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Original Article

# Clinical Value of Systemic Immune Inflammation and Pan-Immune Inflammation in Adenoid Hypertrophy

Tuğba Yemiş[1], Mehmet Birinci[1], Metin Çeliker[1], Gökçe Aydın Balaban[2], Erdal Eren Askeroğlu[1], Özlem Çelebi Erdivanlı[1]

[1]Recep Tayyip Erdoğan University Faculty of Medicine, Department of Otorhinolaryngology, Rize, Turkey
[2]Rize State Hospital, Clinic of Otorhinolaryngology, Rize, Turkey

**ABSTRACT**

**Aim:** This study aimed to investigate the relationship between adenoid hypertrophy, the most common cause of obstructive sleep apnea (OSA) in children, with the systemic immune inflammation index (SII) and the pan-immune inflammation value (PIV), and to evaluate the clinical utility of SII and PIV in prognostic and predictive aspects.

**Materials and Methods:** The retrospective data from 29 patients presenting to the otorhinolaryngology clinic with dyspnea and undergoing adenoidectomy for OSA between June, 2022 and June, 2023 were reviewed. Thirty age- and sex-matched healthy subjects were included as the control group. The preoperative and postoperative 6-month SII and PIV values of both groups were compared.

**Results:** There was no significant difference between the groups in terms of age and gender ($p>0.05$). Platelet SII and PIV were statistically significantly higher in patients in the preoperative period compared to the control group ($p<0.05$). No significant differences were found in the preoperative neutrophil, lymphocyte, and monocyte counts between the patients and the control subjects ($p>0.05$). Postoperative neutrophil, platelet, and monocyte counts, as well as the SII and PIV values of the patients, were significantly higher than of those in the control group ($p<0.05$).

**Conclusion:** Our study highlights the potential utility of SII and PIV in assessing systemic inflammation in adenoid hypertrophy-related OSA. However, the unexpected increase in postoperative SII and PIV values underscores the need for further research into their clinical implications.

**Keywords:** Pan-immune inflammation value, systemic immune inflammation index, adenoid hypertrophy, obstructive sleep apnea

## Introduction

Adenoid tissue situated in the nasopharynx can undergo hypertrophy, leading to the obstruction of the air passage from the nasal cavity to the nasopharynx (1). If left untreated, adenoid hypertrophy can contribute to conditions such as nocturnal hypoxia and obstructive sleep apnea (OSA). Risk factors for snoring, including adenotonsillar hypertrophy, chronic tonsillitis, obesity, and male gender, have been identified (2). Untreated adenoid hypertrophy in children may result in chronic upper airway obstruction, potentially leading to secondary enuresis, severe morning headaches, loss of appetite, behavioral disorders, impaired school performance, and growth-development retardation. Progressive cases can lead to various cardiopulmonary complications such as pulmonary ventilation deficiency, chronic hypoxia, hypercapnia, right heart hypertrophy, cor pulmonale and pulmonary edema (3). In these instances, systemic inflammatory markers and proinflammatory

**Address for Correspondence**
Tuğba Yemiş, Recep Tayyip Erdoğan University Faculty of Medicine, Department of Otorhinolaryngology, Rize, Turkey
**Phone:** +90 506 967 09 32 **E-mail:** tugba.yemis@erdogan.edu.tr **ORCID:** orcid.org/0000-0001-8713-0251
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cytokines increase, promoting lymphoid tissue proliferation (4).

The systemic immune inflammation index (SII) and pan-immune inflammation value (PIV) are derived from complete blood count elements using specific formulas. While studies have extensively explored SII and PIV in diseases such as colorectal cancer, breast cancer, and rheumatoid diseases, their utility extends to assessing severity and prognosis in other diseases (5,6).

In this study, our aim was to investigate the associations between SII and PIV in relation to adenoid hypertrophy-induced OSA in children. Additionally, we sought to evaluate the potential of SII and PIV as clinical indicators supporting surgical interventions for patients with adenoid hypertrophy.

## Materials and Methods

Upon receiving approval from the Recep Tayyip Erdoğan University Non-Interventional Clinical Research Ethics Committee (approval no.: 2024/26, date: 18.01.2024), the records of patients visiting the otorhinolaryngology clinic between June, 2022 and June, 2023 were meticulously examined. Informed consent was obtained from the parents of all patients, with acknowledgement of the study objectives and possible publication of the medical data. Inclusion criteria encompassed those individuals with an active complaint of dyspnea and a history of adenoidectomy due to OSA. Exclusions were made for patients over 18 years of age, those categorized as overweight or obese, individuals with genetic syndromes, congenital malformations, nasal septum deviation, sinonasal infections, otitis media, as well as those with chronic or hematological diseases. A cohort of 29 patients meeting the specified criteria was identified and enrolled into this study. Additionally, data from 30 healthy subjects matched in terms of age and sex were utilized as the control group for comparative analysis.

