

HEMATOLOGICAL PARAMETERS IN RHEUMATOID ARTHRITIS AND THEIR RELATIONSHIP WITH DISEASE ACTIVITY

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ABSTRACT:

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Background: Inflammatory changes in rheumatological diseases encompass alterations in shape, number, and size of peripheral blood cells. Complete blood cell parameters may be used as an index of inflammation and disease activity.

Aim of the work: Assess the hematological parameters in rheumatoid arthritis (RA) and identify their relationship with disease activity.

Methods: 141 patients with rheumatoid arthritis and 100 healthy controls were included in this study. Full medical history, general and musculoskeletal examination, assessment of disease activity using the DAS 28 score, markers of inflammation, rheumatoid factor (RF) titer, anti-cyclic citrullinated peptide (anti-CCP) titer and complete blood picture were done.

Results: RA patients had lower RBCs, Hb, MPV, PWD and Hb/RDW% ratio and higher RDW% than controls. Active RA patients had higher WBCs, neutrophils, and NLR. WBCs and neutrophils were positively correlated with DAS score and CRP titre. NLR ratio correlated positively with the DAS score, CRP and Anti CCP titres. Active RA had higher RDW% and lower HCT, Hb, Hb/PLT, RDW%/PLT, Hb/RDW% ratios. RDW% was positively correlated with DAS score, ESR, CRP, RF and Anti CCP titres. The RDW% differentiated active and inactive RA with best cut-off value >12. Active patients had higher platelets and PLR, which were positively correlated with DAS score .

Conclusion: Changes in haematological parameters are significantly associated with disease activity in RA patients and they correlate positively with inflammatory markers. RDW%, platelets count and PLR are the most affected hematologic parameters in relation to DAS score and parameters of disease activity.

Key words: Rheumatoid arthritis, disease activity, hematologic parameters.

INTRODUCTION:

Inflammatory reactions play a crucial role in rheumatological diseases and encompass alterations in peripheral blood cells' number, shapes, and sizes. Complete blood cell parameters could act as indicators of inflammation and disease activity ^[1].

Recent studies investigated the association between the activity of RA and the haematological parameters ^[2]. Some studies assessed the correlation between platelets (PLT), red blood cells (RBC), red blood cells-platelet ratio (RPR) and haemoglobin-platelet ratio (HPR) as regards the disease activity. Little is known about

the significance of the PLT and parameters of RBC in differentiating active from inactive disease^[3]. Studies found negative correlation between disease activity and haemoglobin (Hb) level and thrombocytosis with high disease activity, but results were not conclusive as regard the mean platelet volume (MPV) ^[2].

Another study revealed a presence of an increase in the number of platelets in patients with RA during disease activity, then a decrease in their number with remission^[4]. Consequently, a correlation between platelet indices and disease activity in RA has been proposed ^[5].

Moreover, studies have shown that Platelet/lymphocyte ratio (PLR), red blood cell distribution width (RDW), Red blood cell distribution width/platelet ratio (RPR) neutrophil/lymphocyte ratio (NLR) and mean platelet volume (MPV) could be used as inflammatory markers in autoimmune diseases and indicator of mortality in some diseases ^[3,6]. However, the relationship between RPR value and the disease activity in RA patients has not been widely investigated ^[7].

Few studies have investigated the association between all the haematological parameters, markers of inflammation and disease activity in RA.

AIM OF THE STUDY:

To study the hematological parameters and their relation with the disease activity in patients with rheumatoid arthritis.

PATIENTS AND METHODS:

This case control study included 141 rheumatoid arthritis patients diagnosed according to 2010 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) criteria for RA ^[8], and 100 healthy controls who were

matched according to age and sex. Patients were allocated from Ain Shams University hospitals outpatient clinics. Patients with blood diseases, malignancies, advanced kidney disease, advanced liver disease and other autoimmune diseases were excluded. **Ethical approval was taken from the Faculty of Medicine, Ain Shams University Ethical Committee of Scientific Research No. FWA 000017585.** A written informed consent was taken from all participants. A full medical history, general and musculoskeletal examination and assessment of the disease activity using the DAS 28 score-ESR were done. According to DAS 28 score; a score <2.6 was considered inactive, 2.6-3.2 was considered low disease activity, >3.2-5.1 was considered moderate disease activity and >5.1 was considered high disease activity ^[9]. Patients with active disease were those having low, moderate and severe activity.

Complete blood picture showing red blood cells (RBCs) count and indices, white blood cells (WBCs); both total and differential counts, and platelets parameters was done to all patients. Complete blood count was done using a Coulter Counter (T660; Beckman Coulter, Brea, CA) . Markers of disease activity including Erythrocyte sedimentation rate (ESR) (Westergren method) was done, C reactive protein (CRP) titre [performed on Modular P auto analyzer (Roche Diagnostics, Mannheim, Germany)], RF titre and anti-CCP titre (determination by a COBAS Autoanalyzer (Roche Diagnostics, Mannheim, Germany) were also done. Comparison between active RA patients, inactive RA patients and healthy controls regarding the hematological parameters was done. Then a comparison between active and inactive groups regarding the WBCs, RBCs and platelet indices, and a correlation of the hematological parameters with DAS score and parameters of disease activity were assessed. Collected data were tabulated and statistically analysed using the statistical

package for social sciences (SPSS) version 17.0. Variables as frequencies and percentages, mean ± standard deviation and range were used. Chi-square and Mann Whitney U tests for comparison were also implemented. A P value of 0.05 or less was considered significant.

