

The Implication of Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio Between Diabetic and Non-Diabetic Patients Diagnosed with Bell's Palsy

● Melis Demirağ Evman, ● Hakan Avcı, ● Sedat Aydın

Department of Ear, Nose and Throat Diseases, University of Health Sciences İstanbul Kartal Dr. Lütfi Kırdar Training and Research Hospital, İstanbul, Turkey

Submitted: 10.09.2018
Accepted: 18.10.2018

Correspondence:
Melis Demirağ Evman,
SBÜ İstanbul Kartal Dr. Lütfi Kırdar Eğitim ve Araştırma Hastanesi, KBB Kliniği, İstanbul, Turkey
E-mail: melisdemirag@hotmail.com



Keywords: Bell's palsy; lymphocyte; neutrophil; platelet; Type 2 diabetes mellitus.

ABSTRACT

Objective: Acute facial paralysis (AFP) is one of the most common complaints of patients who were admitted to the otolaryngology emergency clinics. It is important to diagnose and provide accurate treatment for AFP because misdiagnosis or late treatment may result with permanent unwanted outcomes. The aim of the present study was to investigate the usefulness of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) in patients diagnosed with Bell's palsy (BP) with or without diabetes for the differential diagnosis and alternative treatment modalities of patients with BP.

Methods: Patients who were admitted to the Kartal Dr. Lütfi Kırdar Training and Research Hospital emergency department with a complaint of acute peripheral facial paralysis diagnosed with BP between January 2013 and February 2017 were evaluated retrospectively. Eighteen patients with BP and 17 patients with BP and type 2 diabetes mellitus (T2DM) were included in the study.

Results: Thirty-five patients diagnosed with facial paralysis were evaluated. It was statistically significant that the number of diabetic females with BP was higher than that of males ($p=0.035$). Seventeen patients with BP and 18 patients with T2DM and BP were evaluated, and there was no statistical significance between both groups' NLR and PLR values.

Conclusion: There was no statistically significant difference between NLR and PLR between patients with BP with T2DM and non-DM.

INTRODUCTION

Acute facial paralysis (AFP) is characterized by sudden onset peripheral, unilateral facial weakness. The incidence of AFP is found to be 30/100,000 in the literature.^[1] It can be caused by many diseases, such as cancer, trauma, Bell's palsy (BP), Ramsay Hunt syndrome (RHS), and iatrogenic injury.^[1,2] The most common causes among these are BP and RHS.^[1,3] The incidence of BP is 15–30/100,000 in the literature.^[4] The etiology of the disease is not clear, but vascular causes, autoimmune diseases, and inflammation of the nerve sheath are indicated in the pathogenesis.^[5] There are evidences in the literature suggesting that BP is an inflammatory disorder of the facial nerve.^[6,7] As a result of inflammation, edema occurs in the fallopian tubes, especially in the labyrinth segment of the facial nerve.^[8] Patients who benefit from corticosteroid therapy and observation of the facial nerve during decompression surgery are strong predictive factors showing that BP is an inflammatory process.^[9,10]

Neutrophil-to-lymphocyte ratio (NLR) is a marker used in the diagnosis of general inflammation condition of the human body, and it is considered to be a useful marker in the etiological investigation of inflammatory disorders.^[9,11,12] It is shown in many studies that NLR is a valuable indicator in diseases, such as vestibular neuritis, sudden hearing loss, rheumatoid arthritis, cystic fibrosis, and BP in which the inflammatory process occurs in etiology.^[10]

Platelet-to-lymphocyte ratio (PLR) can be used in the follow-up of inflammation, vascular disorders, and gynecologic and hepatobiliary system malignancies.^[13,14]

Mean platelet volume and red cell distribution width are markers that can also be used in inflammatory diseases.^[15]

Diabetes mellitus (DM) is increasing worldwide. Many studies are made to determine its pathophysiology, prevention, and new treatment modalities. Studies have shown the association between inflammatory biomarkers and the occurrence of type 2 DM (T2DM) and its complications.^[16]

The aim of the present study was to investigate the usefulness of NLR and PLR in patients diagnosed with BP with or without diabetes for the differential diagnosis and alternative treatment modalities of patients with BP.

