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Prognostic importance of the pan-immune-inflammation value and potential serological biomarkers of complicated peritonsillar abscesses

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ABSTRACT

Aims: A peritonsillar abscess (PTA) is the most common deep infection of the head and neck and can sometimes be associated with life-threatening complications. Clinical symptoms in patients with a complicated peritonsillar abscess (CPTA) may not always reflect the severity of this disease. Therefore, monitoring these patients with inexpensive and easily accessible hematological parameters is essential. Recently, certain inflammatory monitoring markers have gained acceptance. In this study, we aimed to determine the role of the pan-immune-inflammation value (PIV) in patients with a PTA at a high risk of complications.

Methods: Patients aged 18 years and older who were diagnosed with a PTA and hospitalized in our clinic between October 10, 2022, and October 1, 2024 were retrospectively analyzed. The patients were divided into the CPTA group and the uncomplicated peritonsillar abscess (UPTA) group. Demographic characteristics, laboratory findings, and complications observed in the emergency department were evaluated.

Results: A total of 104 patients were included in the study, with 71 in the UPTA group and 33 in the CPTA group. PIV values were significantly higher in the CPTA group compared to the UPTA group. The diagnostic value of PIV in predicting PTA-related complications was assessed using receiver operating characteristic curve analysis. A PIV cutoff value of 989.6 (AUC: 0.838; 95% confidence interval: 0.753-0.903) demonstrated a sensitivity of 72.7% and a specificity of 85.9%, indicating superior predictive power for PTA-related complications compared to NLR, MLR, and SII.

Conclusion: Our findings suggest that the PIV is a rapid, simple, and reliable marker for predicting the severity of PTAs and potential complications.

Keywords: Complication, emergency department, pan-immune-inflammation value, peritonsillar abscess

INTRODUCTION

A peritonsillar abscess (PTA) is characterized by the accumulation of suppuration in the space between the tonsillar capsule and the superior constrictor muscles. A PTA is the most common deep infection of the head and neck observed in the emergency department (ED) and frequently occurs in young adults.[1] Delayed or inadequate treatment of severe progressive infections can lead to the spread of the infection into the deep cervical spaces of the neck, resulting in serious or life-threatening complications.[2] Therefore, complicated peritonsillar abscesses (CPTAs), which have clinical importance, most commonly affect the retropharyngeal, parapharyngeal, and peritonsillar spaces. These abscesses may lead to severe morbidity and mortality, particularly when associated with conditions such as mediastinitis, sepsis, and airway obstruction.[3]

Needle aspiration is essential for a definitive diagnosis of a PTA, while surgical drainage and antimicrobial therapy constitute the cornerstone of treatment. In patients with a PTA, who often require hospitalization, surgical intervention and tonsillectomy may also be necessary.[4] Most PTAs resolve without complications with abscess drainage and appropriate antibiotic therapy. However, as the infection spreads to deep neck spaces, surrounding tissues, or distant tissues via hematogenous dissemination, clinical deterioration occurs.[5] Early diagnosis and prompt, effective treatment of this severe infection are crucial. In patients with CPTA, the clinical presentation is highly variable, and early symptoms may not always reflect the severity of this disease.[6] Therefore, monitoring patients with a CPTA using inexpensive and easily accessible hematological parameters is necessary.