RESULTS:

The mean age of RA patients was 50.404± 11.945 years. 77.3 % of them were females and 22.7 % were males. 91(64.54 %) patients were active while 50 patients (35.46%) were inactive.

RA patients showed statistically significant lower RBCs, Hb, MPV, PWD and Hb/RDW% ratio, while they had statistically significant higher RDW% compared with the controls (table 1).

WBCs, neutrophil, RDW%, PLT, NLR and PLR were significantly higher in active RA patients while HCT, Hb, Hb/PLT, RDW%/PLT, Hb/RDW% and RBCs/PLT ratios were significantly lower compared to the inactive patients (table 2).

The number of tender joints was significantly positively correlated with RDW%, PLT count, NLR and PLR. On the contrary, it was significantly negatively

correlated with RBCs count, Hb levels, Hb/PLT, RDW%/PLT, RBCs/PLT and Hb/RDW% ratios. The number of swollen joints showed statistically significant positive correlations with RDW%, PLT count, PLR. On the other hand, it was negatively correlated with the Hb, Hb/PLT, RDW%/PLT, RBCs/PLT and Hb/RDW% ratios. DAS28 score was positively correlated with WBCs, neutrophils, PLTs, RDW%, NLR and PLR in RA patients. On the contrary, HCT, Hb levels, Hb/PLT, RDW%/PLT, RBCs/PLT and Hb/RDW% ratios were negatively correlated with DAS28 score (table 3).

There was statistically significant positive correlation between ESR and RDW%, PLT count, PLR while it was significantly negatively correlated with HG levels, Hb/PLT ratio, RDW%/PLT ratio, RBCs/PLT ratio, Hb/RDW% ratio. Other significant correlations are shown in table3 and 4.

Both RF and Anti CCP titres were positively correlated to RDW%, PLT count and PLR, but they were negatively correlated with HG levels, Hb/PLT, RDW%/PLT, RBCs/PLT and Hb/RDW% ratios. However, anti CCP titre was positively correlated with NLR (table 4).

Table 1: Comparison between RA patients and controls as regard WBCs, RBCs and platelet parameters.

Hematological indices	Groups						T-Test	
	RA			Control			t	P-value
	Mean	±	SD	Mean	±	SD		
WBCS(10 ⁹ /L)	7.136	±	2.491	6.977	±	1.990	0.555	0.580
NEUT(10 ⁹ /L)	4.287	±	2.321	4.112	±	1.629	0.685	0.494
Lympho(10 ⁹ /L)	2.283	±	0.690	2.294	±	0.768	-0.115	0.908
HCT (%)	36.149	±	2.364	36.099	±	2.453	0.165	0.869
RBCs(10 ¹² /L)	4.786	±	0.523	5.480	±	4.096	-1.991	0.048*
Hb(g/L)	11.984	±	0.810	12.344	±	0.717	-3.729	<0.001*
MCV(fL)	78.865	±	7.346	80.477	±	5.782	-1.918	0.056
MCH(pg)	26.457	±	3.021	27.107	±	2.625	-1.814	0.071
RDW%	13.776	±	2.234	13.171	±	1.473	2.493	0.013*
PLT(10 ⁹ /L)	402.752	±	174.647	365.704	±	140.972	1.838	0.067
MPV/fl	9.177	±	1.009	10.921	±	2.043	-8.898	<0.001*
PDW%	10.445	±	1.655	12.282	±	1.882	-8.301	<0.001*
Hb/PLT ratio	0.037	±	0.020	0.040	±	0.017	-1.158	0.248

RDW%/PLT ratio	0.040	±	0.015	0.042	±	0.015	-0.912	0.363
RBCs/PLT ratio	0.015	±	0.008	0.017	±	0.013	-1.685	0.093
Hb/RDW% ratio	0.896	±	0.177	0.951	±	0.132	-2.719	0.007*
NLR ratio	2.093	±	1.508	1.977	±	1.136	0.682	0.496
PLR ratio	200.002	±	139.664	178.532	±	112.876	1.331	0.184

SD: Standard Deviation, No: number, %: percentage, mm/h: millimeter per hour, mg/L: milligram per Liter, IU/ml: International unit per milliliter, U/L: Unit per liter, mg/dL: milligram per Deci Liter WBCs: White blood cells, HCT: Hematocrit, RBCs: Red blood cells, Hb: Hemoglobin, MCV: Mean corpuscular volume, MCH: Mean corpuscular Hemoglobin, RDW: Red cell distribution width, PLT: Platelets, MPV: Mean platelet volume, PDW: Platelet distribution width, Hb/PLT ratio: Hemoglobin/Platelet ratio, RDW/PLT ratio: Red cell distribution width/ Platelet ratio, RBCs/PLT ratio: Red blood cells/Platelet ratio, Hb/RDW ratio: Hemoglobin/ Red cell distribution width ratio, NLR: Neutrophil/Lymphocyte ratio, PLR: Platelet/Lymphocyte ratio, /mm³: Per cubic millimeter, %: percentage, g/dL: Gram per deci Liter, fl: femtoliter, pg: picogram, t: independent sample t test, P: probability value, *: p<0.05 is statistically significant, **: p≤0.001 is statistically highly significant

Table 2: Comparison between active and inactive RA patients as regard WBCs, RBCs and platelet parameters.