### Adenoidectomy Procedure

All patients underwent a comprehensive preoperative assessment, including endoscopic nasal examination, nasopharynx examination, otoscopic and endoscopic ear examination, as well as tympanometry. Preoperative tympanograms consistently displayed type A patterns in all patients. Adenoidectomy was conducted under general anesthesia with patients in a supine position employing an adenoidectomy curette. Hemostasis was meticulously ensured through tamponade post-procedure. Notably, none of the pediatric patients exhibited clinical signs of infection during the adenoidectomy procedure.

### Laboratory Analyses

Preoperative routine blood samples were collected from the antecubital vein into tubes containing ethylenediaminetetracetic acid. Hemogram analysis was performed on a Mindray BC-600 Hematology Analyzer. The following formulas were used to calculate PIV and SII (5,7):

$$PIV = \frac{\text{neutrophil\#} * \text{platelet\#} * \text{monocyte\#}}{\text{lymphocyte\#}}$$

$$SII = \frac{\text{neutrophil\#} * \text{monocyte\#}}{\text{lymphocyte\#}}$$

The patients were scheduled for follow-up appointments at the 1st week, 3rd month, and 6th month following surgery. At the 6-month follow-up, transnasal flexible endoscopy revealed the absence of adenoid tissue in all patients. Additionally, those patients who underwent blood tests for any other medical reason during the 6th postoperative month or thereafter were retrospectively included in this study.

### Statistical Analysis

Data analysis was conducted using the SPSS 25.0 statistical package program. The normal distribution of continuous variables was assessed using the Shapiro-Wilk test. Descriptive statistics are presented according to normality as mean±standard deviation or median (minimum-maximum). The Mann-Whitney U test was used to compare independent groups, specifically the "control group" and the "patient group" in the preoperative and postoperative periods. Additionally, the Wilcoxon signed-rank test was used to compare dependent groups, specifically the preoperative and postoperative measurements within the patient group. A p value <0.05 was considered statistically significant.

## Results

The mean age of the patient group (n=29; 16 males, 13 females) was 5.2±2 years, while the control group had a mean age of 6.3±3.8 years (n=30; 17 males, 13 females). Age and gender distributions were similar between both groups (p>0.05).

The hematological parameters and inflammatory indices of both the control and patient groups before and after surgery are presented in Table I. Statistical analysis revealed that platelet count, SII, and PIV were significantly higher in the preoperative patient group compared to the control group (p=0.002, p=0.027, and p=0.006 respectively), as

**Table I.** Comparison of hematological parameters and inflammatory indices between control and patient groups before and after surgery for adenoid hypertrophy-induced OSA

| Parameters | Control group (n=30) | Patient group (n=29) | |
|---|---|---|---|
| | | Preoperative values | Postoperative values at the 6th month |
| Neutrophil ($10^3$/mm$^3$) | 3.4±0.9 | 4.1±1.8 | 5.5±2.3$^{+,++}$ |
| Platelet ($10^3$/mm$^3$) | 320.8±43.4 | 372.4±69.3$^{*}$ | 382.7±74.4$^{++}$ |
| Lymphocyte ($10^3$/mm$^3$) | 3.7±1.2 | 3.7±1.3 | 3.3±1.5 |
| Monocyte ($10^3$/mm$^3$) | 0.5±0.2 | 0.6±0.2 | 0.7±0.3$^{++}$ |
| SII | 324.9±156.1 | 471±277$^{*}$ | 783.8±806.5$^{+,++}$ |
| PIV | 173.4±104.6 | 296.2±211.5$^{*}$ | 544.5±585.3$^{+,++}$ |

$^{*}$Significantly high compared to control values (Mann-Whitney U test)
$^{+}$Significantly high compared to preoperative values (Signed-rank test)
$^{++}$Significantly high compared to control values (Mann-Whitney U test)
OSA: Obstructive sleep apnea, SII: Systemic immune inflammation index, PIV: Pan immune inflammation value

determined by the Mann-Whitney U test. Conversely, there were no significant differences in the preoperative values of neutrophils, lymphocytes, and monocytes between the patient group and the control group ($p>0.05$).

Comparing preoperative and postoperative values within the patient group, significantly higher values for neutrophils, SII, and PIV were observed postoperatively compared to the preoperative values ($p=0.012$, $p=0.008$, and $p=0.020$ respectively), as determined by the Wilcoxon signed-rank test. However, there were no significant differences between preoperative and postoperative platelet, lymphocyte, and monocyte levels ($p>0.05$).

In the comparison of measurement values between the postoperative patient group and the control group, significantly higher levels of neutrophils, platelets, monocytes, SII, and PIV were observed in the postoperative patient group ($p<0.001$, $p<0.001$, $p<0.001$, $p=0.011$, $p<0.001$, and $p<0.001$ respectively), as determined by the Mann-Whitney U test. Conversely, there were no significant differences in lymphocyte levels between the postoperative patient group and the control group ($p>0.05$).

