Kulak Burun Bogaz Ihtis Derg 2017;27(5):221-225 doi: 10.5606/kbbihtisas.2017.22847

Original Article* / *Çalışma - Araştırma

Red blood cell distribution width in patients with nasal polyposis

Nazal polipli hastalarda kırmızı kan hücresi dağılım genişliği

Özgül Topal, MD., Selim Sermed Erbek, MD.

Department of Otolaryngology, Medical Faculty of Başkent University, Ankara, Turkey

ABSTRACT

Objectives: This study aims to evaluate the red blood cell distribution width (RDW) levels of patients with nasal polyposis (NP), and investigate its value as an inflammatory parameter and possible correlation with the severity of the disease.

Patients and Methods: Between January 2003 and September 2016, a total of 139 NP patients (87 males, 52 females; mean age 46.6 years; range 22 to 87 years) and 80 controls (59 males, 21 females; mean age 30.3 years; range 17 to 64 years), who underwent nasal septal reconstruction surgery, were included in this retrospective controlled study. Data including polyp stage, computed tomography (CT) score, number of eosinophils in peripheral blood, total serum immunoglobulin E (IgE) and RDW were obtained from medical records.

Results: Red blood cell distribution width was above normal values in 56 NP patients (40.28%). Mean RDW was 15.3906±1.41805% in NP group and 14.6413±0.83191% in the control group. The difference was statistically significant between the two groups ($p<0.001$). There was no statistically significant correlation between RDW and total serum IgE, number of total eosinophils in peripheral blood, polyp stage, and CT scores.

Conclusion: Patients with NP showed significantly increased RDW values compared to controls. Although we failed to demonstrate an association of elevated RDW with the disease severity, this preliminary study may give rise to further prospective studies.

Keywords: Inflammation; nasal polyp; red blood cell distribution width.

ÖZ

Amaç: Bu çalışmada nazal polipli (NP) hastaların kırmızı kan hücresi dağılım genişliği (KKDG) seviyeleri değerlendirildi ve enflamatuvar bir parametre olarak önemi ve hastalık şiddeti ile muhtemel ilişkisi araştırıldı.

Hastalar ve Yöntemler: Ocak 2003 - Eylül 2016 tarihleri arasında 139 NP hastası (87 erkek, 52 kadın; ort. yaş 46.6 yıl; dağılım 22-87 yıl) ve nazal septal rekonstrüksiyon cerrahisi olmuş 80 kontrol hastası (59 erkek, 21 kadın; ort. yaş 30.3 yıl; dağılım 17-64 yıl) bu retrospektif kontrollü çalışmaya dahil edildi. Polip evresi, bilgisayarlı tomografi (BT) skoru, periferik kanda eozinofil sayısı, total serum immünoglobulin E (IgE) ve KKDG verileri tıbbi kayıtlardan elde edildi.

Bulgular: Elli altı NP'li hastada (%40.28) KKDG normal değerlerin üzerindeydi. Ortalama KKDG, NP'li grupta %15.3906±1.41805, kontrol grubunda ise %14.6413±0.83191 idi. İki grup arasındaki fark istatistiksel olarak anlamlı bulundu ($p<0.001$). Total serum IgE ve KKDG, periferik kanda total eozinofil sayısı, polip evresi ve BT skorları arasında istatistiksel olarak anlamlı ilişki yoktu.

Sonuç: Nazal polipli hastalar, kontrol grubu ile karşılaştırıldığında KKDG değerlerinde anlamlı olarak artış gösterdi. Yüksek KKDG değerlerinin hastalık şiddeti ile ilişkisi ortaya konmamış olsa da, bu ön çalışma ileriye yönelik prospektif çalışmalara yol gösterici olabilir.

Anahtar Sözcükler: Enflamasyon; nazal polip; kırmızı kan hücresi dağılım genişliği.