RA	DAS 28 Activity						T-Test	
	Inactive			Active			t	P-value
	Mean	±	SD	Mean	±	SD		
WBCs(10 ⁹ /L)	6.568	±	2.016	7.448	±	2.676	-2.028	0.044*
NEUT(10 ⁹ /L)	3.752	±	1.665	4.581	±	2.574	-2.053	0.042*
Lympho(10 ⁹ /L)	2.288	±	0.573	2.280	±	0.750	0.063	0.950
HCT (%)	36.680	±	2.437	35.857	±	2.284	1.999	0.048*
RBCs(10 ¹² /L)	4.833	±	0.499	4.760	±	0.536	0.787	0.432
Hb(g/L)	12.254	±	0.783	11.835	±	0.791	3.020	0.003*
MCV (fL)	78.432	±	8.032	79.103	±	6.975	-0.518	0.605
MCH (pg)	25.942	±	3.142	26.741	±	2.931	-1.509	0.134
RDW%	11.560	±	1.188	14.993	±	1.665	-12.883	<0.001*
PLT(10 ⁹ /L)	238.740	±	99.662	492.868	±	137.419	-11.511	<0.001*
MPV/fl	9.142	±	0.871	9.196	±	1.082	-0.302	0.763
PDW%	10.250	±	1.633	10.553	±	1.667	-1.039	0.301
Hb/PLT ratio	0.057	±	0.018	0.026	±	0.011	12.631	<0.001*
RDW%/PLT ratio	0.053	±	0.014	0.033	±	0.009	10.585	<0.001*
RBCs/PLT ratio	0.023	±	0.007	0.011	±	0.004	13.009	<0.001*
Hb/RDW% ratio	1.071	±	0.120	0.801	±	0.121	12.741	<0.001*
NLR ratio	1.701	±	0.761	2.308	±	1.758	-2.320	0.022*
PLR ratio	110.268	±	53.937	249.307	±	147.742	-6.415	<0.001*

SD: Standard Deviation, No: number, %: percentage, mm/h: millimeter per hour, mg/L: milligram per Liter, IU/ml: International unit per milliliter, U/L: Unit per liter, mg/dL: milligram per Deci Liter WBCs: White blood cells, HCT: Hematocrit, RBCs: Red blood cells, Hb: Hemoglobin, MCV: Mean corpuscular volume, MCH: Mean corpuscular Hemoglobin, RDW: Red cell distribution width, PLT: Platelets, MPV: Mean platelet volume, PDW: Platelet distribution width, Hb/PLT ratio: Hemoglobin/Platelet ratio, RDW/PLT ratio: Red cell distribution width/ Platelet ratio, RBCs/PLT ratio: Red blood cells/Platelet ratio, Hb/RDW ratio: Hemoglobin/ Red cell distribution width ratio, NLR: Neutrophil/Lymphocyte ratio, PLR: Platelet/Lymphocyte ratio, /mm³: Per cubic millimeter, %: percentage, g/dL: Gram per deci Liter, fl: femtoliter, pg: picogram, t: independent sample t test, P: probability value, *: p<0.05 is statistically significant, **: p≤0.001 is statistically highly significant

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Table 3: Correlation between WBCs, RBCs and platelet parameters with clinical parameters of the disease activity

RA	Tender j		Swollen j		DAS 28	
	r	P-value	r	P-value	R	P-value
WBCs($10^9/L$)	0.075	0.451	0.023	0.816	0.164	0.052*
NEUT($10^9/L$)	0.112	0.256	0.019	0.849	0.180	0.033*
Lympho($10^9/L$)	-0.152	0.125	-0.130	0.183	-0.073	0.392
HCT (%)	-0.068	0.492	-0.095	0.332	-0.206	0.014*
RBCs($10^{12}/L$)	-0.236	0.016*	-0.023	0.813	-0.126	0.136
Hb(g/L)	-0.303	0.002*	-0.222	0.022*	-0.378	<0.001*
MCV(fL)	0.177	0.073	0.037	0.702	0.072	0.394
MCH (pg)	0.094	0.340	0.008	0.934	0.097	0.254
RDW%	0.745	<0.001*	0.634	<0.001*	0.876	<0.001*
PLT($10^9/L$)	0.775	<0.001*	0.611	<0.001*	0.859	<0.001*
MPV/fl	-0.011	0.915	0.097	0.319	0.027	0.751
PDW%	0.105	0.291	0.162	0.096	0.109	0.199
Hb/PLT ratio	-0.654	<0.001*	-0.527	<0.001*	-0.753	<0.001*
RDW%/PLT ratio	-0.593	<0.001*	-0.474	<0.001*	-0.692	<0.001*
RBCs/PLT ratio	-0.544	<0.001*	-0.420	<0.001*	-0.704	<0.001*
Hb/RDW% ratio	-0.745	<0.001*	-0.588	<0.001*	-0.855	<0.001*
NLR ratio	0.199	0.043*	0.111	0.254	0.240	0.004*
PLR ratio	0.602	<0.001*	0.433	<0.001*	0.665	<0.001*