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Recently, the use of various inflammatory biomarkers derived from complete blood count parameters as prognostic indicators of severity in infections and sepsis has become increasingly common.[7-9] These biomarkers include C-reactive protein (CRP), the neutrophil-to-lymphocyte ratio (NLR), the platelet-to-lymphocyte ratio (PLR), the monocyte-to-lymphocyte ratio (MLR), and the Systemic Immune-Inflammation Index (SII). Additionally, the pan-immune-inflammation value (PIV), which is calculated as the neutrophil count×platelet count×monocyte count)/ lymphocyte count, is a novel inflammatory index developed to assess patients' levels of inflammation and their prognoses. The PIV can be calculated easily from routine complete blood count tests without incurring additional costs and is commonly available in most clinical laboratories. Previous studies have shown that the PIV is an accurate marker for determining the clinical severity and prognosis of various types of cancer, such as esophageal, colorectal, and breast cancers, as well as conditions such as rheumatoid disease and septic shock.[10-14] Inflammation is prominently observed in PTAs, thus resulting in changes in the PIV. Therefore, the PIV is likely to be a predictive factor for complications of PTAs. To the best of our knowledge, there have been no prior studies on the use of the PIV in the follow-up and treatment process of PTAs in adults. The utility of the PIV as a predictor for distinguishing uncomplicated peritonsillar abscesses (UPTAs) from CPTAs has yet to be clarified.

Therefore, this study aimed to evaluate whether serological biomarkers with prognostic significance, such as the NLR, PLR, MLR, SII, and PIV, which can be derived easily from a complete blood count, can be used to predict PTAs. Additionally, we aimed to assess whether the PIV, a novel serological biomarker, is a reliable predictor for CPTAs.

METHODS

Study Design and Participants

This study was conducted in the Emergency Department of Ankara Etlik City Hospital, which is a tertiary care center with an annual average of 850,000 patient visits, between October 10, 2022 and October 1, 2024. Ethical approval for the study was obtained from the Ankara Etlik City Hospital Scientific Researches Evaluation and Ethics Committee before its commencement (Date: 06.11.2024, Decision No: AEŞH-BADEK-2024-962). The study was conducted in accordance with the Declaration of Helsinki, and the patient data collected by the researchers were kept confidential. Informed consent was not obtained because the study involved retrospectively collected data. The inclusion criteria were as follows: 1) patients older than 18 years of age who presented to the ED with a sore throat; 2) patients whose diagnosis was confirmed by an otolaryngology specialist through needle aspiration, laboratory tests, ultrasonography (US), and computed tomography (CT), and who were hospitalized for clinical treatment; and 3) patients with complete medical records available for inclusion in the study. The exclusion criteria were as follows: patients who did not accept hospitalization; patients referred from external centers; pregnant patients; patients with trauma, active infection of other sites, a history of inflammatory disease, fever of unknown origin, or active hematological or liver disease; patients diagnosed with a tumor according to pathology results; patients who have had any surgery in the last 3 months or who developed symptoms after surgery; patients without complete records; and patients diagnosed with peritonsillar cellulitis owing to the absence of pus in peritonsillar drainage.

Procedure, Data Collection, and Laboratory Analyses

In the ED, patients with medially displaced tonsils underwent US to evaluate suspected PTA and CT imaging to assess the potential spread of deep neck infections. During the consultation, the otolaryngology specialist performed a 1-cm incision using a No. 15 scalpel and aspiration with an 18-gauge needle at the most prominent area of swelling, which was located at the junction of the upper pole of the medially swollen tonsils and the base of the uvula. Patients with pus drainage were diagnosed with a PTA.

The patients were divided into the UPTA group and the CPTA group. The UPTA group comprised patients who were diagnosed with UPTA. The CPTA group consisted of patients who showed airway obstruction, tongue base abscess, para- or retropharyngeal abscess or phlegmon, mediastinitis, carditis, or sepsis, or required tracheostomy or intubation. These conditions were based on imaging obtained during their ED visit or clinical follow-up during hospitalization. Data for both groups were obtained using the hospital's electronic database. Laboratory parameters from complete blood samples taken during the patients' initial ED visits, along with neck US and CT findings, demographic data, clinical characteristics, complications, and laboratory values (white blood cell, neutrophil, monocyte, lymphocyte, and platelet counts, and CRP concentrations) were recorded. In patients with a PTA confirmed both clinically and radiographically in the ED, the PIV was calculated as an indicator of clinical outcomes. The data of patients in the CPTA group were then compared with those of patients in the UPTA group.