## Discussion

The SII and PIV were significantly higher in the preoperative patient group compared to the control group. In comparing preoperative and postoperative values within the patient group, significantly higher levels of neutrophils, SII, and PIV were observed postoperatively compared to preoperative levels. In the comparison of measurement values between the postoperative patient group and the control group, significantly higher values for SII and PIV were observed in the postoperative patient group.

In our study, we investigated the association between SII and PIV values and chronic systemic inflammation in patients undergoing adenoidectomy for OSA induced by adenoid hypertrophy. This study represents the first evaluation of SII and PIV in the context of adenoid hypertrophy. Adenoidectomy is one of the most common procedures in otorhinolaryngology practice, primarily due to adenoid hypertrophy being a leading cause of OSA in children, potentially resulting in nocturnal hypoxia if left untreated (8). In cases of hypoxia, systemic inflammatory markers and proinflammatory cytokines increase, triggering lymphoid tissue proliferation (4). Additionally, obstructive sleep disorders are associated with elevated inflammatory markers. While the precise mechanisms underlying various diseases, such as cardiovascular and cerebrovascular diseases, infections, and malignancies, remain unclear, chronic inflammation is believed to play a significant role in their pathogenesis (9). Therefore, analyzing the relationship between the inflammatory status of a disease or cancer and its prognosis can be achieved by evaluating systemic inflammation (10).

Previous studies have indicated that easily obtainable ratios, such as the neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR), are useful tools in assessing systemic inflammation. Subsequent research has shown that the SII value is related to disease severity and prognosis (6,11). Moreover, studies have investigated the prognostic and predictive value of PIV, a newer inflammatory marker. Fucà et al. (5) found PIV to be more significant than other known inflammation markers in metastatic colorectal cancer patients, while Şahin et al. (12) demonstrated its importance in breast cancer patients. However, Truffi et

al. (13) found no correlation between PIV and prognosis in breast cancer. The prognostic and predictive roles of SII and PIV in patients with adenoid hypertrophy remain unknown.

Considering this information, we anticipated a decrease in the inflammatory process after adenoidectomy, leading to a reduction in parameters indicating systemic inflammation. A study by Uygur et al. (14) demonstrated the severity of OSA with NLR, indicating a correlation between PLR and the apnea-hypopnea index. Another notable finding in this study is that NLR can also serve as a marker for cardiac and vascular diseases (14,15). However, Korkmaz et al. (16), in their study, found no correlation between the severity of OSA and the NLR value.

In our findings, platelet count, SII, and PIV values in the preoperative patient group were statistically significantly higher than those in the control group. This disparity between the preoperative group and the control group supports the hypothesis that hypoxia-induced systemic inflammation is triggered in adenoid hypertrophy causing OSA, and that inflammatory factors decrease after adenoidectomy. However, contrary to our expectations, significantly higher levels of neutrophils, SII, and PIV were observed in the postoperative Patient Group compared to preoperative values. This unexpected difference in preoperative and postoperative SII and PIV values could be attributed to the marked increase in the neutrophil count, which typically reflects ongoing inflammation (8). However, neither these patients nor the control group exhibited signs of active infection. Therefore, the notable rise in postoperative SII and PIV values may be attributed to unknown effects of surgery, anesthesia, or the healing phase. Additionally, it is plausible that six months post-surgery is not a sufficient time period to observe a decrease in inflammatory markers.

In the comparison of measurement values between the postoperative patient group and the control group, significantly higher levels of neutrophils, platelets, monocytes, SII, and PIV were observed in the postoperative patient group. Conversely, no significant correlation was found between lymphocyte levels in the postoperative patient group and those in the control group.

### Study Limitations

The retrospective nature of our study limited the use of biochemical markers to further elucidate the underlying mechanisms of systemic inflammation. Additionally, while the differences in SII and PIV values between the control group and preoperative patient group indicate potential utility in assessing systemic inflammation, the unexpected increase in postoperative SII and PIV values presents a challenge in the interpretation. The numerous unknowns surrounding these indices, coupled with the potential effects of the postoperative period on inflammatory markers, warrant further investigation.

## Conclusion

Our study highlights the potential utility of SII and PIV in assessing systemic inflammation in patients with adenoid hypertrophy-related OSA. However, the unexpected increase in postoperative SII and PIV values underscores the need for additional research to better understand the underlying mechanisms and clinical implications of these inflammatory indices in the context of adenoidectomy and OSA.

### Ethics

**Ethics Committee Approval:** This study was approved by the Recep Tayyip Erdoğan University Non-Interventional Clinical Research Ethics Committee (approval no.: 2024/26, date: 18.01.2024).

**Informed Consent:** Informed consent was obtained from the parents of all patients, with acknowledgement of the study objectives and possible publication of the medical data.

### Authorship Contributions

Surgical and Medical Practices: T.Y., M.B., M.Ç., Ö.Ç.E., Concept: T.Y., Design: T.Y., Ö.Ç.E., Data Collection and/or Processing: G.A.B., E.E.A., Analysis and/or Interpretation: T.Y., M.B., Literature Search: T.Y., M.Ç., Ö.Ç.E., Writing: T.Y.

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