SD: Standard Deviation, No: number, %: percentage, mm/h: millimeter per hour, mg/L: milligram per Liter, IU/ml: International unit per milliliter, U/L: Unit per liter, mg/dL: milligram per Deci Liter WBCs: White blood cells, HCT: Hematocrit, RBCs: Red blood cells, Hb: Hemoglobin, MCV: Mean corpuscular volume, MCH: Mean corpuscular Hemoglobin, RDW: Red cell distribution width, PLT: Platelets, MPV: Mean platelet volume, PDW: Platelet distribution width, Hb/PLT ratio: Hemoglobin/Platelet ratio, RDW/PLT ratio: Red cell distribution width/ Platelet ratio, RBCs/PLT ratio: Red blood cells/Platelet ratio, Hb/RDW ratio: Hemoglobin/ Red cell distribution width ratio, NLR: Neutrophil/Lymphocyte ratio, PLR: Platelet/Lymphocyte ratio, /mm³: Per cubic millimeter, %: percentage, g/dL: Gram per deci Liter, fl: femtoliter, pg: picogram, t: independent sample t test, P: probability value, *: p<0.05 is statistically significant, **: p≤0.001 is statistically highly significant

Table 4: Correlation between WBCs, RBCs and platelet parameters with laboratory parameters of the disease activity.

RA	ESR		CRP		RF		ANTI CCP	
	r	P-value	r	P-value	r	P-value	r	P-value
WBCs($10^9/L$)	0.125	0.139	0.265	0.001*	-0.036	0.675	0.059	0.487
NEUT($10^9/L$)	0.143	0.090	0.294	<0.001*	0.019	0.819	0.102	0.227
Lympho($10^9/L$)	-0.002	0.981	-0.024	0.776	-0.212	0.012	-0.196	0.020
HCT (%)	-0.097	0.255	-0.085	0.314	-0.098	0.246	-0.065	0.445
RBCs($10^{12}/L$)	-0.120	0.156	-0.056	0.509	-0.139	0.101	-0.118	0.164
Hb(g/L)	-0.376	<0.001*	-0.185	0.028*	-0.236	0.005*	-0.185	0.028*
MCV(fL)	-0.020	0.817	0.076	0.368	-0.117	0.168	0.000	0.999
MCH (pg)	0.062	0.468	-0.073	0.392	0.074	0.381	0.148	0.080
RDW%	0.577	<0.001*	0.396	<0.001*	0.283	0.001*	0.294	<0.001*
PLT($10^9/L$)	0.551	<0.001*	0.325	<0.001*	0.272	0.001*	0.355	<0.001*
MPV/fl	-0.014	0.867	0.016	0.852	-0.039	0.644	-0.010	0.908
PDW%	0.145	0.087	0.102	0.231	-0.002	0.978	-0.069	0.417
Hb/PLT ratio	-0.476	<0.001*	-0.311	<0.001*	-0.268	0.001*	-0.326	<0.001*
RDW%/PLT ratio	-0.409	<0.001*	-0.252	0.003*	-0.226	0.007*	-0.299	<0.001*
RBCs/PLT ratio	-0.425	<0.001*	-0.304	<0.001*	-0.300	<0.001*	-0.308	<0.001*

Hb/RDW% ratio	-0.593	<0.001*	-0.375	<0.001*	-0.325	<0.001*	-0.316	<0.001*
NLR ratio	0.159	0.059	0.295	<0.001*	0.112	0.187	0.188	0.026*
PLR ratio	0.386	<0.001*	0.220	0.009*	0.341	<0.001*	0.393	<0.001*

SD: Standard Deviation, No: number, %: percentage, mm/h: millimeter per hour, mg/L: milligram per Liter, IU/ml: International unit per milliliter, U/L: Unit per liter, mg/dL: milligram per Deci Liter WBCs: White blood cells, HCT: Hematocrit, RBCs: Red blood cells, Hb: Hemoglobin, MCV: Mean corpuscular volume, MCH: Mean corpuscular Hemoglobin, RDW: Red cell distribution width, PLT: Platelets, MPV: Mean platelet volume, PDW: Platelet distribution width, Hb/PLT ratio: Hemoglobin/Platelet ratio, RDW/PLT ratio: Red cell distribution width/ Platelet ratio, RBCs/PLT ratio: Red blood cells/Platelet ratio, Hb/RDW ratio: Hemoglobin/ Red cell distribution width ratio, NLR: Neutrophil/Lymphocyte ratio, PLR: Platelet/Lymphocyte ratio, /mm³: Per cubic millimeter, %: percentage, g/dL: Gram per deci Liter, fl: femtoliter, pg: picogram, t: independent sample t test, P: probability value, *: p<0.05 is statistically significant, **: p<0.001 is statistically highly significant.