Routine blood samples collected from patients during ED visits were drawn into tubes containing ethylenediaminetetraacetic acid. A complete blood count analysis was performed using a XN (Sysmex, Kobe, Japan) analyzer. The following ratios and indices were calculated: the NLR, MLR, PLR, SII, (calculated as platelet count×neutrophil count/lymphocyte count),[7,8,15] and the PIV (calculated as neutrophil count×platelet count× monocyte count)/lymphocyte count).[9]

Statistical Analysis

The data analysis was performed using the Statistical Package for Social Sciences (SPSS) version 26 (IBM SPSS Inc., Armonk, NY, USA). In the evaluation of the collected data, descriptive statistical methods (percentage calculations, median, mean, and standard deviation) were calculated. Continuous variables are expressed as the mean±standard deviation (SD) or median (minimum-maximum value) according to the normality of distribution, while categorical variables are expressed as numbers and percentages. The normal distribution of the data was evaluated using the Kolmogorov-Smirnov test. The student T test was used to compare continuous variables with a normal distribution, and the Mann-Whitney U test was used

to compare variables without a normal distribution. Pearson's chi-squared or Fisher's test was used to compare categorical variables. The diagnostic ability of the variables that were statistically significant in-group comparisons was evaluated by a receiver operating characteristic (ROC) curve analysis, and the Youden Index was used to determine the cutoff value. In the tests used, p values <0.05 were considered statistically significant.

RESULTS

During the study period, ED physicians requested a total of 4,015 emergency consultations from the otolaryngology clinic. Of these, 263 patients (15.2%) were suspected of having a PTA. A total of 159 patients were excluded from the study for the following reasons: 15 patients were referred from external centers; 45 patients had comorbidities, such as hypertension, diabetes, metabolic syndrome, coronary heart disease, thyroid dysfunction, renal or hepatic dysfunction, malignancy, a history of surgery within the past 3 months, nasal septum deviation, systemic inflammatory diseases, anemia, or chronic obstructive pulmonary disease, or they smoked, were on medications for chronic inflammation, or had other inflammatory diseases; 73 patients were diagnosed with peritonsillar cellulitis owing to the absence of pus during peritonsillar drainage; 6 patients declined admission to the otolaryngology clinic; and 20 patients had incomplete medical records or lacked imaging studies. A total of 104 patients were included in the study, with 71 in the UPTA group and 33 in the CPTA group.

The mean age of the patients was 34.4±9.7 years in the UPTA group and 34.7±11.1 years in the CPTA group. Male patients constituted 54.7% of the UPTA group and 61.6% of the CPTA group. There was no significant difference in age or sex between the groups. The demographic data and hematological parameters of the patients included in the study are shown in Table 1. The median NLR and mean MLR were significantly higher in the CPTA group than in the UPTA group [3.52 (2.61-4.19) vs. 2.45 (1.83-3.86), p=0.005; 0.39±0.19 vs. 0.68±0.36, p<0.001, respectively]. Additionally, the median SII and mean PIV values were significantly higher in the CPTA group than in the UPTA group [1011 (795-1314) vs. 705 (559-1172), p=0.004; 1201.9±401.6 vs. 695.6±380.6, p<0.001, respectively]. There was no significant difference in PLR values between the CPTA and UPTA groups (p=0.055).

