.441 9.0±1.7 0.838	With anemia	153.7±64.9		124.7±68.4	
With anemia 653.8±326.1 483.3±241.4 RDW Without anemia 13.3±0.9 <0.001 12.8±1.1 0.129 With anemia 15.2±2.4 13.1±1.3 MPV Without anemia 10.1±1.7 0.441 9.0±1.7 0.838	SII				
With anemia 653.8±326.1 483.3±241.4 RDW Without anemia 13.3±0.9 <0.001 12.8±1.1 0.129 With anemia 15.2±2.4 13.1±1.3 MPV Without anemia 10.1±1.7 0.441 9.0±1.7 0.838	Without anemia	538.1±321.6	0.035	549.6±332.8	0.201
Without anemia 13.3±0.9 <0.001 12.8±1.1 0.129 With anemia 15.2±2.4 13.1±1.3 MPV Without anemia 10.1±1.7 0.441 9.0±1.7 0.838				483.3±241.4	
With anemia 15.2 ± 2.4 13.1 ± 1.3 MPV Without anemia 10.1 ± 1.7 0.441 9.0 ± 1.7 0.838	RDW				
MPV Without anemia 10.1±1.7 0.441 9.0±1.7 0.838	Without anemia	13.3±0.9	< 0.001	12.8±1.1	0.129
MPV Without anemia 10.1±1.7 0.441 9.0±1.7 0.838	With anemia	15.2±2.4		13.1±1.3	
	Without anemia	10.1±1.7	0.441	9.0±1.7	0.838
	With anemia			8.9±1.6	

RA: Rheumatoid artritis; r-AxSpA: Radiographic axial spondyloarthritis; RF: Rheumatoid factor; DAS-28: Disease Activity Score in 28 Joints; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score with CRP; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; WBC: White blood cell count; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; SII: Systemic inflammatory immune index; RDW: Red blood cell distribution width; MPV: Mean platelet volume. Bold values are signficant at p<0.05

Table 3: The correlations between hemoglobin value and other parameters amoung patients.

		Hemoglobin					
Variables	RA		r-AxSpA				
	r value	P value	r value	P value			
Age (in years)	0.174	0.108	-0.024	0.797			
Body mass index (BMI)	0.038	0.726	-0.173	0.063			
Disease duration (years)	-0.059	0.586	0.167	0.073			
DAS-28	-0.205	0.056	-	-			
BASDAI	-	-	0.078	0.403			
ASDAS-CRP	-	-	0.149	0.109			

Continued.

		Hemoglobin						
Variables	RA		r-AxSpA	r-AxSpA				
	r value	P value	r value	P value				
RF	0.002	0.984	-	-				
Anti-CCP	0.012	0.909	-	-				
HLA-B27	-	-	0.036	0.725				
CRP	-0.041	0.708	-0.184	0.048				
ESR	-0.390	< 0.001	-0.318	< 0.001				
WBC	0.135	0.213	-0.202	0.030				
Neutrophil count	0.060	0.578	-0.215	0.020				
Lymphocyte count	0.108	0.318	0.047	0.619				
Monocyte count	0.092	0.394	0.304	< 0.001				
Platelet count	-0.300	0.005	0.033	0.727				
NLR	-0.093	0.391	0.117	0.212				
PLR	-0.280	0.009	0.003	0.976				
SII	-0.194	0.072	0.114	0.222				
RDW	-0.469	< 0.001	-0.348	< 0.001				
MPV	0.069	0.523	0.000	1.000				

RA: Rheumatoid artritis; r-AxSpA: Radiographic axial spondyloarthritis; RF: Rheumatoid factor; Anti-CCP: Antibodies against cyclic citrullinated peptides; DAS-28: Disease Activity Score in 28 Joints; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score with CRP; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; WBC: White blood cell count; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; SII: Systemic inflammatory immune index; RDW: Red blood cell distribution width; MPV: Mean platelet volume. Bold values are signficant at p<0.05.

