New Predictive Hematologic Parameters in Chronic Rhinosinusitis: A Multicenter Study

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Abstract

Introduction: Our aim was to investigate whether Neutrophil-Lymphocyte Ratio (NLR), Platelet-Lymphocyte Ratio (PLR) and Mean Platelet Volume parameters (MPV) may be utilized as inflammatory markers of chronic rhinosinusitis with nasal polyps (CRSwNP) and without nasal polyps (CRSsNP).

Methods: This retrospective multicenter study was performed on 647 patients who underwent endoscopic sinus surgery. Clinical and preoperative laboratory data of patients were screened retrospectively. The study and control groups were compared for the parameters NLR, PLR, MPV, neutrophils, lymphocytes, and platelets.

Results: Of the 647 patients, 313 were in the CRSwNP group, 334 were in the CRSsNP group. There were 93 individuals in the control group. NLR and PLR levels were significantly higher in study groups compared to control group (p < 0.001). But no statistically significant differences were identified between CRSwNP group and CRSsNP group in terms of NLR, PLR, MPV levels.

Conclusion: We speculate that high NLR and PLR values may be useful inflammatory indicator for CRSwNP and CRSsNP groups. We believe these parameters will have increasing clinical use in the future on treatment options and prognosis.

Keywords: Neutrophil- Lymphocyte Ratio, Platelets-Lymphocyte Ratio, Mean Platelet Volume, Inflammatory Indicators, Chronic Rhinosinusitis.

Introduction

Chronic rhinosinusitis (CRS) is a prevalent disease characterized by mucosal inflammation of the sinuses for a minimum of 12 weeks. It is categorized depending on whether it exists with nasal polyps or not, either as CRS with polyp (CRSwNP) or CRS without polyp (CRSsNP) (1). Long-standing inflammation observed in these patients may have an association with chronic bacterial sinusitis, allergic rhinitis, cystic fibrosis, allergic fungal sinusitis, or autonomic nervous system dysfunction (2). The recognized histopathological factors include inflammatory cell and T-cell patterns, remodeling patterns (TGF-b), eicosanoid, and Ig E production, microorganisms, and epithelial barrier dysfunction (3). For CRS without polyp, there is mostly neutrophilic inflammation and T helper 1 (Th1) cell presence in the stroma (4). There is an abundance of pro-inflammatory cytokines associated with Th1 type inflammation, and cellular infiltration of neutrophils, macrophages, and lymphocytes (5). Cytokines such as IL-1α, IL-1β, IL-6, interferon-α, TNF, and IL-8 have been reported to play important roles in inflammatory response (6). CRSwNP develops as a result of prolonged inflammation of the nasal passages. Airborne irritants and allergens, fungi, staphylococcal enterotoxins, and biofilms have been blamed as inflammatory stimulants. Disorders of innate immune system and the combination of host susceptibility and environmental exposure contribute to the chronic inflammatory state. Despite all these, the etiopathogenesis of CRS is not fully understood and is thought to be multifactorial (7).

Besides cytokines, neutrophils, macrophages, and lymphocytes, recent studies have shown the importance of platelets in inflammation. Increased platelet activation has an important role in the development of inflammation, and significantly contributes in chronic inflammation (8). The neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR), and the mean platelet volume (MPV) are parameters commonly
analyzed in complete blood count. There are many reports suggesting the use of these parameters as inflammatory markers in diseases associated with inflammation, including head and neck cancers, Fibromyalgia Syndrome, gastrointestinal diseases, Crimean–Congo Hemorrhagic Fever, and sinonasal diseases (9-13). The aim of the present study was to investigate whether the parameters NLR, PLR, and MPV are valid inflammatory markers to be used in patients with CRS.

Materials and Method

We retrospectively reviewed the medical files of 647 patients that underwent endoscopic sinus surgery due to an initial diagnosis of chronic rhinosinusitis between 2005 to 2015. All procedures were performed at the Ear-Nose-Throat clinics of Dicle University, Cumhuriyet University, Abant Izzet Baysal University and Recep Tayyip Erdogan University. We obtained approval of the local department ethics committee. The study conforms with the declaration of Helsinki as amended in 2013.