In the 33 patients with complications, the most common complication observed was upper respiratory tract obstruction, which occurred in 78.8% of the patients. One patient required tracheostomy, and another required intubation. The types and frequencies of complications that developed following PTA in the study population are shown in Figure 1. A ROC curve analysis was performed to calculate the diagnostic values of the NLR, MLR, PLR, SII, and PIV in predicting complications associated with PTAs. The area under the curve (AUC) value for the NLR was 0.673 [95% confidence interval (CI): 0.574-0.761], that for the MLR was 0.776 (95% CI: 0.684-0.852), that for the PLR was 0.617 (95% CI: 0.517-0.711), that for the SII was 0.674 (95% CI: 0.575-0.763), and that for the PIV was 0.838 (95% CI: 0.753-0.903). The highest diagnostic value was found for the PIV, with an AUC of 0.838 (95% CI: 0.753-0.903), which indicated that the PIV was a stronger predictive tool than the NLR, MLR, SII, and PLR alone. The optimal cutoff values were 2.98 for the NLR (69.7% sensitivity, 67.6% specificity), 0.51 for the MLR (63.6% sensitivity, 76.0% specificity), 130.6 for the PLR (63.7% sensitivity, 60.5% specificity), 802.2 for the SII (75.7% sensitivity, 61.9% specificity), and 989.6 for the PIV (72.7% sensitivity, 85.9% specificity) (Table 2). The ROC curve of PIV evaluating CPTA is shown in Figure 2.

Table 1. Comparison of peritonsillar abscess patients with and without complications

	Peritonsillar abscess		
Variables	Complication absent (n=71)	Complication present (n=33)	p-value
Age, (years)	34.4±9.7	34.7±11.1	0.978
Male gender,	58 (54.7%)	61 (61.6%)	0.317
WBC (x10^9/L)	15.7±4.4	18.1+±2.7	0.006
Neutrophil, (x10^9/L)	6.07 (4.89-7.64)	7.01 (4.81-8.39)	0.082
Monocyte, (x10^9/L)	0.86±0.41	1.22±0.44	<0.001
Lymphocyte, (x10^9/L)	2.39±0.84	2.05±0.78	0.092
Platelet, (x10^9/L)	303.1±67.5	296.9±61.4	0.655
CRP mg/dl	134.8±91.2	168.1±57.0	0.002
NLR	2.45 (1.83-3.86)	3.52 (2.61-4.19)	0.005
MLR	0.39±0.19	0.68±0.36	<0.001
PLR	124.6 (105.2-175.8)	146.6 (118.2-199.8)	0.055
SII	705 (559-1172)	1011 (795-1314)	0.004
PIV	695.6±380.6	1201.9±401.6	<0.001

Data are presented as mean±standard deviation, median (25%-75% quartiles) or n (%), WBC: White blood cell, CRP: C-reactive protein, NLR: Neutrophil to lymphocyte ratio, MLR: Monocyte to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, SII: Systemic İmmune-İnflammation Index, PIV: Pan-immune-inflammation value

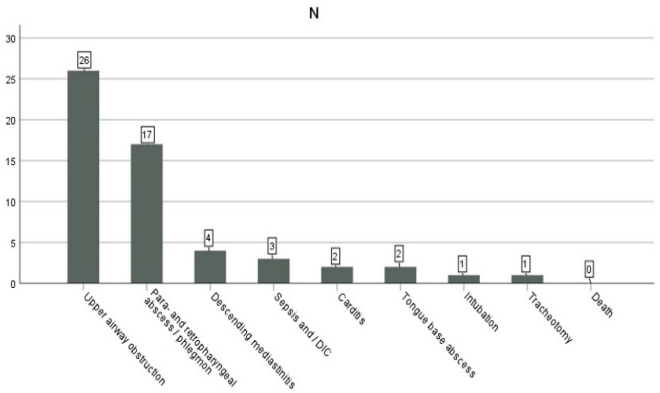

Figure 1. Types and rates of complications following peritonsillar abscess in the study population. *Since some patients experienced more than one complication, the total number of complications exceeded the number of patients with complications (n=56)

DISCUSSION

A PTA is one of the most common causes of deep space head and neck infections, and it represents the most frequent otolaryngology emergency because of its life-threatening complications.[16,17] Radiological methods, such as US and CT, are used in the diagnosis of PTAs and the investigation of their associated complications.[18,19] However, these imaging modalities have certain disadvantages. US requires an

Table 2. Analysis of the area under the ROC curve for NLR, MLR, PLR, SII, and PIV in patients with complicated peritonsillar abscess