MATERIAL AND METHODS

Patients who were admitted to our hospital's emergency department with a complaint of peripheral facial paralysis between January 2013 and February 2017 were evaluated retrospectively. They underwent physical examination by neurology and otolaryngology specialists. They were all diagnosed with BP. Patients with acute or chronic ear disease and who had another inflammatory disease other than T2DM were excluded from the study. Overall, 17 patients with BP and 18 patients with BP and T2DM were included in the study. Whole blood analysis results were evaluated retrospectively. NLR was calculated by dividing absolute neutrophil count by lymphocyte count per microliter, and PLR was calculated by dividing absolute platelet count by lymphocyte count per microliter. Demographic characteristics were also collected. The results were expressed as mean (25th–75th percentile) for numerical variables and percentages for categorical variables. The chi-square test and the Mann–Whitney U test were used with MedCalc Statistical Software version 16.4.3 (MedCalc Software bvba, Ostend, Belgium; <https://www.medcalc.org>; 2016).

RESULTS

In the aforementioned period, 35 patients diagnosed with facial paralysis were evaluated. Of the 35 patients, there

were 21 (60%) male and 16 (40%) female patients. Of the 21 males, 7 (33.3%) had T2DM, and of the 16 females, 11 had T2DM (68.7%). It was statistically significant that the number of diabetic females with BP was higher than that of males ($p=0.035$) (Table 1).

The median NLR of 18 patients with BP and T2DM was 2.55, and it was 2.25 with patients with non-DM BP ($p=0.235$). There was no statistical significance between the groups. The median PLR of 18 patients with BP and T2DM was 1.58, and it was 1.28 with patients with non-DM BP ($p=0.212$). There was no statistical significance between the groups (Table 2).

DISCUSSION

The incidence of AFP in the literature is found to be 30/100,000, and the most common causes are BP and RHS.^[1,3] The etiopathogenesis of BP is still unclear. Infection, genetic factors, microvascular circulatory impairment, immunological factors, and inflammation have been blamed.^[17] Owing to microvascular circulatory impairment, neuritis was associated with vascular inflammation.^[9]

The immune response to physiological changes is characterized by increased neutrophil and decreased lymphocyte counts.^[18] Neutrophils play an important role in cytokine production during inflammation, and lymphopenia due to apoptosis is seen in the inflammatory process.^[10] NLR may provide information about inflammatory disorders.^[11,12] It is an inexpensive and easily available parameter in studying inflammatory disorders.

Platelets are important blood elements especially in coagulation. They also play a role in inflammation. PLR is also a parameter evaluated in the literature. It was found to be increased in some diseases, such as peripheral vascular diseases, coronary artery disease, and in some malignancies.^[19,20] It is also found to be associated with sudden hearing loss in the literature.^[21]

Since vestibular neuritis and BP are considered to have the same etiology, some investigations are made on NLR and PLR in vestibular neuritis.^[12,22] In a study of 70 patients with acute sensorineural hearing loss, Chung et al.^[12] concluded that NLR and PLR levels are higher in patients with hearing loss than in controls.

Table 1. Comparison between male and female patients in terms of their diabetes status

	Patients with DM				Total	
	DM (–)		DM (+)		n	%
	n	%	n	%		
Male	14	66.7	7	33.3	21	56.8
Female	5	31.2	11	68.7	16	43.2
Total	19	51.4	18	48.6	37	100

DM: Diabetes mellitus.

Table 2. Hemogram parameters of patients with Bell's palsy

	Bell's palsy group without DM			Bell's palsy group with DM			p ^a
	n	Median	Average rank	n	Median	Average rank	
PLT	19	295.0000	17.0789	18	317.0000	21.0278	0.2674
NE (%)	17	62.1000	16.2059	18	66.6000	19.6944	0.3141
LYM (%)	19	27.5000	21.1842	18	25.2150	16.6944	0.2073
Neutrophil to lymphocyte ratio	17	2.2582	15.8824	18	2.5519	20.0000	0.2348
Platelet to lymphocyte ratio	19	1.2854	16.8421	18	1.5825	21.2778	0.2128

^aMann-Whitney U test. DM: Diabetes mellitus; PLT: Platelet, NE: Neutrophil, LYM: Lymphocyte.

