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Inflammatory Biomarkers and Clinical Course in Deep Neck Infections: Role of Comorbidities and Etiology

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ABSTRACT

Objective: Deep neck infections (DNI) may present a complex clinical picture depending on etiological factors and comorbidities. The effects of these predisposing factors on biomarkers – systemic inflammatory response index, pan-immune-inflammation value, neutrophil-to-lymphocyte-to-platelet ratio, C-reactive protein–albumin–lymphocyte index (CALLY index), and hemoglobin–albumin–lymphocyte and platelet score (HALP score) – and their relationship with the disease course were evaluated.

Materials and Methods: This retrospective cohort study evaluated patients hospitalized with DNI. Demographic, clinical, and laboratory data were recorded and biomarker values calculated. Patients were grouped by infection source and comorbidities into Group A (fewer than two risk factors) and Group B (two or more). They were also classified by treatment as medical (Group 1) or surgical drainage (Group 2). Biomarkers and laboratory parameters were compared between groups, and their association with disease course was assessed.

Results: Among 82 patients, demographic features and treatment distribution were similar across groups. Group 2 (surgical drainage) had longer hospital stays (p=0.003) and lower hemoglobin (p=0.013) than Group 1. Lymphocyte counts were lower in Group B and higher in Group 2 (p=0.023, p=0.050). Group B showed reduced CALLY index and HALP score (p≤0.001), while other biomarkers were comparable. CALLY index had high sensitivity (94.9%), and HALP score showed high specificity (74.4%).

Conclusion: The coexistence of infectious sources and systemic comorbidities significantly affects the clinical trajectory and therapeutic strategies in DNI. Accordingly, biomarkers such as the CALLY index and HALP score serve as valuable tools for predicting their influence on disease progression.

Keywords: Biomarker, C-reactive protein–albumin–lymphocyte index, Deep neck infection, Hemoglobin –albumin–lymphocyte and platelet score

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INTRODUCTION

A deep neck infection (DNI) is a serious and potentially life-threatening condition that involves an infection of the deep fascial spaces of the neck. Bacteria can cause these infections, and they often arise from the spread of an infection from another area in the head or neck, such as the tonsils, teeth, salivary glands, or lymph nodes.[1] Such infections have the potential to result in significant complications, including airway obstruction and mediastinitis, which require prompt medical intervention. The management of DNIs typically involves empirical antibiotic therapy, followed by surgical incision and drainage if necessary.[1,2] The most common cause of DNIs is dental infection, particularly those involving chronic problem teeth.[1-3] Older adults, particularly those with diabetes and elevated blood glucose levels, as well as patients with chronic kidney disease, are often at increased risk of more severe disease progression and poorer prognoses due to underlying immune system dysfunction.[4,5]

Empirical intravenous antibiotics (β-lactamase-resistant β-lactam antibiotics, the third-generation cephalosporin antibiotics, metronidazole, and clindamycin) were administered before the culture results were available, then the antibiotic regimen was modified based on the culture and sensitivity results.[1,6] In cases where antibiotics prove ineffective or in instances of airway obstruction, incision and drainage are crucial.[7] New models are being developed to predict outcomes based on factors such as serum creatinine levels and the presence of mediastinitis.[8] The mortality risk is increased in cases where there are multiple infected sites, renal insufficiency, and advanced age.[7,8] While DNIs are severe, timely diagnosis and treatment can significantly improve outcomes. However, the presence of comorbidities and delayed treatment can lead to life-threatening complications, underscoring the importance of early intervention and comprehensive care strategies.[4-8]