Available online at
www.kbbihtisas.org
doi: 10.5606/kbbihtisas.2017.22847
QR (Quick Response) Code

Received / *Geliş tarihi:* August 11, 2012 Accepted / *Kabul tarihi:* August 24, 2012

Correspondence / İletişim adresi: Özgül Topal, MD. Başkent Üniversitesi Konya Uygulama ve Araştırma Merkezi Kulak Burun Boğaz Kliniği, 42100 Selçuklu, Konya, Turkey.

Tel: +90 332 - 257 06 06 e-mail *(e-posta):* ozgultopal75@yahoo.com

Nasal polyposis (NP) is a chronic inflammatory disease characterized by edematous masses originating from the mucous membrane of the nasal cavity or paranasal sinuses.[1] Nasal polyposis significantly reduces quality of life because of symptoms like nasal obstruction, nasal/postnasal dripping, hyposmia/anosmia, and headache.[2,3] Although the exact etiology is still unknown, tissue eosinophilia is accepted to be a characteristic histological appearance.[4]

Red blood cell distribution width (RDW) is calculated by dividing the standard deviation of red blood cell volume by mean corpuscular volume (MCV).[5] It has diagnostic value in differentiating anemia. Nowadays, there is growing evidence that RDW is a useful inflammatory parameter in assessing the disease severity of various chronic inflammatory diseases.[6-8]

The aim of this study was to evaluate the RDW values of patients with NP, and investigate its correlation with severity of the disease.

PATIENTS AND METHODS

This study was approved by Başkent University School of Medicine Review Board (Project no: KA16/105). Informed consent was not obtained from the patients because the study was retrospective and only the anonymous data was used. Medical records of 139 patients operated on for NP were evaluated retrospectively. Nasal polyposis was defined as the presence of bilateral polyps in the middle meatus by using anterior rhinoscopy and/or endoscopic endonasal examination, and bilateral mucosal disease on paranasal computed tomography (CT).[9] Eighty patients who were operated on for nasal septum deviation with no medical history of any other inflammatory or systemic diseases were used as control group.

Nasal polyposis patients who had data about hematological parameters and disease severity were included in the study. In predicting the severity of NP, number of total eosinophils in complete blood count (CBC), total serum immunoglobulin E (IgE), polyp stage, and paranasal sinus CT score parameters were used. Polyp stage was predicted as 1-3 as reported by Lildholdt et al.[10] The Lund-Mackay system[11] was used to score opacification of the paranasal sinuses. Prior to preoperative anesthesia consultation and oral steroid administration for planned endoscopic sinus surgery, complete blood count measurements were performed with a hematology analyzer (Beckman Coulter LH780; Beckman Coulter, Brea, CA, USA). The reference range for RDW was 11.6-15.5%.

Patients who presented to our clinic between January 2003 and September 2016, and for whom clinical, laboratory, and radiological information were completely retrievable were included to the study. Exclusion criteria were: history of previous operation for NP, local or systemic usage of steroid therapy during the last four weeks, anemia, malignancy, diabetes mellitus, immunosupression, and any other chronic or acute systemic inflammatory diseases.

Table 1. Clinical characteristics of patients with nasal polyposis

	n	Mean±SD	Mean	Range
Mean age (year)			46.6	22-87
Gender				
Male	87			
Female	52			
Polyp stage				
Stage 1	44			
Stage 2	55			
Stage 3	40			
Mean computed tomography score			16.76	4-24
Total immunoglobulin E (IU/mL)		152.0±198.3		
Total eosinophil (K/μL)		0.365±0.245		

SD: Standard deviation.

Table 2. Red blood cell distribution width characteristics in nasal polyposis and control groups

	Number of patients	Mean±SD*
Nasal polyposis	139	15.4±1.4%
Control group	80	14.6±0.8%

SD: Standard deviation; * Red blood cell distribution width.

