Al-Azhar International Medical Journal

Volume 4 | Issue 7 Article 28

2023

Section: Biochemistry, Clinical Pathology, Pathology, Rheumatology and Medical Rehabilitation

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How to Cite This Article

Ibrahim, Omar Ashraf Mohamed; Ghit, Mohamed Magdy; Assem, Ahmed Ali; and Hamoud, Hesham Salah (2023) "The Relationship between ESR/CRP Ratio, Platelet Indices and Rheumatoid Disease Activity," *Al-Azhar International Medical Journal*: Vol. 4: Iss. 7, Article 28.
DOI: https://doi.org/10.58675/2682-339X.1897

ORIGINAL ARTICLE

The Relationship Between Erythrocyte Sedimentation Rate/C-Reactive Protein Ratio, Platelet Indices and Rheumatoid Disease Activity

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Abstract

Background: **Measurement of Rheumatoid arthritis (RA) disease activity helps guide therapeutic decision and follow-up. Several disease activity scores (DAS) have been developed. DAS28 is the most frequently utilized score and the backbone for the European League Against Rheumatism (EULAR) response criteria.**

Objective: **To evaluate the possible association between erythrocyte sedimentation rate/C-reactive protein (ESR/CRP) ratio, MPV, and PDW and rheumatoid disease activity.**

Patients and methods: **Ninety individuals were included and subdivided into three age and gender matched groups: group A: 30 RA patients who received conventional disease-modifying antirheumatic drugs (DMARDs), group B: 30 RA patients who received biological DMARDs, Group C: 30 healthy volunteers as a controls. Each participant was subjected to history taking, musculoskeletal examination, disease activity score by DAS 28, laboratory tests including complete blood count (CBC), mean platelet volume (MPV), platelet distribution width (PDW), ESR, and CRP.**

Results: **DAS28-CRP was more significantly reduced in biological DMARDs group than in conventional group at 6 months from baseline ($P < 0.001$) as well as at one year from baseline ($P < 0.001$) and at 12 months from 6 months ($P = 0.003$). Significant positive associations were reported between MPV, PDW and DAS28-CRP all through study duration in conventional group as well as a biological group. A non-significant relationship was reported between DAS28-CRP and ESR/CRP ratio in conventional group as well as biological group.**

Conclusion: **MPV and PDW were significantly higher among RA patients than control individuals. Moreover, they have a significant association with disease activity in RA patients.**

Keywords: Erythrocyte sedimentation rate, C-reactive protein, Platelet indices, Rheumatoid disease activity

1. Introduction

Rheumatoid arthritis (RA) is a chronic, progressive autoimmune disease characterized by synovial proliferation and degeneration of joints and bones.[1] The disease activity scores (DAS) involves composite parameters which include number of tender and swollen joints, patient global health self-report, as well as C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR) levels. The DAS28 is the most frequently utilized score, comprising either CRP or ESR, and it had been demonstrated that a selection of the 28 named joints is as valid and reliable as more comprehensive joint counts in clinical care and trials. Since CRP is generally accessible, and responds in a more timely manner to alterations in inflammatory activity, DAS28 CRP is commonly utilized in clinical practice.[2]

The mean platelet volume (MPV) and platelet distribution width PDW are determinants of platelet function and activation. MPV reflects platelet size

Accepted 10 January 2023.
Available online 30 December 2023

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https://doi.org/10.58675/2682-339X.1897

and activation. Increased MPV values indicate large platelets, which are newer and denser with more activity.[3] The PDW determines the variation in platelet size and active platelet release. MPV and PDW are now an integral part of the complete bold count (CBC) which is the most routinely ordered laboratory test.[4]

The current study investigated the possible association between ESR/CRP ratio, MPV, and PDW and RA disease activity.

2. Patients and methods

90 individuals were included and subdivided into three age and sex matched groups:

Group A: 30 RA patients who received conventional disease-modifying antirheumatic drugs (DMARDs).

Group B: 30 RA patients who received biological DMARDs.

Group C: 30 healthy individuals as controls.

Patients with age 18–60 years, both males and females with disease duration 1–10 years and fulfilling the (ACR) 2010 classification criteria of RA were included. While exclusion criteria were infection, malignancy, hematological, metabolic, endocrinal, and other rheumatological disorders.

2.1. Ethical considerations

Patient informed consent.