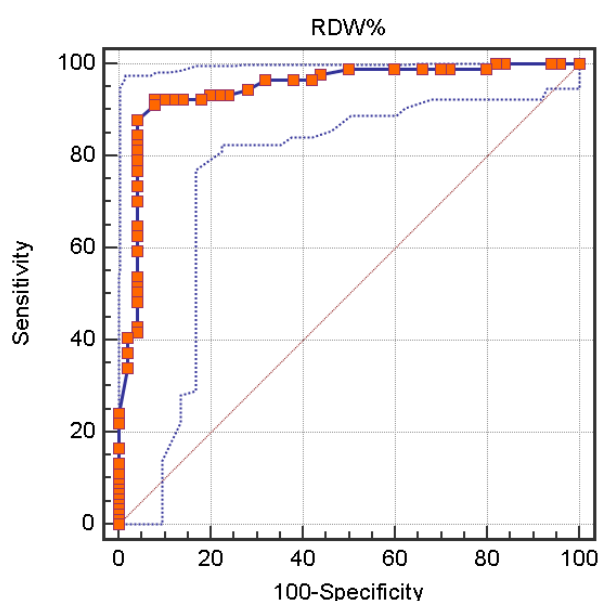


Fig (1) The ROC curve showed that the best RDW% cut-off value for predicting disease activity in RA patients was >12.9 with a sensitivity of 92.31% and a specificity of 92.00%, with positive predictive value is 95.5%.

The best RDW% cut-off value for predicting disease activity in RA patients was >12.9. Fig (1).

DISCUSSION:

Inflammatory process in rheumatic diseases causes changes in the peripheral blood cell counts, morphology and sizes. Therefore, blood cell indices were considered as indicators of inflammation and markers of disease activity [10]. Studies proved a significant role of platelets in the inflammatory response [11]. In addition, RBC-related parameters can be used as

inflammatory markers in autoimmune diseases [12]. Ratios among haematological indices have shown to be useful tools for evaluation of inflammatory activity in various autoimmune diseases including ulcerative colitis and Familial Mediterranean Fever [10]. Few studies investigated the relationship between the parameters of PLT, RBC, WBCs parameters and disease activity; especially their importance in

differentiating active from inactive RA. Therefore, the current study aimed at assessing the association between all these blood biomarkers and rheumatoid arthritis disease activity.

To assess the difference concerning haematological parameters among RA patients and healthy controls, a comparison between both groups regarding the WBCs, RBCs and platelet parameters was done and results showed that the RA patients had higher WBCs, neutrophils and NLR while they had lower lymphocytes compared to healthy controls, but these results did not reach the statistical significance. These results partially agreed with studies by Haitao et al., Mercian et al., and Uslu et al., [13-15] whose results revealed that NLR increased significantly in RA patients compared to controls. Similarly, Helal et al., and Abd-Elazeem et al., [16, 17] found that the NLR and PLR were significantly higher in RA patients than that of the controls.

As regard the RBCs parameters, RA patients had statistically significant higher RDW% and lower RBCs count, Hb level and Hb/RDW% ratio than healthy controls. Lin et al., Al-Rawi et al., and Tecer et al., [18-20] also reported a significant higher RDW in patients with RA compared to controls. Interestingly, Lee et al., [21] found that a higher percentage of RDW was observed in patients with RA than in patients with osteoarthritis.

Similarly, results of Dervišević et al., discerned that RA patients had significantly lower RBCs than control group [22].

While assessing the parameters of platelets, although a high platelets count was observed, it was of no statistical significance. Yet there was a statistically significant lower value of MPV and PDW in patients with RA than controls. These results were in accordance with the results of Dervišević et al., [22] which showed significantly higher platelet count in patients

with RA than healthy controls. While these results disagreed with Khaled et al., [23] results who found that patients with RA had significantly higher PDW values than those of controls.

In order to identify the relationship between different haematological parameters and DAS score and disease activity parameters, the patients with RA were divided into active RA [91 patients (64.6%)] and inactive RA [50 patients (35.46%)] groups. Then comparison between both groups as regards haematological parameters and correlation of haematological indices with parameters of disease activity were done.

Regarding WBCs parameters, there was significantly higher WBCs count, neutrophil count, and NLR in active patients. Also, WBCs and neutrophil counts correlated positively with both DAS score and CRP titre. NLR ratio correlated significantly positively with the DAS score, number of tender joints, CRP and Anti CCP titres. Fu et al., and Mercan et al., [24,14] , reported a positive correlation between the DAS28 score and WBCs count, neutrophil count and NLR in RA patients as in this study. Also Haitao et al., [13] results also proved that high NLR values were positively associated with increase CRP, ESR, and DAS28 values in RA patients.

Helal et al., and Uslu et al., [16,15] detected significant higher NLR in active disease and reported a significant relationship between NLR and PLR with the DAS-28. Another study by Mercan et al., [14] found that the NLR was positively correlated with ESR and CRP and NLR increased with increasing the DAS28 score.

