

## **Are Red Cell Distribution Width and Mean Platelet Volume associated with Rheumatoid Arthritis?**

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### **Abstract**

**Aim:** The aim of this retrospective study was to investigate the correlation between Rheumatoid Arthritis (RA) and Mean Platelet Volume (MPV) and Red Cell Distribution Width (RDW), which are parameters of routine hemogram tests that are suggested to be related with inflammation.

**Methods:** We included 81 patients with RA in this retrospective study. Control group was consisted of 80 healthy subjects admitted to our institution for a routine check-up. White Blood Cell count (WBC), haemoglobin (Hb), RDW, platelet count (PLT) and MPV values of the participants obtained and analyzed.

**Results:** We found that, RDW and MPV values were significantly different in patients with RA compared to control subjects.

**Conclusion:** We think that, MPV reduction and RDW elevation is associated with RA. However, prospective studies with larger population are needed to reveal the relationship between the disease activity and MPV and RDW.

**Keywords** Rheumatoid arthritis, mean platelet volume, red cell distribution width.

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### **Introduction:**

Rheumatoid Arthritis (RA) is a chronic inflammatory disease of unknown cause which characterized by tenderness, swelling and stiffness of the joints, with progressive destruction of cartilage and bone structure [1, 2]. About 40% of the pain present with extra articular involvement [3]. Pathogenesis of RA has been associated with a variety of inflammatory molecules [4]. Detection of platelet associated micro particles in the synovial fluid of RA patients has been attracted authors' interest whether platelets have involved in the inflammation [4, 5]. It is well known that peripheric thrombocytosis accompanies with inflammation in RA [6]. MPV and RDW are hemogram parameters that authors speculate that both two were associated with inflammation and inflammatory conditions [7-9]. Previously, MPV has been introduced as an inflammatory marker in RA and ankylosing spondylitis [10]. Mean platelet volume (MPV) is an indicator of platelet function. It reflects activation of the platelets [11] and it has been found to be related with inflammatory conditions [12-15]. Variability in size of the erythrocytes have been referred to as

red cell distribution width (RDW) and similarly, it has been found to be associated with inflammatory processes [9, 16, 17]. We aimed in this retrospective study to assess RDW and MPV values of the patients with RA and to compare those to normal population.

### **Methods**

A total of 81 patients with RA and 80 healthy controls included in present retrospective study. Exclusion criteria were as follows: iron deficiency anemia, hypo-hyperthyroidism, active infection, cardiovascular and metabolic diseases that may affect MPV and RDW values. Laboratory data of the participants obtained from computerized database of our institution.

We recorded age, gender, white blood cell count (WBC) , hemoglobin (Hb) , red cell distribution width (RDW), platelet count (PLT) and mean platelet volume (MPV) values. All statistics were brought out with SPSS programme (SPSS 15.0, SPSS Inc., Chicago, IL, USA). Variables were expressed as

median (min-max) and compared with Mann Whitney U test. A p value <0.05 was considered as statistically significant. The study was approved by Ministry of Health, Ordu Health Directorate.

## Results

Age of the patients in RA group was 53 (16-95) years and age of the control group was 57.5 (28-81) years. The difference was not statistically significant (p=0.71). There were 17 men and 64 women in RA group and 27 men and 53 women in control group. The difference was not significant (p=0.07). Similarly, WBC (p=0.07), Hb (p=0.13) and PLT (p=0.83) values were not statistically different between study and control groups.

**Table 1.** Characteristics and data of study population.

	RA group	Control group	P
Gender	Men (n)	27	0.07
	Women (n)	53	
Median (Min.- max.)			
Age (years)	53 (16-95)	57.5 (28-81)	0.71
WBC (k/mm <sup>3</sup> )	7.9 (2.3-9.6)	6.8 (4.4-14)	0.07
Hb (g/dl)	12.7 (11-16.5)	13.2 (10.8-14.7)	0.13
RDW (%)	13.8 (12-18)	13.7 (10.2-15.2)	0.04
PLT (k/ mm <sup>3</sup> )	258 (131-689)	260 (109-509)	0.83
MPV (fL)	8 (5.2-14.2)	8.9 (6.9-16.4)	<0.001

Table 1 shows general characteristics and laboratory data of the RA and control groups.

Median RDW of the RA group was 13.8 (12-18) and median RDW of the control group was 13.7 (10.2-15.2). The difference was statistically significant (p=0.04). Median MPV of the RA group was 8 (5.2-14.2) and median MPV of the control group was 8.9 (6.9-16.4). The difference was statistically significant (p<0.001).