An ethical committee approval to start this study.

2.2. Methodology

In this prospective study, each participant was subjected to history taking, musculoskeletal examination, disease activity score by DAS 28, blood tests including CBC, MPV, PDW, ESR, and CRP.

2.3. Statistical analysis

Data were analyzed by the statistical package for social sciences, V 23.0 (SPSS Inc., Chicago, US). Quantitative data were expressed as means± standard deviations and ranges when their distribution. Qualitative variables were expressed as numbers and percent's. Data were tested for normality by Kolmogorov–Smirnov and Shapiro–Wilk Test.

3. Results

Table 1 demonstrates significant difference among groups regarding ACCP Ab (Eu/ml) ($P < 0.001$).

Table 2 demonstrates significant difference among groups as regards ESR/CRP ratio at baseline ($P < 0.001$) as well as at six months following therapy initiation ($P < 0.001$). Meanwhile, a significant difference existed among groups as regards change in ESR/CRP ratio at 6m from baseline ($P = 0.011$) Table 3.

This table shows that DAS28-CRP was significantly lower in biological DMARDs group than in conventional group 6 months following treatment ($P < 0.001$) as well as 12 months after treatment ($P < 0.001$). DAS28-CRP was more significantly lower in biological DMARDs group in comparison with conventional group at 6 months from baseline ($P < 0.001$) as well as at one year from baseline ($P < 0.001$) and at 12 months from 6 months ($P = 0.003$).

Table 4 demonstrates significant difference among groups as regards MPV at baseline ($P < 0.001$) as well as at 6 months ($P < 0.001$) and after one year ($P < 0.05$). A significant difference was found among groups in the change of MPV at 6 months from baseline ($P < 0.05$) as well as at one year from baseline ($P < 0.05$) Table 5.

This table demonstrated a significant difference between groups as regards PDW at baseline ($p < 0.001$) as well as at 6 months ($P < 0.001$) and at one year ($P < 0.05$). A reduction in PDW was

Table 1. Demographics, disease duration and ACCP ab of the studied Groups.

	Conventional DMARDs ($n = 30$)	Biological DMARDs ($n = 30$)	Control ($n = 30$)	Test value	P
Age (y)					
Mean ± SD	41.47 ± 7.91	39.97 ± 9.39	39.13 ± 7.57	F:0.605	0.548
Range	23_55	24_57	26_54		
Sex					
Males	6 (20 %)	6 (20 %)	9 (30 %)	x^2:1.118	0.572
Females	24 (80 %)	24 (80 %)	21 (70 %)		
Disease duration (y)					
Mean ± SD	4.60 ± 1.79	4.63 ± 1.69	–	t:-0.074	0.941
Range	1_8	2_8	–		
ACCP Ab (Eu/ml)					
Mean ± SD	76.90 ± 59.90B	124.5 ± 101.8A	11.57 ± 6.76C	H:20.675	**<0.001***
Range	5_246	0.7_500	5_31		

Table 2. Comparison between the study groups as regards erythrocyte sedimentation rate/C-reactive protein ratio.

	Conventional DMARDs ($n = 30$)	Biological DMARDs ($n = 30$)	Control ($n = 30$)	H-test	*P*
ESR/CRP ratio baseline					
Mean ± SD	3.10 ± 1.27C	3.95 ± 2.64B	4.24 ± 1.02A	11.301	**<0.001***
Range	0.4_5.41	0.45_11.27	2_6.5		
ESR/CRP ratio 6 months					
Mean ± SD	3.53 ± 1.84B	4.21 ± 1.86A	4.28 ± 0.92A	4.070	**0.013***
Range	1.2_10	0.9_7.5	2.4_5.5		
ESR/CRP ratio 12 months					
Mean ± SD	4.46 ± 1.69	5.45 ± 5.50	4.31 ± 1.10	1.554	0.304
Range	1.8_8.3	1.25_30	2_6.3		
Change 6m-baseline	0.43 ± 1.07A	0.39 ± 0.34B	0.04 ± 0.62C	4.263	**0.011***
Change 12m-baseline	1.23 ± 1.40A	1.63 ± 0.74B	0.07 ± 0.17C	2.912	0.054
Change 12m−6m	0.8 ± 0.47A	1.24 ± 0.88A	0.03 ± 0.13B	0.983	0.327

Table 3. Comparison between study groups (G1 and G2) Regarding to disease activity scores28-C-reactive protein.