Biomarkers such as the systemic immune-inflammation index (SII), neutrophil-to-lymphocyte ratio (NLR), and C-reactive protein (CRP) have been the subject of investigation with a view to establishing their prognostic value in DNIs. These biomarkers can assist in the prediction of complications and the guidance of treatment decisions.[9-22] CRP is a commonly used marker for assessing infection severity and has been shown to correlate with length of stay in patients with DNIs.[9] NLR is a cost-effective marker derived from routine blood tests and is comparable to CRP in predicting the length of hospitalization for DNIs.[11] In addition, NLR has been demonstrated to be a valuable tool in predicting necrotizing fasciitis and systemic involvement in DNIs.[12] NLR value can be considered in determining the prognosis of DNI, which may develop as a complication, especially in the early stages of acute bacterial tonsillitis.[11,20] CRP, NLR, and SII have been reported as effective biomarkers in the early diagnosis of deep neck abscess or necrotizing soft-tissue infection that may develop depending on the severity of odontogenic infections.[17] Biomarkers such as the SII and systemic inflammation response index (SIRI), which are derived from laboratory parameters including CRP and NLR, contribute to the optimization of DNI management by complementing clinical and radiological assessments.[16-18] Notably, the SII index has shown high diagnostic accuracy in predicting DNI-related complications.[16] Nutritional deficiencies and immunological impairments associated with chronic comorbid conditions are anticipated to significantly influence both the therapeutic trajectory and clinical outcomes of patients diagnosed with DNIs. Given the multifactorial etiology of DNI, including infection sources and the impact of systemic comorbidities, comprehensive evaluation through emerging biomarkers, novel indices, and advanced scoring systems is of considerable clinical relevance. There are not enough studies investigating the relationship between SIRI, pan-immune-inflammation value (PIV), neutrophil-to-lymphocyte-to-platelet ratio (NLPR), C-reactive protein–albumin–lymphocyte Index (CALLY index), hemoglobin, albumin, lymphocyte, and platelet score (HALP score), and DNI. Therefore, in our study, we aimed to evaluate the impact of comorbidities and infection etiology in patients with DNI on inflammatory parameters such as SIRI, SII, PIV, NLPR, CALLY index, and HALP score; as well as the relationship between changes in these biomarkers, and the clinical course of DNI patients.

MATERIALS AND METHODS

In this retrospective cohort study, cases of DNI diagnosed by otorhinolaryngology specialists and managed through inpatient hospitalization, follow-up, and treatment were evaluated. This study includes patients who presented to the emergency department or otorhinolaryngology clinic between January 1, 2019, and June 31, 2024, and were confirmed to have a diagnosis of DNI. This study was conducted in accordance with the principles outlined in the Declaration of Helsinki and received approval from the Local Ethics Committee (Approval No: 16/9, Date: October 24, 2024).

Patients requiring hospitalization due to DNI were included in the study. The decision for hospitalization was made for patients presenting with prominent clinical findings such as erythema, swelling, heat sensation in the head-and-neck region, trismus, along with difficulty in eating and/or breathing, and a need for intravenous antibiotic therapy. Patients were excluded from the study if they were under 18 years of age, had a history of head and neck surgery or penetrating infected wounds, had been diagnosed with head and neck cancer, or had previously undergone radiotherapy or chemotherapy. Further exclusion criteria included the presence of tumors in other anatomical regions (including both solid and hemato-

logical malignancies), immunosuppressive disease, abscesses resulting from foreign bodies, resistance to treatment with multiple intravenous antibiotics, and incomplete medical records.

Demographic data, including age, gender, length of hospital stay, and details of medical, interventional, or surgical treatments administered to the patients included in the study, were recorded. In addition, hemogram and biochemical parameters measured at the time of hospital admission, such as hemoglobin (Hb) levels (g/dL), white blood cell (WBC) count and its subtypes (10^3/mm^3), platelet (PLT) count (10^3/mm^3), albumin (g/L), and CRP levels (mg/L), were collected. Using these hematological and biochemical laboratory data, the biomarkers evaluated in the study were calculated.

The calculated parameters included SII, SIRI, PIV, and NLPR values, as well as the CALLY index and HALP score. The SII was calculated by multiplying the peripheral platelet count by the neutrophil count and dividing the result by the lymphocyte count. SIRI was calculated using the formula in which the monocyte count is multiplied by the neutrophil count, and the resulting value is then divided by the lymphocyte count. The PIV is calculated by multiplying the neutrophil count, monocyte count, and platelet count, and then dividing the result by the lymphocyte count. The NLPR was calculated by dividing the neutrophil count by the product of the lymphocyte count and the platelet count. The CALLY index is determined by multiplying the serum albumin concentration by the peripheral lymphocyte count, followed by division of the resulting product by the CRP level scaled by a factor of ten. This composite metric integrates nutritional and inflammatory parameters to provide prognostic insight in various clinical settings. The HALP score was calculated by multiplying the Hb level by the albumin concentration and the lymphocyte count, and then dividing the result by the platelet count.