## Discussion

In present retrospective study, we showed that the patients with RA have significantly lower MPV and higher RDW values compared to age-sex matched healthy subjects.

We shall discuss the reasons of elevated MPV in RA patients here. MPV is the marker of platelet activation. Activated platelets become enlarge in size. Kısacık et al reported that MPV was significantly decreased in RA patients compared to controls [10]. Similarly, Aktas et al reported significantly decreased MPV values in patients with nasal polyps, another inflammatory condition, compared to healthy population [18]. Boilard et al reported the important role of platelets in the course of inflammatory arthritis [19]. Literature is full of data about the relation between MPV and inflammatory conditions

[4, 5, 20, 21]. Therefore, the decrease of MPV in RA is not surprising.

What are the possible mechanisms of MPV reduction in RA? First of all, activated platelets in response to the inflammatory processes are tend to be in larger size. After their utilization and involvement in inflammatory processes, remaining smaller, inactive platelets may cause a reduction in MPV. Secondly, inflammatory cytokines in blood flow may interact with the megakariopoesis in bone marrow and cause production of smaller platelets which results a decrease in MPV. Red cell distribution width is a marker of erythrocyte indices in routine hemogram test and indicates anisocytosis of the red cells. Elevation in RDW has been reported in various inflammatory conditions in literature [8, 22]. The data about the association between RDW and inflammation in literature is conflicting. Authors reported an association between inflammation and RDW increase [23-25] while others not [26].

One of these conflicting reports in literature, the study by Vaya et al, which showed elevated RDW levels in patients with systemic lupus erythematosus compared to control subjects [27]. Unfortunately, Hb levels of patients with SLE were significantly lower than that of the controls in their study. Iron deficiency, the most common cause of anaemia may induce RDW elevation.

On the other hand, Hb levels were not different between study and control groups in our report and similar to literature, we found increased RDW in RA patients compared to healthy subjects. Inflammatory burden of RA may interfere with erythropoiesis and cause production of erythrocytes in different sizes. Two major limitations of present study are retrospective design and relatively small study cohort.

## Conclusion

In conclusion, we think that, MPV reduction and RDW elevation is associated with RA. However, prospective studies with larger population are needed to reveal the relationship between the disease activity and MPV and RDW.

## References:

1. Scott DL, Symmons DP, Coulton BL, Popert AJ. Long-term outcome of treating rheumatoid arthritis: results after 20 years. *Lancet* 1987; 1: 1108-1111.
2. Wolfe F. The natural history of rheumatoid arthritis. *The Journal of rheumatology Supplement* 1996; 44: 13-22.
3. Turesson C, Jacobsson LT. Epidemiology of extra-articular manifestations in rheumatoid arthritis. *Scandinavian journal of rheumatology* 2004; 33 :65-72.
4. Choy EH, Panayi GS. Cytokine pathways and joint inflammation in rheumatoid arthritis. *The New England journal of medicine* 2001; 344: 907-916.
5. Knijff-Dutmer EA, Koerts J, Nieuwland R, Kalsbeek-Batenburg EM, van de Laar MA. Elevated levels of platelet microparticles are associated with disease activity in