	Conventional DMARDs ($n = 30$)	Biological DMARDs ($n = 30$)	U-test	*P*
DAS28-CRP baseline				
Mean ± SD	6.56 ± 0.65	6.73 ± 0.40	−1.253	0.215
Range	5.2_7.6	6.1_7.5		
DAS28-CRP 6 months				
Mean ± SD	3.54 ± 0.44	2.94 ± 0.30	−8.867	**<0.001***
Range	2.9_4.1	2.7_3.7		
DAS28-CRP 12 months				
Mean ± SD	2.92 ± 0.29	2.13 ± 0.09	9.575	**<0.001***
Range	2.6_3.5	1.8_2.88		
Change 6m-baseline	−3.02 ± 0.56	−3.79 ± 0.92	13.336	**<0.001***
Change 12m-baseline	−3.64 ± 0.94	−4.43 ± 0.75	13.723	**<0.001***
Change 12m−6m	−0.62 ± 0.29	−0.81 ± 0.59	3.127	**0.003**

Table 4. Comparison between study groups as regards to mean platelet volume.

	Conventional DMARDs ($n = 30$)	Biological DMARDs ($n = 30$)	Control ($n = 30$)	H-test	*P*
MPV baseline					
Mean ± SD	11.38 ± 1.57A	12.53 ± 1.91A	8.84 ± 0.83B	26.850	**<0.001***
Range	8.7_13.4	9.3_14.9	7.3_10.3		
MPV 6 months					
Mean ± SD	9.46 ± 1.48B	8.58 ± 1.36A	8.62 ± 0.59C	16.107	**<0.001***
Range	7.2_11.9	6.3_11.6	7.6_9.6		
MPV 12 months					
Mean ± SD	8.54 ± 1.26A	7.41 ± 1.10A	8.80 ± 0.65B	6.620	**0.002***
Range	7.5_10.8	6.22_10.5	7.4_10.1		
Change 6m-baseline	−1.92 ± 0.45A	−2.95 ± 1.5B	−0.22 ± 0.18C	6.496	**0.002***
Change 12m-baseline	−2.84 ± 0.91A	−4.12 ± 0.90A	−0.04 ± 0.18C	6.015	**0.004***
Change 12m−6m	−0.92 ± 0.42	−1.17 ± 0.46	0.17 ± 0.14	2.556	0.083

reported in the current study along the study period. Meanwhile, there was difference between groups according to change at 6m from baseline ($P < 0.05$) Table 6.

This table shows progression of ESR/CRP ratio, DAS28 CRP, MPV, and PDW through study period in Conventional DMARDs group Table 7.

This table shows progression of ESR/CRP ratio, DAS28 CRP, MPV, and PDW through study period in biological DMARDs group.

Tables 8 and 9 show significant positive correlations between MPV, PDW and DAS28-CRP all through study duration in conventional group as well as biological group. Moreover, significant positive correlations between DAS28-CRP and CRP as well as ESR all through study duration in conventional group as well as biological group. A nonsignificant relationship was found between DAS28-CRP and ESR/CRP ratio in both conventional and biological groups.

Table 5. Comparison between the study groups as regards platelet distribution width.

	Conventional DMARDs ($n = 30$)	Biological DMARDs ($n = 30$)	Control ($n = 30$)	H-test	*P*
PDW at baseline					
Mean ± SD	17.85 ± 2.13A	18.68 ± 2.27A	11.48 ± 0.98B	13.480	**<0.001***
Range	13.5_21.3	14.1_23.9	9.6_13.2		
PDW 6 months					
Mean ± SD	14.83 ± 1.76B	12.94 ± 1.68A	11.57 ± 0.83C	10.120	**<0.001***
Range	11.4_16.8	10.3_15.1	9.5_12.9		
PDW 12 months					
Mean ± SD	13.52 ± 1.64A	11.15 ± 1.29A	11.19 ± 0.80B	4.307	**0.016***
Range	9.3_15.4	9.3_14.9	9.3_12.9		
Change 6m-baseline	−3.02 ± 1.27A	−5.74 ± 1.39A	0.09 ± 0.46B	3.296	**0.042***
Change 12m-baseline	−4.33 ± 1.49	−7.54 ± 2.43	−0.29 ± 0.15	2.759	0.069
Change 12m−6m	−1.31 ± 0.52	−1.79 ± 0.49	−0.38 ± 0.32	0.060	0.942

Table 6. Comparison between baseline of erythrocyte sedimentation rate/C-reactive protein ratio, disease activity scores28 C-reactive protein, mean platelet volume, platelet distribution width and other measurements "6 months and 12 months" in Conventional DMARDs group.