Variables	NLR	MLR	PLR	SII	PIV
AUC (95% CI)	0.673 (0.574-0.761)	0.776 (0.684-0.852)	0.617 (0.517-0.711)	0.674 (0.575-0.763)	0.838 (0.753-0.903)
Cut-off value	>2.98	>0.51	>130.6	>802.2	>989.6
Sensitivity	69.7%	63.6%	63.7%	75.7%	72.7%
Specificity	67.6%	76.0%	60.5%	61.9%	85.9%
+LR	2.15	2.66	1.61	1.99	5.16
-LR	0.45	0.48	0.60	0.39	0.32
PPV	50.0%	55.3%	42.9%	48.1%	70.6%
NPV	82.8.6%	81.8%	78.2%	84.6%	87.1%

ROC: Receiver operating characteristic, NLR: Neutrophil to lymphocyte ratio, MLR: Monocyte to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, SII: Systemic Immune-Inflammation Index, PIV: Pan-immune-inflammation value, AUC: Area under the ROC curve, CI: Confidence interval, +LR: Positive likelihood ratio, -LR: Negative likelihood ratio, PPV: Positive predictive value, NPV: Negative predictive value

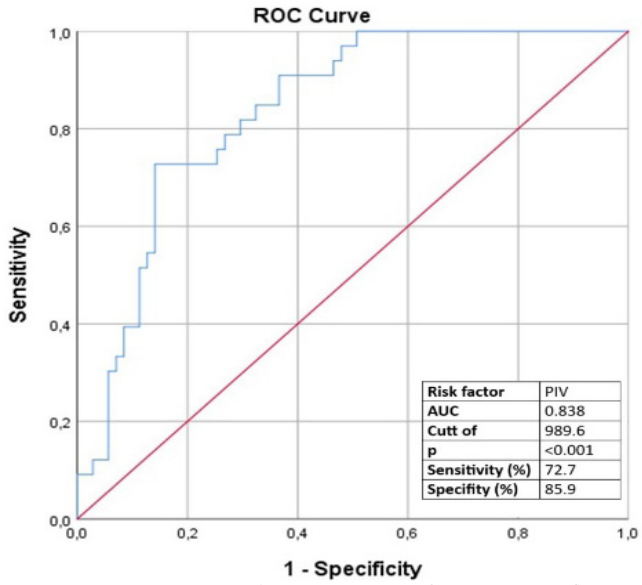

Figure 2. Receiver-operating characteristic curve of pan-immune-inflammation value for prediction of complicated peritonsillar abscess

experienced radiologist, has a limited field of view, and faces challenges in evaluating deep tissues. CT is associated with higher costs, a prolonged hospital stay, the requirement for intravenous contrast agents, and exposure to radiation.[20-22] A complete blood count can be performed in most EDs, and biomarkers calculated from complete blood count parameters are easily accessible because of their relatively low cost. In recent years, the use of biomarkers has gained considerable popularity.[23] The use of novel serological biomarkers in conjunction with imaging modalities may assist ED physicians in managing treatment and predicting the prognosis of UPTAs and CPTAs. To the best of our knowledge, the role of the PIV in distinguishing between UPTAs and CPTAs remains unclear. Therefore, in this study, we investigated whether the PIV can differentiate between a UPTA and a CPTA.

In this study, we found significantly higher PIV values in patients with CPTAs than in those with UPTAs. The AUC value of the PIV in predicting CPTAs was higher than the AUC values of the NLR, MLR, PLR, and SII when considered individually. We found that patients with a PTA and a PIV >989.6 had a higher risk of developing CPTA than those with a lower PIV value. In the ROC curve analysis, the PIV showed a sensitivity of 72.7% and a specificity of 85.9% in predicted CPTAs (AUC: 0.838). These findings suggest that the PIV could serve as a useful and prognostic biomarker in predicting CPTAs.