Abd -Elazeem et al., and Koiwa et al., [17,25]. found that the DAS28 positively correlated with the NLR and PLR. These studies support the present study and may reflect the importance of WBCs indices as a

marker of inflammation and disease activity in patients with RA.

Current results showed that the RBCs parameters may give an idea about the inflammatory status and activity status in RA patients, and that the alterations in these parameters go hand in hand with alterations in the inflammatory markers. The current study found that active patients had significantly higher RDW%, while HCT value, Hb levels, Hb/PLT ratio, RDW%/PLT ratio, Hb/RDW% ratio and RBCs/PLT ratio were significantly lower than the inactive patients. Also the RDW% was positively correlated with DAS score and other clinical and laboratory activity parameters "number of tender and swollen joints, ESR, CRP, RF and Anti CCP titres". These results are in concordance to Yunchun et al., [26] who observed that the RDW was associated with the level of inflammatory markers and autoantibodies in RA patients. Lin et al., [18] also supported the results and demonstrated that CRP and ESR correlated positively with RDW in patients with RA patients.

Moreover, Tecer et al., [20] found that RDW was positively correlated with DAS-28 and proposed its use as a marker of activity in RA and that RDW was positively correlated with ESR and CRP in reflecting the inflammatory state that go hand in hand with the current results.

The current results are in line with Talukdar et al., [3] who observed that Patients with high disease activity had a significantly lower Hb values. Also Xue et al., [27] illustrated that active RA patients showed significantly lower levels of RBC counts, Hb, Red blood cell /platelets ratio and haemoglobin-platelet ratio compared to inactive RA and that Hb, RPR and HPR were negatively related with DAS28-CRP.

On the other hand, Al-Rawi et al., [19] showed that there was no significant correlation between DAS28-ESR, RF, and ACPA with RDW. Also, Rodríguez-

Carrio et al., [28] did not find correlation between RDW and DAS-28.

Al -Rawi et al., and Lin et al., [19,18] found that RDW could differentiate between RA and controls. Although the current study did not assess the diagnostic value of RDW in RA, but RDW% showed its value in differentiating active from inactive RA with best cut-off value >12.9%.

Platelet parameters in RA patients revealed that it could be a reflection of the inflammatory and activity status. The present study found that active patients had significantly higher platelets count and PLR. Moreover, Platelet count and PLR were positively correlated with DAS score and all other clinical and laboratory activity parameters. These results are in accordance to other results [27,4] who showed that active RA patients had higher PLT counts, and that PLT count was positively correlated with DAS28 score. Similarly, Yildirim et al., [5] observed a relationship between platelet indices and disease activity in RA.

Results of Talukdar et al., [3] agree with our results as they found significantly higher platelet count and MPV in high disease activity patients. Although the higher MPV in active patients did not reach the statistical significance in the present results.

MPV showed significant importance as a marker of inflammation and disease activity [29]. In one study by Tekeoglu et al., [6] MPV was significantly associated with RA disease activity. Although the current results found higher MPV in active patients than in inactive patients yet it did not reach statistical significance.

Briggs et al., and Gürol et al., [30,31] also supported this study and concluded that parameters of the blood cells may be used in evaluation of disease activity in autoimmune inflammatory disorders generally.

In conclusion, alterations in WBCs, RBCs and PLTs parameters proved to be significantly related to the disease activity in

patients with RA, and these changes go hand in hand with inflammatory markers. Therefore, they may be used as indicators of the inflammation and activity in RA patients. RDW%, platelets count and PLR were among the most hematologic parameters connected with DAS score, parameters of disease activity followed by WBCs count, neutrophil count and NLR. CBC and haematological parameters are simple, available and cheap laboratory investigation that could be used in the future to assess and follow up RA patients. Larger prospective studies with huge number of patients are recommended to confirm and explain the importance of haematological parameters in RA patients in comparison with other autoimmune diseases.

Conflict of interest:

We declare that there are no conflicts of interest for this paper

REFERENCES:

1. **Al-Osami MH, Awadh NI, Khalid KB, et al.** Neutrophil/lymphocyte and platelet/lymphocyte ratios as potential markers of disease activity in patients with Ankylosing spondylitis: a case-control study. *Adv Rheumatol.* 2020; 60(1):13.
2. **Möller B, Scherer A, Förger F, et al.** Anaemia may add information to standardised disease activity assessment to predict radiographic damage in rheumatoid arthritis: a prospective cohort study. *Ann Rheum Dis.* 2014; 73(4):691–96.
3. **Talukdar M, Barui G, Adhikari A, et al.** A study on association between common haematological parameters and disease activity in rheumatoid arthritis. *J Clin Diagn Res.* 2017; 11(1):EC01–EC04.
4. **Harifi G and Sibilia J.** Pathogenic role of platelets in rheumatoid arthritis and systemic autoimmune diseases: perspectives and therapeutic aspects. *Saudi Med J.* 2016; 37(4):354–360.
5. **Yildirim A, Karabiber M, Surucu GD, et al.** The changes of mean platelet volume and platelet distribution width in patients with rheumatoid arthritis and their correlation with disease activity. *Acta Med Mediterr.* 2015; 31:1105–1111.
6. **Tekeoglu I, Gurol G, Harman H, et al.** Overlooked haematological markers of disease activity in rheumatoid arthritis. *Int J Rheum Dis.* 2016; 19(11):1078–1082.
7. **Charbonneau M, Lavoie RR, Lauzier A, et al.** Platelet-derived growth factor receptor activation promotes the prodestructive invadosome -forming phenotype of synoviocytes from patients with rheumatoid arthritis. *J Immunol.* 2016; 196 (8):3264–3275.
8. **Aletaha D, Neogi T, Silman A J., et al.** Rheumatoid arthritis classification criteria: An American College of Rheumatology/ European League Against Rheumatism collaborative initiative. *Arthritis. Rheum.* 2010; 62 (9): 2569-81.
9. **Prevoo ML, van 't Hof MA, Kuper HH, et al.** Modified disease activity scores that include twenty-eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. *Arthritis and Rheumatism* 1995, 38 (1): 44-8.
10. **Gasparyan AY, Ayvazyan L, Mukanova U, et al.** The Platelet-to-Lymphocyte Ratio as an Inflammatory Marker in Rheumatic Diseases. *Ann Lab Med.* 2019; 39(4):345-357.
11. **Bakogiannis C, Sachse M, Stamatiolopoulos K, et al.** Platelet-derived chemokines in inflammation and atherosclerosis. *Cytokine.* 2019; 122:154157.
12. **Xu T, Zhang G, Lin H, et al.** Clinical characteristics and risk factors of diffuse alveolar hemorrhage in systemic lupus erythematosus: a systematic review and meta-analysis based on observational studies. *Clin Rev Allergy Immunol.* 2020; 59:295–303.
13. **Fu H, Qin B, Hu Z, et al.** Neutrophil- and platelet-to-lymphocyte ratios are correlated

- with disease activity in rheumatoid arthritis. *Clin Lab.* 2015; 61(3-4):269-73.
14. **Mercan R, Bitik B, Tufan A, et al.** The Association Between Neutrophil/ Lymphocyte Ratio and Disease Activity in Rheumatoid Arthritis and Ankylosing Spondylitis. *J. Clin. Lab. Anal.* 2016; 30: 597–601.
 15. **Uslu AU, Küçük A, Şahin A, 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; 18(7):731-5.
 16. **Helal R M, El naggar M H, Zahraa MK, et al.** Neutrophil to Lymphocyte Ratio and Platelet to Lymphocyte Ratio as Marker of Disease Activity in Rheumatoid Arthritis. *Medical journal of Cairo university.*2019; 87:139-145.
 17. **Abd-Elazeem M I and Mohamed R A.** Neutrophil-lymphocyte and platelet-lymphocyte ratios in rheumatoid arthritis patients: Relation to disease activity. *Egypt. Rheumatol.* 2018; 40:227–231.
 18. **Lin F, Wang X, Liang Y, et al.** Red Blood Cell Distribution Width in Rheumatoid Arthritis, Ankylosing Spondylitis and Osteoarthritis: True Inflammatory Index or Effect of Anemia? *Ann Clin Lab Sci.* 2018; 48(3):301-307.
 19. **Al-Rawi Z S, Gorial F I, and Al-Bayati A.** Red Cell Distribution Width in Rheumatoid arthritis. *Mediterr J Rheumatol.* 2018; 29(1): 38–42.
 20. **Tecer D, Sezgin M, Kamk A, et al.** Can mean platelet volume and red blood cell distribution width show disease activity in rheumatoid arthritis? *Biomark Med* 2016; 10:967-74.
 21. **Lee WS and Kim TY.** Relation between red blood cell distribution width and inflammatory biomarkers in rheumatoid arthritis. *Arch Pathol Lab Med.* 2010; 134:505-6.
 22. **Dervišević A, Muhić A, Začiragić A, et al.** Red blood cell distribution width-to-platelet ratio inversely correlates with indicators of disease activity status in rheumatoid arthritis patients. *Rom J Intern Med.* 2021; 59(2):180-186.
 23. **Khaled SAA, NasrEldin E, Makarem YS, et al.** Value of Platelet Distribution Width and Mean Platelet Volume in Disease Activity Score of Rheumatoid Arthritis. *J Inflamm Res.* 2020;13:595-606
 24. **Fu H, Qin B, Hu Z, et al.** Neutrophil- and platelet-to-lymphocyte ratios are correlated with disease activity in rheumatoid arthritis. *Clin Lab* 2015; 61(3–4):269–273.
 25. **Koiwa M, Goto S, Takahashi K, et al.** Neutrophil/Lymphocyte Ratio in Patients with Rheumatoid Arthritis Treated with Biological Agents. *J Nippon Med Sch.* 2016; 83(3):118-24.
 26. **Yunchun L, Yue W, Jun FZ, et al.** Clinical Significance of Red Blood Cell Distribution Width and Inflammatory Factors for the Disease Activity in Rheumatoid Arthritis. *Clin Lab.* 2016; 62(12):2327-2331.
 27. **Xue L, Tao L, Sun H, et al.** Association Between Blood PLT and RBC Related Indices and Disease Activity in Patients with Rheumatoid Arthritis. *Int J Gen Med.* 2022; 15:573-581.
 28. **Rodríguez-Carrio J, Alperi-López M, López P, et al.** Red cell distribution width is associated with endothelial progenitor cell depletion and vascular-related mediators in rheumatoid arthritis. *Atherosclerosis.* 2015; 240:131-6.
 29. **Gasparyan AY, Ayvazyan L, Mikhailidis DP, et al.** Mean Platelet Volume: A Link Between Thrombosis and Inflammation? *Curr Pharm Des.* 2011; 17(1):47–58.
 30. **Briggs C.** Quality counts: new parameters in blood cell counting. *Int J Lab Hematol.* 2009; 31(3):277–297.
 31. **Gürol G, Harman H, Karakeçe E, et al.** Overlooked haematological markers of disease activity in rheumatoid arthritis. *Int J Rheum Dis.* 2016; 19(11):1078–1082.