Table 3. Computed tomography score, total immunoglobulin E, and total eosinophil characteristics in nasal polyposis according to red blood cell distribution width

	RDW	
	Normal	High
	Mean±SD	Mean±SD
Computed tomography score	16.7±6.1	16.9±5.4
Total immunoglobulin E (IU/mL)	160.3±225.1	139.4±151.1
Total eosinophil (K/µL)	0.4±0.3	0.3±0.2

RDW: Red blood cell distribution width; SD: Standard deviation.

Statistical analysis

Statistical analysis was performed by using SPSS for Windows version 15.0 (SPSS Inc., Chicago, IL, USA). Student t test was used for the comparison of RDW values between two groups. Pearson correlation was used for correlation analysis. A value of $p<0.05$ was considered statistically significant.

RESULTS

The study included 139 NP patients (87 males, 52 females; mean age 46.6 years; range 22 to 87 years) and 80 septoplasty patients (control group) (59 males, 21 females; mean age 30.3 years; range 17 to 64 years). In the NP group, 44 (31.7%) patients were stage 1, 55 (39.6%) patients were stage 2, and 40 (28.8%) patients were stage 3.

Mean serum total IgE was 152.0±198.3 IU/mL, and mean number of total eosinophils was 0.4±0.2 K/µL in NP group.

Table 4. Red blood cell distribution width values according to polyp stage in nasal polyposis

Stage	Mean±SD*
1	15.4±1.5%
2	15.4±1.4%
3	15.3±1.4%

SD: Standard deviation; * Red blood cell distribution width.

Table 1 shows the clinical characteristics of patients with NP.

The RDW was above normal values in 56 (40.3%) NP patients and nine (11.25%) patients in the control group. Among these patients mean RDW was 16.53±1.54%. Table 2 shows RDW characteristics in NP and control groups. Mean RDW was 15.39±1.42% in NP group. Mean RDW was 14.64±0.83% in the control group. The difference was statistically significant between two groups ($p<0.001$).

There were no statistically significant correlation between RDW and total IgE ($p=0.58$), number of total eosinophils ($p=0.58$), CT scores ($p=0.78$) (Table 3), and polyp stage ($p=0.798$) (Table 4).

DISCUSSION

In this study, the mean RDW value significantly increased in NP patients, compared to the controls. The RDW was above normal values in 56 (40.3%) NP patients and nine (11.25%) patients in the control group. To the best of our knowledge, this is the first study showing the RDW increase in NP.

Nasal polyposis is an inflammatory disease in which tissue eosinophilia is accepted to be a characteristic histological appearance.[4,12] Toxic inflammatory mediators secreted by activated

eosinophils and other inflammatory cells cause a series of pathological processes like epithelial injury, excessive mucus secretion, increase in vascular permeability, and edema within the nasal and paranasal sinus mucosa. One of these mediators is interleukin-5 (IL-5) which is known to have a key importance in maintenance of tissue eosinophilia and reported to be increased in NP compared to healthy controls.[13] On the other hand, a variety of other cytokines like IL-6, IL-8, IL-11, IL-16 are nonspecific markers of the inflammation in these patients.[14,15] IL-16 is a highly potent chemotactic and chemoattractant molecule for eosinophils. Lackner et al.[15] reported a local increase of IL-16 in nasal polyp tissue. However, Keseroglu et al.[16] showed that levels of IL-16 in NP patients were also significantly increased in peripheral blood and concluded that it supports the presence of a systemic eosinophil activation in NP. Based on this, it can be speculated that NP is a chronic systemic inflammation.

It has been demonstrated that a positive association exists between RDW and conventional inflammatory biomarkers.[6] Even a low grade inflammation may result in anisocytosis.[17,18] There is growing literature about various inflammatory diseases such as psoriasis vulgaris, hepatitis B, familial Mediterranean fever, Takayasu arteritis revealing that RDW is a valuable inflammatory marker to assess disease activity in patients without anemia.[19-22] Our study also revealed a significant RDW elevation in NP as in other systemic inflammatory diseases.