- rheumatoid arthritis. *Arthritis and rheumatism* 2002; 46: 1498-1503.
6. Dahlqvist SR, Nilsson TK, Norberg B. Thrombocytosis in active rheumatoid arthritis. Relation to other parameters of inflammatory activity and confounding effect of automated cell counting. *Clinical rheumatology* 1988; 7 : 335-341.
  7. Polinska B, Matowicka-Karna J, Kemon H. Assessment of the influence of the inflammatory process on the activation of blood platelets and morphological parameters in patients with ulcerative colitis (colitis ulcerosa). *Folia histochemica et cytobiologica / Polish Academy of Sciences, Polish Histochemical and Cytochemical Society* 2011; 49: 119-124.
  8. Song CS, Park DI, Yoon MY, Seok HS, Park JH, Kim HJ, Cho YK, Sohn CI, Jeon WK, Kim BI. Association Between Red Cell Distribution Width and Disease Activity in Patients with Inflammatory Bowel Disease. *Digest Dis Sci* 2012; 57: 1033-1038.
  9. Aktaş G, Alçelik A, Tekçe BK, Şavlı H, Üyetürk Ü, Kurt M, Tekelioğlu V, Yüce Y. Mean Platelet Volume and Red Cell distribution width in Hepatosteatos. *National Journal of Medical Research* 2013; 3: 264-266.
  10. Kisacik B, Tufan A, Kalyoncu U, Karadag O, Akdogan A, Ozturk MA, Kiraz S, Ertenli I, Calguneri M. Mean platelet volume (MPV) as an inflammatory marker in ankylosing spondylitis and rheumatoid arthritis. *Joint Bone Spine* 2008; 75: 291-294.
  11. Briggs C, Mellors I, Roderick A, Ward A, O'Malley C, Barker J, De La Salle B, McTaggart P, Hyde K, Machin SJ, Advis UNGHS. Quality counts: new parameters in blood cell counting. *Int J Lab Hematol* 2009; 31: 277-297.
  12. Choi CU, Seo HS, Kim YK, Na JO, Lim HE, Kim JW, Kim EJ, Rha SW, Park CG, Oh DJ. Can mean platelet volume predict coronary vasospasm? *Platelets* 2011; 22: 173-178.
  13. Endler G, Klimesch A, SunderPlassmann H, Schillinger M, Exner M, Mannhalter C, Jordanova N, Christ G, Thalhammer R, Huber K. Mean platelet volume is an independent risk factor for myocardial infarction but not for coronary artery disease. *British journal of haematology* 2002; 117: 399-404.
  14. Gasparyan AY, Stavropoulos-Kalinoglou A, Toms TE, Douglas KM, Kitis GD. Association of mean platelet volume with hypertension in rheumatoid arthritis. *Inflammation & allergy drug targets* 2010; 9: 45-50.
  15. Ha SI, Choi DH, Ki YJ, Yang JS, Park G, Chung JW, Koh YY, Chang KS, Hong SP. Stroke prediction using mean platelet volume in patients with atrial fibrillation. *Platelets* 2011; 22: 408-414.
  16. Cakal B, Akoz AG, Ustundag Y, Yalinkilic M, Ulker A, Ankarali H. Red Cell Distribution Width for Assessment of Activity of Inflammatory Bowel Disease. *Digest Dis Sci* 2009; 54: 842-847.
  17. Clarke K, Sagunathy R, Kansal S. RDW as an additional marker in inflammatory bowel Disease/Undifferentiated colitis. *Digest Dis Sci* 2008; 53: 2521-2523.
  18. Aktas G, Sit M, Tekce H, Alcelik A, Savli H, Simsek T, Ozmen E, Isci AZ, Apuhan T. Mean platelet volume in nasal polyps. *The West Indian medical journal* 2013; 62: 515-518.
  19. Boilard E, Blanco P, Nigrovic PA. Platelets: active players in the pathogenesis of arthritis and SLE. *Nature Reviews Rheumatology* 2012; 8: 534-542.
  20. Bathon JM, Martin RW, Fleischmann RM, Tesser JR, Schiff MH, Keystone EC, Genovese MC, Wasko MC, Moreland LW, Weaver AL, Markenson J, Finck BK. A comparison of etanercept and methotrexate in patients with early rheumatoid arthritis. *The New England journal of medicine*. 2000; 343: 1586-1593.
  21. Breedveld FC, Dayer JM. Leflunomide: mode of action in the treatment of rheumatoid arthritis. *Annals of the rheumatic diseases* 2000; 59: 841-849.
  22. Yuksel O, Helvacı K, Basar O, Koklu S, Caner S, Helvacı N, Abaylı E, Altıparmak E. An overlooked indicator of disease activity in ulcerative colitis: mean platelet volume. *Platelets* 2009; 20: 277-281.
  23. Anderson JL, Ronnow BS, Horne BD, Carlquist JF, May HT, Bair TL, Jensen KR, Muhlestein JB. Usefulness of a complete blood count-derived risk score to predict incident mortality in patients with suspected cardiovascular disease. *The American journal of cardiology* 2007; 99: 169-174.
  24. Ani C, Ovbiagele B. Elevated red blood cell distribution width predicts mortality in persons with known stroke. *Journal of the neurological sciences* 2009; 277: 103-108.
  25. Brusco G, Di Stefano M, Corazza GR. Increased red cell distribution width and coeliac disease. *Digestive and liver disease : official journal of the Italian Society of Gastroenterology and the Italian Association for the Study of the Liver* 2000; 32: 128-130.
  26. Agarwal S, Kumar P, Kapadia S. Association between red cell distribution width (RDW), inflammatory markers and cardiovascular fitness in healthy adults: data from national health and nutrition examination survey 1999-2004. *Journal of the American College of Cardiology* 2012; 59: E1779.
  27. Vaya A, Alis R, Hernandez JL, Calvo J, Mico L, Romagnoli M, Ricarte JM. RDW in patients with systemic lupus erythematosus. Influence of anaemia and inflammatory markers. *Clinical hemorheology and microcirculation* 2013; 54: 333-339.

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