Patients were divided into two groups based on clinical, radiological, and histopathological findings: chronic rhinosinusitis with nasal polyp (CRSwNP) and chronic rhinosinusitis without nasal polyp (CRSsNP). Demographical properties, clinical findings, laboratory results, operation findings, and histopathological information were reviewed retrospectively from patient files present from the ENT archives. As laboratory parameters, neutrophil (NEU), lymphocyte (LYMP), mean platelet volume (MPV), platelet (PLT), white blood cells (WBC), and hemoglobin (HGB) were noted. The NLR was determined as the ratio of neutrophil count to lymphocyte count, and the PLR was determined as the ratio of platelet count to lymphocyte count. Study exclusion criteria are as follows: history of chronic inflammatory diseases, autoimmune disease, acute or chronic infectious disease, hematological disorders, malignancies, systemic corticosteroid use, and/or chronic renal failure. The control group was selected among individuals that did not have sinusitis or rhinitis during the last year, or history of any chronic disease. The study and control groups were compared for the parameters NLR, PLR, MPV, NEU, LYMP, and PLT. In addition, CRSwNP and CRSsNP groups were compared between each other.

Result

Of the 647 patients that underwent endoscopic sinus surgery, 313 were in the CRSwNP group, and 334 were in the CRSsNP group. There were 97 females and 216 males in the CRSwNP group that had a mean age of 40.83 ±16.16 (6-78) years; whereas, there were 113 females and 221 males with a mean age of 36.63±15.24 (3-77) years in the CRSsNP group. There were 93 individuals in the control group, of which 37 were female and 56 were male, and the mean age was 35.05 ±16.49 (13-69) years. The groups did not show statistically significant differences in terms of age (p = 0.64) and sex distribution (p = 0.157). Table 1 summarizes the data related to the hematological parameters. According to comparison of PLT, NEU, LYMP, MPV, NLR, and PLR values, NEU, LYMP, NLR, and PLR parameters showed significant difference between groups. Interestingly, PLT and MPV parameters did not show any significant difference (see Table 1). In comparison to the control group, NLR, PLR, NEU, and LYMP values were significantly higher in both the CRSwNP group (p < 0.001) and CRSsNP group (p < 0.001). These parameters did

Table 1. Demographic characteristics and laboratory parameters of study groups.

<table>
<thead>
<tr>
<th>Variables</th>
<th>CRSwNP Group Mean ± SD</th>
<th>CRSsNP Group Mean ± SD</th>
<th>Control Group Mean ± SD</th>
<th>p* value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>313</td>
<td>334</td>
<td>93</td>
<td></td>
</tr>
<tr>
<td>Age mean (years)</td>
<td>40.8 (6-78)</td>
<td>36.0 (3-77)</td>
<td>35.0 (13-69)</td>
<td>0.64</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>97</td>
<td>113</td>
<td>37</td>
<td>0.157</td>
</tr>
<tr>
<td>Male</td>
<td>216</td>
<td>221</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>PLT (K/uL)</td>
<td>271±71</td>
<td>274±76</td>
<td>257±54</td>
<td>0.121</td>
</tr>
<tr>
<td>NEU (10^3 u)</td>
<td>4,47±2,5</td>
<td>4,37±2,0</td>
<td>2,36±0,6</td>
<td>0.001</td>
</tr>
<tr>
<td>LYMP (10^3 u)</td>
<td>2,77±1,4</td>
<td>2,69±1,17</td>
<td>7,66±1,96</td>
<td>0.001</td>
</tr>
<tr>
<td>MPV (fl)</td>
<td>7,92±1,38</td>
<td>8,07±1,32</td>
<td>8,15±1,37</td>
<td>0.619</td>
</tr>
<tr>
<td>NLR</td>
<td>1,96±1,85</td>
<td>1,90±1,12</td>
<td>0,31±0,07</td>
<td>0.001</td>
</tr>
<tr>
<td>PLR</td>
<td>114,00±53,88</td>
<td>116,31±49,31</td>
<td>35,28±10,10</td>
<td>0.001</td>
</tr>
</tbody>
</table>


p*: Significance of Kruskal–Wallis Test
Discussion

There have been many studies in the recent years that have examined NLR, PLR, and MPV as useful inflammatory markers for various inflammatory diseases. Our findings indicate that NLR and PLR, as a result of the inflammatory process, are increased in chronic sinusitis with or without polyp in comparison to control group.