Patients were stratified based on the presence of infectious sources and comorbidities associated with DNI. Among the DNI cases included in this study, identifiable etiological sources comprised odontogenic infections (e.g., dental abscesses and periodontitis), tonsillitis and peritonsillar abscesses, pharyngeal infections, salivary gland obstruction or infection, lymphadenitis, infected congenital neck cysts (including branchial cleft cysts and thyroglossal duct cysts), and skin or soft-tissue infections, particularly cellulitis extending into the deep neck spaces. The comorbidities assessed in this cohort included hypertension, diabetes mellitus, cardiopathy, anemia, endocrinopathies (excluding diabetes), chronic kidney disease, alcohol and substance abuse, chronic liver disease, and chronic obstructive pulmonary disease. Regardless of the presence or absence of a defined infectious source, two distinct cohorts were established to evaluate relevant biomarkers. A cohort was formed comprising patients who presented with two or more infectious sources or comorbidities (Group B); those with fewer than two of these risk factors were categorized into a distinct group (Group A). The impact of multiple concurrent etiological and comorbid risk factors on the severity of inflammation and infection was comparatively analyzed through biomarker profiling. In addition to medical therapy (Group 1), patients enrolled in the study were further classified according to their requirement for either ultrasound-guided drainage or incisional open surgical drainage (Group 2). The demographic data of the patients, length of hospital stay, laboratory parameters, and evaluated biomarkers were compared between Groups A and B, as well as between Groups 1 and 2. To assess the relationship between the CALLY index and HALP score with hospital stay duration, the length of hospital stay was categorized into short stay (SS) (<7 days) and extended stay (LS) (≥7 days).

Statistical Analysis

The statistical analyses were conducted using the Statistical Package for Social Sciences for Windows 27.0 program. Categorical data were defined as percentages and frequencies. The numeric data were determined, and a distribution analysis was performed. Data sets that conformed to a normal distribution were defined as mean±standard deviation (SD). For data sets that did not conform to a normal distribution, the median and interquartile range (IQR) were defined. The Chi-square test was employed to ascertain the relationship between categorical data. The analysis of numeric tests that followed a normal distribution was conducted using parametric tests (t-test and analysis of variance [ANOVA]); nonparametric tests were used in the analysis of numeric tests that did not follow a normal distribution. Subsequent comparisons were made using paired t-tests and ANOVA. The receiver operating characteristic test was employed to calculate the effect power of the dependent variable. A threshold value was determined, and the sensitivity and specificity were subsequently calculated based on this value. Statistical findings with a p-value below 0.05 were considered to be statistically significant.

RESULTS

A total of 82 patients were included in the analysis, having met the pre-established inclusion criteria. There was no significant difference in gender distribution or age across the groups ($p>0.05$). Similarly, there was no significant difference in the medical therapy and drainage rates between Group A and B, Group 1 and 2 ($p>0.05$). However, patients who underwent drainage had a significantly longer treatment time ($p=0.003$) (Table 1). Hb levels were significantly lower in Group 2 compared to Group 1 ($p=0.013$). Regarding lymphocyte counts, statistically significant differences were observed both between Group B and Group A ($p=0.023$), and between Group

Table 1. Baseline patient characteristics and initial clinical findings in patients with and without a number of risk factors and drainage of a deep neck infection

	Number of etiological and comorbid disease factors			Drainage required		
	Group A <2 (n=43)	Group B ≥2 (n=39)	p	Group 1 No (31)	Group 2 Yes (51)	p
Gender, Female (n, %)	12 (27.9)	12 (30.8)	0.184	9 (29)	15 (29.4)	0.197
Age (mean±SD)	42.81±21.63	42.71±18.64	0.440	42.54±19.08	42.9±20.95	0.356
Treatment (n, %)						
Observation	17 (39.5)	14 (35.9)	0.575	31 (100)		
Incisional drainage	19 (44.2)	20 (51.3)			39 (76.5)	
Interventional drainage	7 (16.3)	5 (12.8)			12 (23.5)	
Lenght of hospital stay, day (mean±SD)	7.67±5.22	9.48±6.06	0.139	6.13±3	9.98±6.42	0.003

2 and Group 1 (p=0.050). Lymphocyte levels were lower in Group B, which included patients with two or more infectious sources or comorbidities. Conversely, patients who underwent surgical or interventional drainage (Group 2) exhibited higher lymphocyte counts.