The NLR has been reported as a reliable biomarker for distinguishing patients with suspected infections from those without infections in EDs.[23] Furthermore, de Jager et al.[24] showed that the NLR outperformed CRP concentrations, white blood cell count, and neutrophil count in identifying bacteremia in patients who presented to the ED. Baglam et al.[25] studied a pediatric patient population and proposed a cutoff value of 5.4 for the NLR as a predictor of deep neck infections resulting from acute bacterial tonsillitis. Şentürk et al.[2] found that an NLR of 3.08 was the optimal cutoff value, and the sensitivity, specificity, positive predictive value, and negative predictive value were all 90.9%. They found that the NLR in the pre-treatment PTA group was higher than that in the post-treatment PTA group and the control group. Additionally, they reported a decrease in the NLR after treatment compared with pre-treatment. In our study, we found that the NLR had a sensitivity of 69.7% and a specificity of 67.6% in predicting complications in patients with PTA. We consider the NLR an important biomarker for distinguishing between complicated and uncomplicated cases of PTAs.

The SII has been reported as a prognostic biomarker that reflects the host's inflammatory response in various diseases and conditions.[26,27] A recent study proposed that an SII cutoff value of 2975 serves as a predictor of a high risk of complications in deep neck infections.[7] Additionally, this SII cutoff value is associated with airway obstruction requiring tracheostomy, an increased risk of mediastinitis, and a higher mortality rate. In our study, we found that an SII cutoff value of 802.2 showed a sensitivity of 75.7% and a specificity of 61.9% in predicting CPTAs. Despite variations in threshold values, we believe that the SII could be an important biomarker for distinguishing between complicated and uncomplicated PTA cases.

The recently discovered PIV is a Next-Generation Comprehensive Inflammatory Index that has been reported as a prognostic biomarker in various conditions, such as peritoneal dialysis, malignancies, autoimmune diseases, and sepsis.[28] A large-scale cross-sectional study showed an association between the PIV and stage III/IV periodontitis.[29] An association between the PIV and mortality has been

investigated in various coronary diseases.[30] However, the role of the PIV in patients with PTAs at a high risk of complications has not been previously evaluated. In our study, the PIV was significantly higher in patients with CPTAs than in those with UPTAs. We found that a PIV cutoff value of 989.6 was a predictor of a high risk of complications in patients with PTAs.

The PIV is derived from neutrophil, platelet, monocyte, and lymphocyte counts measured during admission to the ED. Therefore, the PIV can be calculated to identify patients at a high risk of complications. The accessibility and low cost of obtaining the PIV make it a useful tool in ED for assessing PTAs, which are one of the most common causes of deep neck space infections. The PIV is useful for predicting disease severity, potential complications, and the requirement for surgical intervention.

Limitations

Our study has certain limitations. First, because of the retrospective design of the study, the data were obtained by reviewing electronic patient records, and patients with incomplete data or those referred from external hospitals were excluded. These factors may have affected the PIV results. Second, the study was limited by its single-center design and relatively small cohort size. Third, we calculated the NLR, MLR, PLR, SII, and PIV using blood samples collected at the time of ED admission. We were unable to examine post-treatment changes in these indices by repeated measurements. Finally, the study lacked a healthy control group, which limits the ability to compare the findings with baseline values in a non-diseased population.

CONCLUSION

Delayed diagnosis and inadequate treatment in patients with PTAs can lead to life-threatening morbidities. Therefore, early diagnosis and close monitoring of PTAs are crucial for such patients. The PIV, with a cutoff value of 989.6, is useful in predicting complications in patients with PTAs. The accessibility and ease of calculation of the PIV make it a useful tool for assessing disease severity and potential complications. Moreover, the PIV can be effectively used in emergency settings in which access to imaging is limited or contraindicated, such as in pediatric or pregnant patients. Larger multicenter studies with broader patient populations are required to validate our findings and enhance the clinical utility of this biomarker.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Ankara Etlik City Hospital Scientific Researches Evaluation and Ethics Committee (Date: 06.11.2024, Decision No: AEŞH-BADEK-2024-962).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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