There are few studies on PLR and BP. Atan et al.^[22] revealed that PLR is significantly higher in the BP group than in the control group. Yilmaz et al.^[17] found that inflammatory cytokines, serum interleukin (IL)-6, IL-8, and tumor necrosis factor-alpha levels are significantly higher in patients with BP than in healthy control group patients.^[24] Ulu et al.^[23] found that NLR is significantly higher in patients with sudden hearing loss than in the control group, and they also reported that high NLR is a predictor of poor prognosis.

The presence of NLR in BP was demonstrated in recent studies. Eryilmaz et al. studied NLR in pediatric patients with BP, and NLR was found to be significantly higher in patients with BP than in the control group.^[10] NLR was found to be higher in patients with BP in another study by Özler et al.^[24] Atan et al.^[22] found that NLR and PLR are significantly higher in 99 patients with BP than in the 99 patient control group in their study. Sahin et al.^[11] also found that NLR is significantly higher in the BP group than in the healthy control group.

T2DM is very common worldwide. As the number of patients with DM increases, related complications begin to cause morbidity and mortality. T2DM and its complications have proven that DM is an inflammatory disease, and several studies have shown that an altered immune system plays an important role in the pathogenesis of DM.^[18,25] Many studies have determined that DM is associated with chronic inflammation, and several studies explored that chronic inflammation promotes the acceleration of diabetic microangiopathy.^[18] In a review about DM and inflammation, recent evidence linking low-grade chronic inflammation with the occurrence of T2DM and its related complications were discussed. It was concluded that available evidence supports the role of low-grade chronic inflammation connection between obesity and T2DM by inflammation-induced insulin resistance.^[16] One recent study has shown that the NLR values of patients with diabetes are significantly higher than those of the healthy control group.^[18] Understanding the inflammatory mechanism between inflammation and T2DM and its complications stimulated the interest of using anti-inflammatory drugs in treatment. Some drugs used routinely in DM, such as statins, have been shown to lower inflammatory mediators.^[16] There are newly made trials on the subject, but none of them have been yet accepted in clinical use.

In the present study, we found no significant statistical difference between both NLR and PLR between the two groups. Patients with T2DM are individuals with diagnosed DM, and even some of them are on antidiabetic drugs, meaning that their blood glucose is regulated. This made us think that patients with DM under controlled blood glucose have similar inflammatory features with patients with BP. Prospective studies with more patients should be designed to have a significant conclusion. In the present study, while working on the demographic analysis of patients, we realized that patients with T2DM were younger than patients with no diabetes, and it was statistically significant ($p=0.005$). According to this, we may conclude

that patients with DM are more prone to BP at earlier ages than the normal population. It may be because of the chronic inflammatory process of DM causing changes in the immune system of individuals. Further studies about this issue can answer this question. In our study, it was statistically significant that the number of diabetic females with BP was higher than that of males. We may say that females with BP and T2DM are higher in number than males. This may alter according to the demographic differences between patients, and our study group was not randomized enough to conclude the data this way. Studies of patients with diabetes from different areas of Turkey with different demographic properties may lead to more significant results.

Our study had several limitations. First, the number of cases was limited. Second, it was a retrospective study, and we did not have the chance to evaluate patients after treatment. Further prospective studies with more number of cases for the evaluation of NLR and PLR especially with new treatment modalities applied will lead to new data for the literature.

In conclusion, there was no significant difference between NLR and PLR between patients with BP with T2DM and non-DM. NLR and PLR were studied in many BP cases in the literature, but to our knowledge, NLR and PLR were studied for the first time in patients with T2DM BP. Further prospective studies with larger volume of patients are highly recommended.

Ethics Committee Approval

Approved by the local ethics committee.

Informed Consent

Retrospective study.

Peer-review

Internally peer-reviewed.

Authorship Contributions

Concept: S.A., Design: M.D.E.; Data Collection: H.A., Analysis and/or interpretation: M.D.E.; Literature Search: H.A.; Writing: M.D.E.; Critical Review: S.A.

Conflict of Interest

None declared.