قياسات الخلايا الدموية في مرض المفاصل الروماتويدي وعلاقتها بنشاط المرض

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الخلفيه:

ان التغيرات الالتهابيه المصاحبه للأمراض الروماتيزمية تؤثر على تغيرات في عدد وشكل وأحجام خلايا الدم المختلفه.

تحليل صورة الدم الكامله يمكن استخدامه كمؤشر للالتهاب ونشاط الأمراض الروماتيزميه.

هدف الدراسه:

الهدف من هذه الدراسه هو قياس التغيرات المختلفه في تحليل صورة الدم الكامله وتحديد علاقتها بنشاط مرض الروماتويد المفصلي .

منهجية الدراسه:

اجريت هذه الدراسه المقارنه علي المرضى الذين تأكد تشخيصهم كمرضى التهاب المفاصل الروماتيدي .تم اختيار مجموعه مكونه من ١٤١ مريض التهاب مفصلي روماتويدي بشكل عشوائي ثم تم تقسيمهم الي مجموعتين علي حسب نشاط المرض (مجموعه ذات نشاط عالي للمرض ومجموعه خامله .) تمت مقارنة هاتين المجموعتين مع

مجموعه ضابطه اخري لا تعاني من الالتهاب المفصلي الروماتويدي او اي أمراض مفصليه اخري.تضمنت المقارنه القياسات المختلفه لصورة الدم الكامله وعلاقتها بنشاط المرض.

نتائج الدراسه:

أظهرت نتائج هذه الدراسه ان مرضى الروماتويد لديهم نسبة اقل في عدد خلايا حمراء ، والهيموجلوبين ، و متوسط حجم الصفائح الدموية ، و عرض توزيع الصفائح الدموية. وتبين ان عرض توزيع خلية حمراء أعلى من المجموعه الضابطه. كان لدى المرضى النشطين عدد أعلى من الخلايا البيضاء ، و العدلات ، ونسبة العدلات الى الخلايا الليمفاوية ارتبطت خلايا الدم البيضاء والعدلات ارتباطاً إيجابياً بدرجة نشاط المرض و عيار البروتين التفاعلي C . ايضاً ارتبطت نسبة العدلات الى الخلايا الليمفاوية ارتباطاً إيجابياً بمقياس نشاط المرض ، وعدد المفاصل المؤلمه ، والبروتين التفاعلي C ومعايير البيبتيد المضاد للسيترولين الحلقي. كان لدى المرضى النشطين عرض أعلى لتوزيع الخلايا الحمراء وانخفاض في الهيموجلوبين. كان عرض توزيع الخلايا الحمراء مرتبطاً إيجابياً بمقياس نشاط المرض وعدد المفاصل المؤلمه والمتورمة ومعدل ترسيب كرات الدم الحمراء والبروتين التفاعلي C وعامل الروماتويد ومعايير البيبتيد المضاد للحلقية. كما أوضح ان لدى المرضى النشطين نسبة أعلى من الصفائح الدموية ونسبة الصفائح الدمويه الخلايا الليمفاوية . ارتبطت الصفائح الدمويه ونسبة الصفائح الدمويه الى الخلايا الليمفاوية بشكل إيجابي مع درجة نشاط المرض وجميع معاملات النشاط السريرية والمخبرية الأخرى.

يمكن استخدام عرض توزيع الخلية الحمراء للتمييز بين الروماتويد النشط وغير النشط لوجود نسبة أفضل قيمته

قطع < ١٢,٩

خلاصة الدراسه:

ارتبطت التغيرات في معايير الدم بشكل كبير مع نشاط المرض في مرضى التهاب المفاصل الروماتويدي وكانت موازية لعلامات الالتهاب. كانت عرض توزيع خلايا الدم الحمراء ، وعدد الصفائح الدموية ونسبة الخلايا الليمفاوية الصفيحة الأكثر ارتباطاً بدرجات نشاط المرض ومعايير نشاط المرض.