Table 4: The correlations between hemogram parameters and disease activity indices and acute phase reactants.

Variables	r/p value	CRP	ESR	NLR	PLR	SII	RDW	MPV
RA								
DAS-28	r value	0.856	0.768	0.228	0.312	0.273	0.061	-0.138
	p value	< 0.001	< 0.001	0.034	0.003	0.011	0.573	0.203
CRP	r value	1.000	0.565	0.330	0.135	0.298	-0.012	-0.085
	p value	-	< 0.001	0.002	0.212	0.005	0.915	0.436
ESR	r value	0.565	1.000	0.275	0.257	0.273	0.109	-0.183
	p value	< 0.001	-	0.010	0.016	0.010	0.313	0.089
NLR	r value	0.330	0.275	1.000	0.526	0.873	0.111	-0.060
	p value	0.002	0.010	-	< 0.001	< 0.001	0.307	0.581
PLR	r value	0.135	0.257	0.526	1.000	0.718	0.160	-0.139
	p value	0.212	0.016	< 0.001	-	< 0.001	0.138	0.200
SII	r value	0.298	0.273	0.873	0.718	1.000	0.177	-0.135
	p value	0.005	0.010	< 0.001	< 0.001	-	0.102	0.212
RDW	r value	-0.012	0.109	0.111	0.160	0.177	1.000	0.257
	p value	0.915	0.313	0.307	0.138	0.102	-	0.016
MPV	r value	-0.085	-0.183	-0.060	-0.139	-0.135	0.257	1.000
	p value	0.436	0.089	0.581	0.200	0.212	0.016	-
r-AxSpA								
BASDAI	r value	0.567	0.186	0.233	0.000	0.181	0.062	-0.028
	p value	< 0.001	0.045	0.012	0.997	0.052	0.506	0.764
ASDAS-CRP	r value	0.806	0.349	0.358	0.128	0.359	0.006	-0.159
	p value	< 0.001	< 0.001	< 0.001	0.171	< 0.001	0.952	0.088
CRP	r value	1.000	0.433	0.394	0.185	0.390	-0.094	-0.169
	p value	-	< 0.001	< 0.001	0.047	< 0.001	0.313	0.070
ESR	r value	0.433	1.000	0.296	0.204	0.252	0.135	0.027
	p value	< 0.001	-	0.001	0.028	0.006	0.149	0.773
NLR	r value	0.394	0.296	1.000	0.572	0.873	-0.004	0.000
	p value	< 0.001	< 0.001	-	< 0.001	< 0.001	0.969	1.000
PLR	r value	0.185	0.204	0.572	1.000	0.692	0.142	0.000

Continued.

Variables	r/p value	CRP	ESR	NLR	PLR	SII	RDW	MPV
	p value	0.047	0.028	< 0.001	-	< 0.001	0.129	0.996
SII	r value	0.390	0.252	0.873	0.692	1.000	0.073	-0. 043
	p value	< 0.001	0.006	< 0.001	< 0.001	-	0.436	0.644
RDW	r value	-0.094	0.135	-0.004	0.142	0.073	1.000	0.205
	p value	0.313	0.149	0.969	0.129	0.436	-	0.027
MPV	r value	-0.169	0.027	0.000	0.000	-0.043	0.205	1.000
	p value	0.070	0.773	1.000	0.996	0.644	0.027	-

DISCUSSION

The prevalence of anemia in patients with RA ranged between 33% and 60%. ²⁶ Previous studies have shown that the frequency of anemia in axSpA patients varies between 20% and 56%. ^{1,3,27,28} In this study, the anemia rate was 47.1% in RA patients and 31.9% in r-axSpA patients. The results are compatible with the literature. Moreover, the frequency of anemia was significantly higher in RA patients than in r-axSpA patients.