REFERENCES

1. Cai Z, Li H, Wang X, Niu X, Ni P, Zhang W, et al. Prognostic factors of Bell's palsy and Ramsay Hunt syndrome. *Medicine (Baltimore)* 2017;96:e5898.
2. Hohman MH, Hadlock TA. Etiology, diagnosis, and management of facial palsy: 2000 patients at a facial nerve center. *Laryngoscope* 2014;124:E283-93.
3. Volk GF, Klingner C, Finkensieper M, Witte OW, Guntinas-Lichius O. Prognostication of recovery time after acute peripheral facial palsy: a prospective cohort study. *BMJ Open*. 2013;3. pii: e003007.
4. Morris AM, Deeks SL, Hill MD, Midroni G, Goldstein WC, Mazzulli T, et al. Annualized incidence and spectrum of illness from an outbreak investigation of Bell's palsy. *Neuroepidemiology* 2002;21:255-61.

5. McCaul JA, Cascarini L, Godden D, Coombes D, Brennan PA, Kerawala CJ. Evidence based management of Bell's palsy. *Br J Oral Maxillofac Surg* 2014;52:387–91.
6. Peitersen E. Bell's palsy: the spontaneous course of 2,500 peripheral facial nerve palsies of different etiologies. *Acta Otolaryngol Suppl* 2002;4–30.
7. Yanagihara N, Honda N, Hato N, Murakami S. Edematous swelling of the facial nerve in Bell's palsy. *Acta Otolaryngol* 2000;120:667–71.
8. Kefalidis G, Riga M, Argyropoulou P, Karotomichelakis M, Gouveris C, Prassopoulos P, et al. Is the width of the labyrinthine portion of the fallopian tube implicated in the pathophysiology of Bell's palsy?: a prospective clinical study using computed tomography. *Laryngoscope* 2010;120:1203–7.
9. Gantz BJ, Rubinstein JT, Gidley P, Woodworth GG. Surgical management of Bell's palsy. *Laryngoscope* 1999;109:1177–88.
10. Eryilmaz A, Basal Y, Tosun A, Kurt Omurlu I, Basak S. The neutrophil to lymphocyte ratios of our pediatric patients with Bell's palsy. *Int J Pediatr Otorhinolaryngol* 2015;79:2374–7.
11. Uslu AU, Küçük A, Şahin A, Ugan Y, Yılmaz R, Güngör T, 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;18:731–5.
12. Chung JH, Lim J, Jeong JH, Kim KR, Park CW, Lee SH. The significance of neutrophil to lymphocyte ratio and platelet to lymphocyte ratio in vestibular neuritis. *Laryngoscope* 2015;125:E257–61.
13. Toprak C, Tabakci MM, Simsek Z, Arslantas U, Durmus HI, Ocal L, et al. Platelet/Lymphocyte ratio was associated with impaired myocardial perfusion and both in-hospital and long-term adverse outcome in patients with ST-segment elevation acute myocardial infarction undergoing primary coronary intervention. *Postepy Kardiol Interwencyjnej* 2015;11:288–97.
14. Aldemir MN, Turkeli M, Simsek M, Yildirim N, Bilen Y, Yetimoglu H, et al. Prognostic Value of Baseline Neutrophil-Lymphocyte and Platelet-Lymphocyte Ratios in Local and Advanced Gastric Cancer Patients. *Asian Pac J Cancer Prev* 2015;16:5933–7.
15. Danese E, Lippi G, Montagnana M. Red blood cell distribution width and cardiovascular diseases. *J Thorac Dis* 2015;7:E402–11.
16. Lontchi-Yimagou E, Sobngwi E, Matsha TE, Kengne AP. Diabetes mellitus and inflammation. *Curr Diab Rep* 2013;13:435–44.
17. Yilmaz M, Tarakcioglu M, Bayazit N, Bayazit YA, Namiduru M, Kanlikama M. Serum cytokine levels in Bell's palsy. *J Neurol Sci* 2002;197:69–72.
18. Lou M, Luo P, Tang R, Peng Y, Yu S, Huang W, et al. Relationship between neutrophil-lymphocyte ratio and insulin resistance in newly diagnosed type 2 diabetes mellitus patients. *BMC Endocr Disord* 2015;15:9.
19. Bhat T, Teli S, Rijal J, Bhat H, Raza M, Khouery G, et al. Neutrophil to lymphocyte ratio and cardiovascular diseases: a review. *Expert Rev Cardiovasc Ther* 2013;11:55–9.
20. Wang D, Yang JX, Cao DY, Wan XR, Feng FZ, Huang HF, et al. Preoperative neutrophil-lymphocyte and platelet-lymphocyte ratios as independent predictors of cervical stromal involvement in surgically treated endometrioid adenocarcinoma. *Oncol Targets Ther* 2013;6:211–6.
21. Seo YJ, Park YA, Bong JP, Park DJ, Park SY. Predictive value of neutrophil to lymphocyte ratio in first-time and recurrent idiopathic sudden sensorineural hearing loss. *Auris Nasus Larynx* 2015;42:438–42.
22. Atan D, İkinçioğulları A, Köseoğlu S, Özcan KM, Çetin MA, En-sari S, et al. New Predictive Parameters of Bell's Palsy: Neutrophil to Lymphocyte Ratio and Platelet to Lymphocyte Ratio. *Balkan Med J* 2015;32:167–70.
23. Ulu S, Ulu MS, Bucak A, Ahsen A, Yucedag F, Aycicek A. Neutrophil-to-lymphocyte ratio as a new, quick, and reliable indicator for predicting diagnosis and prognosis of idiopathic sudden sensorineural hearing loss. *Otol Neurotol* 2013;34:1400–4.
24. Özler GS, Günak G. Neutrophil-lymphocyte ratio: a new predictive and prognostic factor in patients with Bell palsy. *J Craniofac Surg* 2014;25:944–5.
25. Xu T, Weng Z, Pei C, Yu S, Chen Y, Guo W, et al. The relationship between neutrophil-to-lymphocyte ratio and diabetic peripheral neuropathy in Type 2 diabetes mellitus. *Medicine (Baltimore)* 2017;96:e8289.