	Mean ± SD	*P*
ESR/CRP ratio		
Baseline	3.10 ± 1.27	**<0.001***
6 months	3.53 ± 1.84	**<0.001***
12 months	4.46 ± 1.69	
DAS28-CRP		
Baseline	6.56 ± 0.65	
6 months	3.54 ± 0.44	**<0.001***
12 months	2.92 ± 0.29	**<0.001***
MPV		
Baseline	11.38 ± 1.17	**<0.001***
6 months	9.46 ± 1.48	**<0.001***
12 months	8.54 ± 1.26	
PDW		
Baseline	17.85 ± 2.13	**0.038***
6 months	14.83 ± 1.76	**0.029***
12 months	13.52 ± 1.64	

Table 7. Comparison between baseline erythrocyte sedimentation rate/C-reactive protein ratio, disease activity scores28 C-reactive protein, platelet distribution width, mean platelet volume and other measurements "6 months and 12 months" in biological DMARDs group.

	Mean ± SD	*P*
ESR/CRP ratio		
Baseline	3.95 ± 2.64	0.089
6 months	4.21 ± 1.86	0.109
12 months	5.45 ± 5.50	
DAS28-CRP		
Baseline	6.73 ± 0.40	**<0.001***
6 months	2.94 ± 0.30	**<0.001***
12 months	2.13 ± 0.09	
MPV		
Baseline	11.53 ± 1.91	**<0.001***
6 months	8.58 ± 1.36	**<0.001***
12 months	7.41 ± 1.10	
PDW		
baseline	18.68 ± 2.27	**0.021***
6 months	12.94 ± 1.68	**0.016***
12 months	11.15 ± 1.29	

Table 8. Relationship between DAS28-C-reactive protein with different parameters in Conventional DMARDs group.

	DAS28-CRP					
	Baseline		6 Months		12 Months	
	r	*P*	*r*	*P*	*r*	*P*
Age (y)	0.189	0.318	0.169	0.373	0.194	0.131
RA duration (y)	−0.080	0.675	0.071	0.711	0.128	0.500
RF (IU/ml)	0.521	**0.003***	0.500	**0.005***	0.401	**0.028***
ACCP Ab (Eu/ml)	0.503	**0.005***	0.407	**0.026***	0.411	**0.024***
Number of pack/day	0.403	**0.027***	0.443	**0.014***	0.226	0.231
ESR	0.367	**0.034***	0.452	**0.020***	0.712	**<0.001***
CRP	0.340	**0.041***	0.352	**0.032***	0.410	**0.021***
ESR/CRP ratio	−0.086	0.652	−0.282	0.130	−0.124	0.515
MPV	0.438	**0.033***	0.345	**0.028***	0.384	**0.031***
PDW	0.459	**0.039***	0.378	**0.032***	0.308	**0.024***

4. Discussion

In our study, there was a significant reduction in DAS28-CRP in biological DMARDs group in

Table 9. Correlation between disease activity scores28-C-reactive protein with different parameters in Biological DMARDs group.

	DAS28-CRP					
	Baseline		6 months		12 months	
	r	*P*	*r*	*P*	*r*	*P*
Age (y)	0.264	0.158	0.163	0.208	0.288	0.123
RA duration (years)	0.145	0.446	0.313	0.092	0.136	0.472
RF (IU/ml)	0.517	**0.003***	0.420	**0.021***	0.236	0.209
ACCP Ab (Eu/ml)	0.655	**<0.001***	0.377	**0.040***	0.180	0.342
Number of pack/day	0.463	**0.010***	0.293	0.117	0.150	0.429
ESR	0.462	**0.010***	0.490	**0.004***	0.610	**<0.001***
CRP	0.399	**0.026***	0.427	**0.018***	0.494	**0.012***
ESR/CRP ratio	0.113	0.551	0.023	0.906	0.024	0.899
MPV	0.750	**<0.001***	0.654	**<0.001***	0.599	**<0.001***
PDW	0.653	**<0.001***	0.570	**<0.001**	0.787	**<0.001***

comparison with group at 6 months from baseline ($P < 0.001$) as well as at one year from baseline ($P < 0.001$) and at one year from 6 months ($P = 0.003$). In agreement, in Moghimi et al.[5] study on 60 RA patients, DAS-28 score was evaluated at baseline, 2 and 4 months following initiation of therapy. They reported that DAS-28 score showed gradual reduction within 4 months. Moreover, in Orr et al.[6] study, there was a low sensitivity in the detection of inflammation in most of RA cases in relation to the DAS28-CRP.