As shown in Table 2, no statistically significant differences were observed between Group B, which included patients with two or more infectious sources or comorbidities, and Group A in terms of WBC count, platelet count, neutrophil, monocyte, and eosinophil levels, as well as albumin and CRP values (p>0.05). Similarly, no statistically significant differences were found in these parameters between patients who underwent surgical or interventional drainage (Group 2) and those who were managed with medical therapy (p>0.05) (Table 2). Accordingly, the results of the biomarkers calculated using the parameters as presented in Table 2 and Table 3. Similar to the laboratory parameters, as shown in Table 3, no statistically significant differences were found in the biomarker values we evaluated in our study, namely SII, SIRI, PIV, and NLPR, between Group A and Group B (p>0.05), or between Group 1 and Group 2 (p>0.05) (Table 3). Likewise, no statistically significant differences were observed in the CALLY index and HALP score between patients who underwent surgical or interventional drainage (Group 2) and those who were treated with medical therapy (Group 1) (p>0.05) (Table 3). Statistically significant

Table 2. Comparison of laboratory findings in patients with deep neck infections, classified according to the number of etiological and comorbid disease factors, and the need for surgical or interventional drainage

	Number of etiological and comorbid dis-ease factors			Drainage required		
	Group A <2 (n=43)	Group B ≥2 (n=39)	p	Group 1 No (31)	Group 2 Yes (51)	p
White blood cell (mean±SD)	15.76±4.77	14.81±5.19	0.697	15.12±4.48	15.41±5.29	0.222
Hemoglobine (mean±SD)	13.3±1.37	13.51±1.59	0.503	13.78±1.1	13.17±1.63	0.013
Platelet (mean±SD)	307.58±104.03	293.92±99.83	0.669	293.12±94.81	305.92±106.23	0.838
Neutrophil (mean±SD)	12.13±4.78	11.79±4.95	0.843	11.71±4.27	12.12±5.19	0.147
Lymphocyte (mean±SD)	2.23±0.68	1.56±0.69	0.023	1.86±0.68	1.93±0.98	0.050
Monocyte (median. IQR)	1.27(0.89)	1.19 (1.12)	0.311	1.23 (0.64)	1.27 (1.16)	0.253
Eosinophile (median. IQR)	0.08 (0.22)	0.08 (0.14)	0.727	0.07 (0.1)	0.13 (0.23)	0.324
CRP (mean±SD)	130.9±110.5	184.58±117.05	0.486	160.29±107.69	154.1±121.97	0.671
Albumine (mean±SD)	36.9±8.27	30.53±7.80	0.888	35.38±8.40	32.95±8.69	0.913

CRP: C-Reaktif Protein; SD: Standard Deviation; IQR: Interquartile Range.

Table 3. Biomarker comparison in patients with deep neck infections, grouped by the number of etiological and comorbid conditions, and by the presence or absence of surgical or interventional drainage requirement

	Number of etiological and comorbid disease factors			Drainage required		
	Group A <2 (n=43)	Group B ≥2 (n=39)	p	Group 1 No (31)	Group 2 Yes (51)	p
SII (median. IQR)	1396.18 (1254.27)	1979.08 (3687.78)	0.078	1642.75 (1076.12)	1897.84 (2495.11)	0.563
SIRI (median. IQR)	7.33 (14.92)	9.57 (12.81)	0.770	5.96 (8.92)	9.57 (26.91)	0.142
PIV (median. IQR)	1930.88 (4828.58)	2200.89 (4131.17)	0.930	1854.47 (2108.97)	2479.56 (7237.72)	0.153
NLPR (median. IQR)	0.183 (0.02)	0.022 (0.03)	0.072	0.02 (0.02)	0.022 (0.03)	0.749
CALLY (median. IQR)	0.734 (2.19)	0.273 (0.58)	0.001	0.4 (0.95)	0.46 (1.42)	0.860
Hemoglobin –albumin–lymphocyte and platelet (me-dian. IQR)	3.40 (2.38)	1.82 (2.04)	<0.001	3.14 (2.80)	2.43 (2.32)	0.130

CALLY: C-Reactive Protein–Albumin–Lymphocyte Index; IQR: Interquartile Range; SIRI: Systemic Inflammatory Response Index; SII: Systemic Immuno-Inflammation Index; PIV: Pan-Immune Inflammation Value; NLPR: Neu-trophil–lymphocyte–Platelet Ratio.