The waste products of tissue inflammation are reactive oxygen species (ROS) composed of free radicals, leading to oxidative stress. Nowadays, the relation of free radicals with epithelial events in nasal polyposis is under special interest. There is growing evidence revealing higher oxygen radical levels versus lower antioxidant levels in tissue and blood samples in the patients with NP.[23,24] On the other hand, inverse effects of oxidative stress on erythrocyte homeostasis and survival is already reported.[25] Low serum antioxidant concentrations have been reported to be negatively correlated with RDW.[26] Therefore, it can be speculated that the oxidative stress or chronic hypoxemia caused by NP might be one of the reasons for increased RDW in our study group.

Although it was significantly elevated, we failed to demonstrate the value of RDW in predicting the severity of disease. Further prospective studies including surveys predicting quality of life may be planned for estimating self-perceived severity.

One of the major limitations of this study is its being retrospective. Elevated RDW is also associated with iron deficiency, folate or vitamin B12 deficiency, sickle cell-β-thalassemia, immune hemolytic anemia, cytotoxic chemotherapy, chronic liver disease, myelodysplastic syndrome. However, our study and control groups included otherwise healthy patients by history. All the patients were preoperatively evaluated by the anesthesia department and none of them had anemia on CBC, or elevated preoperative liver enzymes in laboratory tests. Moreover, in a report by Zou et al.,[27] baseline RDW in patients with systemic lupus erythematous was evaluated in anemic and nonanemic patient groups. They concluded that RDW was a valuable predictor of therapeutic outcomes and the risk of disease flare irrespective of anemia status. However, for overcoming these limitations prospective studies considering all these variables are suggested.

In conclusion, although the pathophysiology of NP is still under debate, it is known to be a chronic inflammatory disease characterized by tissue eosinophilia. Red blood cell distribution width is regarded as a systemic inflammatory parameter and a positive association exists between RDW and conventional inflammatory biomarkers. This study revealed that RDW levels in NP are significantly increased compared to healthy controls. Thus, the RDW value may be a valuable predictor in reflecting the inflammatory status. Because we failed to demonstrate an association with the severity of the disease in this retrospective study, further prospective studies are needed to evaluate the exact association.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Little SC, Early SB, Woodard CR, Shonka DC Jr, Han JK, Borish L, Steinke JW. Dual action of TGF-beta1