Both RA and axSpA are chronic inflammatory autoimmune diseases characterized by systemic inflammation and immune dysregulation. In RA, the immune system mistakenly attacks the synovial membrane of joints, leading to inflammation, joint damage and potential systemic manifestations. PAXSpA primarily affects the spine and sacroiliac joints, causing inflammation and eventual fusion of the spine. The chronic inflammatory state in these diseases plays a pivotal role in the development of anemia. A systematic review has suggested that RA patients with anemia are likely to have more severe joint disease and the joint disease will also likely respond to treatment if the anemia is treated successfully. As a systematic review has suggested that RA patients with anemia are likely to have more severe joint disease and the joint disease will also likely respond to treatment if the anemia is treated successfully.

The primary mechanism underlying anemia in RA is an increased production of inflammatory cytokines (such as TNF- α , IL-6) as a result of long-standing disease. These cytokines suppress the production of erythropoietin, a hormone responsible for stimulating red blood cell production in the bone marrow. The shortened red blood cell lifespan, hepcidin-induced pathological iron homeostasis (reduced intestinal iron uptake in the mucosal barrier and iron retention in the reticulo-endothelial system) and blunted response to erythropoietin may contribute to the development of ACD in RA³¹. However, the mechanisms driving anemia in axSpA appear to be some different from those in RA.

In axSpA, chronic inflammation leads to increased levels of hepcidin, a hormone involved in regulating iron metabolism. Elevated hepcidin levels inhibit iron absorption from the gut and sequester iron within macrophages, leading to functional iron deficiency and anemia. 1,27,32 Additionally, comorbidities such as gastrointestinal bleeding, commonly seen in axSpA due to the use of nonsteroidal anti-inflammatory drugs

(NSAIDs), can exacerbate anemia in these patients. ^{1,27} In this study, anemia was more prominent in RA patients. It is thought that the chronic inflammatory state in RA leads to disturbances in erythropoiesis and iron metabolism, resulting in a higher prevalence of anemia compared to axSpA.

There are very few studies in the literature investigating the frequency of anemia in both disease groups and its relationship with hemogram parameters. Lin et al, investigated whether erythrocytopenia and hemoglobin reduction could affect the level of RDW and its relationship with traditional inflammatory or immune markers in patients with RA, ankylosing spondylitis (AS) and osteoarthritis (OA) and compared them with a healthy control group. They observed that the RDW level increased only in RA patients, but not in patients with AS and OA. They also found that the RDW level was much higher in those with erythrocytopenia and Hb depletion.

They suggested that increased RDW and its relationship with CRP may be mainly due to Hb depletion. 17 The results of this study indicate that anemia was associated with ESR and RDW levels in both disease groups, but not with disease activity. It is postulated that elevated RDW reflects underlying inflammation, impaired systemic stress erythropoiesis, oxidative and endothelial dysfunction, all of which contribute to poor clinical outcomes. In the context of anemia, higher RDW values have been linked with increased morbidity and mortality, independent of Hb levels.

Moreover, variations in RBC size may impact blood viscosity, shear stress and tissue oxygenation, further exacerbating tissue damage and organ dysfunction. Monitoring changes in RDW over time may provide valuable insights into disease progression and treatment response. ^{7,33,34} It is concluded that the integration of RDW into routine clinical practice offers a non-invasive, costeffective means of risk stratification and prognostication in patients with anemia and various comorbidities.

Limitations

The study has some limitations such as being singlecenter, small sample size, the absence of serum iron, ferritin, folate, vitamin B12 levels and the lack of serum erythropoietin levels. However, according to the results of this study, anemia is a common condition in both disease groups and appears to be closely related to ESR and RDW.

CONCLUSION

In conclusion, anemia of chronic disease can be seen to a considerable extent in rheumatic diseases. Although the incidence of anemia was not affected by disease activity, female gender involvement was prominent. Moreover, the increase in ESR and RDW values may reflect the possibility of developing anemia in rheumatic diseases and therefore patients should be carefully monitored.

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Institutional Ethics Committee

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