Table 4. Receiver operating characteristic analysis according to risk factor count

	Area under the curve±SD	p	Cut-off	Sensitivity	Specificity
C-reactive protein–albumin–lymphocyte index	0.710±0.057	<0.001	1.676	94.9	37.2
Hemoglobin–albumin–lymphocyte and platelet score	0.715±0.057	<0.001	2.286	61.5	74.4

differences were identified in both the CALLY index and HALP score between Group A and Group B (p≤0.001), as presented in Table 3. Importantly, patients in Group B, characterized by the presence of two or more infectious foci or underlying comorbid conditions, exhibited markedly lower values in both indices compared to those in Group A.

A comparative analysis of the CALLY index and HALP score based on their respective area under the curve (AUC)±SD values demonstrates that the CALLY index yields an AUC of 0.710±0.057, whereas the HALP score presents a slightly higher AUC of 0.715±0.057 (p<0.001). Sensitivity analysis reveals that the CALLY index exhibits superior sensitivity (94.9%) compared to the HALP score (61.5%), indicating greater efficacy in detecting true positive cases. Conversely, specificity, reflecting the ability to correctly identify actual negatives, is higher for the HALP score (74.4%) than for the CALLY index (37.2%), suggesting that HALP is more reliable in excluding false positives. These findings are detailed in Table 4 and Figure 1. The specific clinical or diagnostic context should guide the choice between the CALLY index and HALP score. In situations where minimizing the risk of overlooking actual positive cases is crit-

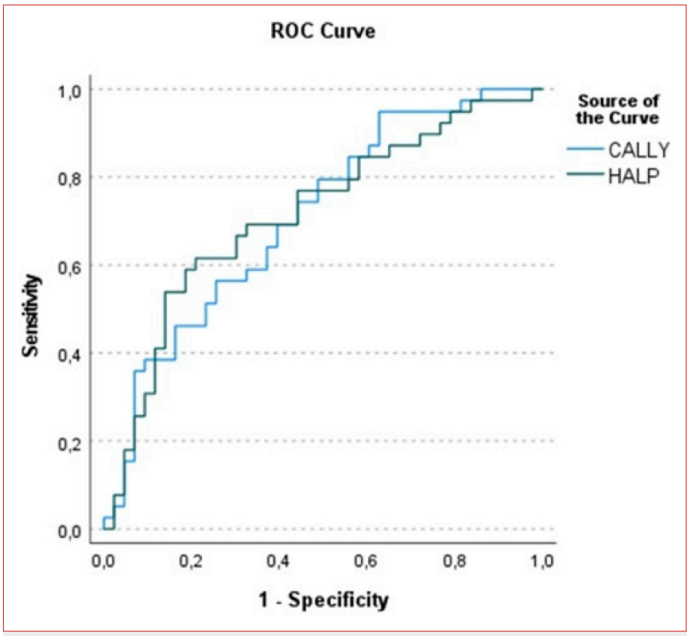

Figure 1. Receiver operating characteristic curves of parameters to predict DNI in number of risk factors group.

ical, such as in early detection or screening protocols, CALLY, with its higher sensitivity, may be the more appropriate tool. Conversely, in settings where the reduction of false-positive results is prioritized – such as in confirmatory diagnostics or resource-limited environments – HALP, owing to its superior specificity, may offer greater clinical utility.

In the assessment based on patients' length of stay in hospital, the median CALLY index value was found to be 0.72 (1.70) for patients with a short length of stay and 0.29 (0.71) for patients with an extended length of stay (p=0.006). A similar assessment was performed within the HALP score regarding length of hospital stay, but no statistically significant result was obtained (p=0.400).