on nasal-polyp derived fibroblasts. Laryngoscope 2008;118:320-4.
2. Damm M, Quante G, Jungehuelsing M, Stennert E. Impact of functional endoscopic sinus surgery on symptoms and quality of life in chronic rhinosinusitis. Laryngoscope 2002;112:310-5.
3. Salhab M, Matai V, Salam MA. The impact of functional endoscopic sinus surgery on health status. Rhinology 2004;42:98-102.
4. Drake-Lee AB. Nasal polyps. In: Kerr AG, Groves J, editors. Scott-Brown's Otolaryngology. London: Butterworths; 1987. p. 142-53.
5. Evans TC, Jehle D. The red blood cell distribution width. J Emerg Med 1991;9:71-4.
6. Lippi G, Targher G, Montagnana M, Salvagno GL, Zoppini G, Guidi GC. Relation between red blood cell distribution width and inflammatory biomarkers in a large cohort of unselected outpatients. Arch Pathol Lab Med 2009;133:628-32.
7. Salvagno GL, Sanchis-Gomar F, Picanza A, Lippi G. Red blood cell distribution width: A simple parameter with multiple clinical applications. Crit Rev Clin Lab Sci 2015;52:86-105.
8. Vayá A, Sarnago A, Fuster O, Alis R, Romagnoli M. Influence of inflammatory and lipidic parameters on red blood cell distribution width in a healthy population. Clin Hemorheol Microcirc 2015;59:379-85.
9. Meltzer EO, Hamilos DL, Hadley JA, Lanza DC, Marple BF, Nicklas RA, et al. Rhinosinusitis: developing guidance for clinical trials. J Allergy Clin Immunol 2006;118:17-61.
10. Lildholdt T, Rundcrantz H, Bende M, Larsen K. Glucocorticoid treatment for nasal polyps. The use of topical budesonide powder, intramuscular betamethasone, and surgical treatment. Arch Otolaryngol Head Neck Surg 1997;123:595-600.
11. Lund VJ, Mackay IS. Staging in rhinosinusitus. Rhinology 1993;31:183-4.
12. Stoop AE, van der Heijden HA, Biewenga J, van der Baan S. Eosinophils in nasal polyps and nasal mucosa: an immunohistochemical study. J Allergy Clin Immunol 1993;91:616-22.
13. Bachert C, Wagenmann M, Hauser U, Rudack C. IL-5 synthesis is upregulated in human nasal polyp tissue. J Allergy Clin Immunol 1997;99:837-42.
14. Bradley DT, Kountakis SE. Role of interleukins and transforming growth factor-beta in chronic rhinosinusitis and nasal polyposis. Laryngoscope 2005;115:684-6.
15. Lackner A, Raggam RB, Stammberger H, Beham A, Braun H, Kleinhappl B, et al. The role of interleukin-16 in eosinophilic chronic rhinosinusitis. Eur Arch Otorhinolaryngol. 2007;264:887-93.
16. Keseroğlu K, Banoğlu E, Kizil Y, Aydil U, Gönül II, Yilmaz M, et al. Serum interleukin-16 levels in patients with nasal polyposis. Laryngoscope 2012;122:961-4.
17. Weiss G, Goodnough LT. Anemia of chronic disease. N Engl J Med 2005;352:1011-23.
18. Kiefer CR, Snyder LM. Oxidation and erythrocyte senescence. Curr Opin Hematol 2000;7:113-6.
19. Kim DS, Shin D, Jee H, Kim TG, Kim SH, Kim DY, et al. Red blood cell distribution width is increased in patients with psoriasis vulgaris: A retrospective study on 261 patients. J Dermatol 2015;42:567-71.
20. Xu WS, Qiu XM, Ou QS, Liu C, Lin JP, Chen HJ, et al. Red blood cell distribution width levels correlate with liver fibrosis and inflammation: a noninvasive serum marker panel to predict the severity of fibrosis and inflammation in patients with hepatitis B. Medicine (Baltimore) 2015;94:612.
21. Özer S, Yılmaz R, Sönmezgöz E, Karaaslan E, Taşkın S, Bütün İ, et al. Simple markers for subclinical inflammation in patients with Familial Mediterranean Fever. Med Sci Monit 2015;21:298-303.
22. Liu Q, Dang AM, Chen BW, Lv NQ, Wang X, Zheng DY. The association of red blood cell distribution width with anemia and inflammation in patients with Takayasu arteritis. Clin Chim Acta 2015;438:205-9.
23. Dagli M, Eryilmaz A, Besler T, Akmansu H, Acar A, Korkmaz H. Role of free radicals and antioxidants in nasal polyps. Laryngoscope 2004;114:1200-3.
24. Topal O, Kulaksızoglu S, Erbek SS. Oxidative stress and nasal polyposis: does it affect the severity of the disease? Am J Rhinol Allergy 2014;28:1-4.
25. Friedman JS, Lopez MF, Fleming MD, Rivera A, Martin FM, Welsh ML, et al. SOD2-deficiency anemia: protein oxidation and altered protein expression reveal targets of damage, stress response, and antioxidant responsiveness. Blood 2004;104:2565-73.
26. Semba RD, Patel KV, Ferrucci L, Sun K, Roy CN, Guralnik JM, et al. Serum antioxidants and inflammation predict red cell distribution width in older women: the Women's Health and Aging Study I. Clin Nutr 2010;29:600-4.
27. Zou XL, Lin XJ, Ni X, Wang J, Liu W, Wei J. Baseline Red Blood Cell Distribution Width Correlates with Disease Activity and Therapeutic Outcomes in Patients with Systemic Lupus Erythematosus, Irrespective of Anemia Status. Clin Lab 2016;62:1841-50.