With an increased focus in sinusitis research, we are beginning to understand the complex and various effects of chronic inflammation on the hemostasis of sinus mucosa. Platelets mainly play a role in thrombosis and hemostasis. Chemokines released from the activated platelet membrane play important roles in immune response. These chemokines are a part of the first immune response as acute phase reactants and function similar to substances released from neutrophils, granulocytes, and monocytes, which have a direct antimicrobial effect (8). When activated, platelets change in shape and size. Their sizes show correlation with their functions. Hence, larger platelets contain more granules and are metabolically and enzymatically more active (14). In other words, when platelets are activated to synthesize inflammatory factors like chemokines and cytokines, the mean platelet volume (MPV) increases. Increased MPV can be used as an indicator of inflammatory diseases characterized with chronic systemic inflammation.

MPV is commonly analyzed in complete blood count from the peripheral blood. Many studies have investigated its association with various diseases, and these studies have some contradicting results (13-17). In their study, Somuk et al. (13) examined the MPV value as an inflammatory marker, and they found significant differences between the patient and control groups. Vizioli et al. (14) evaluated MPV as a risk factor in individuals with cardiovascular disease, and obtained significant results. In their study (including 90 patients) Koç et al. (17) compared MPV and PLT values between patients with chronic sinusitis only without nasal polyp and control group. They found that MPV patients with CRSsNP had significantly higher MPV compared to controls, but did not detect a significant difference regarding PLT. Aktaş et al. (15) evaluated MPV in 43 patients that only had CRSwNP and found that patients with CRSwNP had significantly lower MPV compared to control group. On the other hand, we did not encounter any study that compared the MPV values between CRSwNP and CRSsNP patients. This is the first study to compare MPV between patients with chronic rhinosinusitis with and without nasal polyp. According to our results, CRSwNP and CRSsNP groups did not show significant difference regarding the MPV value. Our study is a multi-centered study; and therefore, is a largest-scale study investigating the NLR, PLR, and MPV in patients with chronic sinusitis. Previous studies on this subject have contradicting results; and their authors pointed out to a requirement for larger-scale, multi-centered studies. We think our study would full this gap in related literature.

The other two parameters easily calculated from complete blood count are NLR and PLR. There are some studies related to NLR and PLR values in some otolaryngological diseases (18-20). In their study, Young et al. (18) stated that NLR and PLR values could be used as prognostic indicators prior for chemotherapy in patients with oropharyngeal cancer. Ulu et al. (19) found higher NLR value in the treatment-non-responsive group in comparison to the treatment-responsive group among patients with sudden hearing loss. They stated that NLR could be used for diagnosis and determining prognosis of the disease. Eryılmaz et al. (20) found that pediatric patients with Bell’s palsy had higher NLR value in comparison to the control group, and stated that high NLR value is associated with inflammatory aspect of the disease. In their study (including 192 patients), Boztepe et al. (21) compared NLR and PLR values between patients with CRSwNP and CRSsNP. They found significantly lower values of NLR and PLR in the control group compared to patients with CRSwNP and CRSsNP, and stated that while NLR could predict recurrence of the disease, PLR could not be used as a predictive factor. They stated further studies were necessary to confirm their results. Our results are consistent with the results of the aforementioned studies. Patients with chronic sinusitis had significantly higher NLR and PLR values in comparison to control group.

In conclusion, high NLR and PLR values may be used as convenient inflammatory markers for CRS. However, our study’s strength is restrained by the retrospective study design and not evaluating the effect of our findings on disease prognosis. We believe these parameters will have increasing clinical use in the future as more information is gathered from large-scale prospective studies that will investigate the effect of hematological parameters on treatment options and prognosis.
References


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