Nötrofil Lenfosit Oranı ve Trombosit Lenfosit Oranının Diyabetik ve Diyabetik Olmayan Bell Paralizili Hastalarda Önemi

Amaç: Akut fasiyal paralizisi (AFP) kulak burun boğaz acil polikliniğine yapılan başvurular arasında sık görülen nedenlerden birisidir. Tanısını koymak ve tedavisini olabildiğince hızlı verebilmek kalıcı hasarların oluşmasını en aza indirecek en önemli yoldur. Bu çalışmanın amacı acil servise akut tek taraflı periferik fasiyal paralizisi ile başvuran Bell paralizisi (BP) tanısı alan ve tip 2 diyabeti (T2DM) olan ve olmayan hastalarda nötrofil-lenfosit oranı (NLR) ve trombosit-lenfosit oranının (PLR) belirlenerek ayırıcı tanı ve alternatif tedavi protokolleri oluşturmak olarak belirlenmiştir.

Gereç ve Yöntem: Ocak 2016 ile Şubat 2017 arasında Kartal Dr. Lütfi Kırdar Eğitim ve Araştırma Hastanesi acil servise başvuran ve KBB Acil Kliniği'ne yönlendirilen hastalar geriye dönük olarak tarandı. On yedi BP tanısı almış hasta, 18 BP tanısı almış ve bilinen tip 2 diyabeti olan hasta çalışmaya dahil edildi.

Bulgular: Çalışmaya alınan 35 hastanın 21'i erkek, 16'sı kadındır. Yirmi bir erkeğin yedisinde T2DM varken 16 kadının 11'inde T2DM rastlanmıştır. T2DM mevcut olan 18 fasiyal paralizisi hastası ve DM olmayan 17 hastanın NLR'si ve PLR'si arasındaki fark istatistiksel olarak anlamlı değildir ($p=0.2348$).

Sonuç: Bell paralizisi olan T2DM hastaları ile diyabetik olmayan BP hastalarının NLR ve PLR değerleri arasında istatistiksel olarak anlamlı fark izlenmemiştir.

Anahtar Sözcükler: Bell paralizisi; lenfosit; nötrofil; tip 2 diyabet; trombosit.