A significant difference also existed among groups as regards MPV at baseline ($P < 0.001$) as well as at 6 months ($P < 0.001$) and after one year ($P < 0.05$). Our study agreed with Tecer et al.[7] study on 100 RA patients and 100 controls that reported significant MPV elevation in RA patients. This was in agreement with Sağ et al.[8] MPV values were greater among RA patients in comparison with controls. In contrast, OZGE et al.[9] who compared RA and ankylosing spondylitis patients with control group, determined no significant difference between patients and controls in terms of MPV. Furthermore, Lee,[10] revealed no significant difference between RA patients and control subjects regarding MPV. Additionally, MPV values were lower among RA patients than in control subjects.[11,12]

A reduction in MPV was reported in the current study along the study period. A significant difference existed between groups in the change of MPV at 6 months from baseline ($P < 0.05$) as well as at one year from baseline ($P < 0.05$). In agreement, Talukdar et al.[13] determined a higher MPV value in RA cases having high disease activity in comparison to that with low disease activity. In another study, it was revealed that MPV values were increased during anti TNF- α therapy.[14] The reasons for controversy between studies were clarified by Gasparian et al.[14] stating that: though the regulation of platelet function and aging depends upon the ploidy and maturity of thrombopoietic progenitors, various cytokines and circulatory factors influence platelet production. These include IL-1; IL-6; aTNF-α and platelet activation in various physiological and pathologic situations causing time-dependent alteration of platelet indices. In contrast, MPV is measured by cell counters utilizing impedance and optical effects.[14]

This study demonstrated a significant difference among groups according to PDW at baseline ($P < 0.001$) as well as at 6 months ($P < 0.001$) and at one year ($P < 0.05$). This was consistent with Sağ et al.[8] who found that PDW values were greater among RA patients in comparison with controls. In disagreement with our findings, OZGE et al.[9] determined no significant difference between RA cases and controls as regards PDW. Boilard et al.[15] demonstrated that platelets have a significant role in inflammatory arthritis.

A reduction in PDW was reported in the current study along the study period. Meanwhile, there was difference between groups according to change at 6m from baseline ($P < 0.05$). This was consistent with Rigby et al.[16] who concluded that treatment with biologics decreased platelet levels.

This study revealed a significant positive association was reported between MPV and DAS28-CRP all through study duration in conventional group as well as biological group. This agreed with Talukdar et al.[13] they reported that those with high DAS 28-3 score had greater MPV values. On the contrary, Tekeoğlu et al.[12] determined a negative association between DAS28 and MPV in RA cases.

In the present work, significant positive associations were reported between DAS28-CRP and CRP as well as ESR all through study duration in conventional group as well as biological group. This is in concordance with Orr et al.[6] who demonstrated a positive association between CRP, ESR and DAS28-CRP with histologic inflammatory alterations in synovial biopsies. On the contrary, Sağ et al.[8] failed to report an association with DAS28 and CRP.

In the current work, significant positive associations were reported between DAS28-CRP and PDW all through study duration in conventional group as well as biological group. This was consistent with Khaled et al.[17] they found significant positive correlation between DAS 28 and PDW in their study on 52 patients with RA. In discordance, a negative correlation was noted between PDW and DAS28 in Targońska-Stępniak et al.[18] study. Such discrepancies may be because of existence of some confounding factors need to be discovered and also because of many additional challenge related to methodology issues. Because of such conflicting reports, more studies are necessary for clarification of these discrepancies.

4.1. Conclusion

MPV and PDW were significantly higher among RA patients in comparison to control subjects. Moreover, they have a strong association with disease activity in RA patients.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article.

Sources of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of interest

Conflict of interest statement: The authors declared that there were NO conflicts of Interest.

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