DISCUSSION

In DNIs, the prevention of life-threatening complications such as sepsis, mediastinitis, and airway obstruction is the primary goal of the follow-up and treatment process. Therefore, being able to predict whether potential sources of infection involved in the etiology will cause DNI development and, if DNI develops, whether it will lead to these complications is of critical importance in clinical management. Studies exist on the presence of an etiological source of infection, patients' comorbidities, and the effects of these risk factors on the clinical course of DNI and the development of complications.[2-4,8, 9,16,21,23-25] These studies report that the presence of an odontogenic infection source, impaired blood sugar regulation due to diabetes, abnormalities in WBC and Hb levels, low blood albumin levels, high creatinine levels, and the presence of cardiopulmonary disease affect the clinical course and severity of infection and the development of complications in DNI patients.[8,9,21,23,25]

In the literature, the relationship between basic laboratory parameters such as WBC, neutrophil, platelet, mean platelet volume, CRP, ESR, and serum creatinine levels and the development and clinical course of DNI has been evaluated.[8,13,14,16,21,22] Furthermore, inflammatory biomarkers such as NLR, PLR, SII, and SIRI have also been similarly investigated in DNI patients.[9-12,14-20,22] These studies indicated that classical laboratory parameters and inflammatory biomarkers could be used as critical predictive markers in the clinical management of DNI and in terms of hospitalization duration, the need for surgical drainage, and the development of complications. Unlike the studies in the literature, new biomarkers such as the CALLY index and HALP score, which we believe can more reliably and comprehensively assess the clinical course of infection, complication risk, and treatment planning in DNI patients in relation to the source of infection and comorbidity, have been examined as predictive markers.

In DNI patients, the correlation of each accompanying disease with the clinical course can be assessed separately. However, as the number of comorbidities and additional risk factors increases, beyond the etiological cause of the infection, clinical evaluation can be performed using multivariate analyses. In clinical studies, multivariate analysis helps clarify the multifaceted nature of risk factors and their relative contribution to outcomes. Studies using multivariate models to analyze DNI prognosis and complication development evaluated large cohorts, but none of the clinical variables consistently demonstrated an independent and meaningful prognostic role.[23] This highlights the complexity and interdependence of various clinical variables contributing to DNI prognosis. Therefore, in DNI patients, cost-effective methods are needed to assess the clinical course and predict complications, independent of the infection's cause, comorbidities, and abundance of risk factors. Inflammatory biomarkers such as SII, SIRI, PIV, and NLPR, easily obtained from laboratory parameters, may be valuable. However, when albumin and Hb levels reflecting nutritional status, lymphocyte count indicating immunological status, and CRP level as an inflammation marker are evaluated with the CALLY index and HALP score, more clinically meaningful and valuable results are obtained.

In this study, it was determined that in patients with DNI, only the lymphocyte count was affected by the source of infection and accompanying comorbidities, whereas other classic laboratory parameters and inflammatory biomarkers, such as SII, SIRI, PIV, and NLPR, did not show significant change. In contrast, the CALLY index and HALP score values were influenced by the infection source and number of comorbidities, with a significant correlation between these parameters. In our study, CALLY's sensitivity was higher than HALP's, at 94.9% versus 61.5%. Selection between CALLY and HALP may depend on specific clinical or diagnostic needs. In scenarios where missing a positive case (high sensitivity) is critical, CALLY may be preferred.

The CALLY index was first defined as a highly predictive tool for stratifying patients with hepatocellular carcinoma.[26,27] It provides a comprehensive assessment of a patient's inflammatory status, nutritional condition, and immune function. Studies on the CALLY index have reported findings related to the clinical course of diseases involving not only gastrointestinal tumors but also systemic inflammatory conditions such as rheumatoid arthritis, peripheral artery disease, ischemic stroke, and sepsis.[28-31] The HALP score, defined for gastric carcinomas, also enables evaluation of disease course in relation to inflammatory status, nutritional condition, and immune function. The prognostic significance of combining preoperative HALP has been reported in gastric carcinomas.[32] HALP has also been evaluated in patients with ischemic stroke and sepsis.[33,34] Both CALLY and HALP are associated with short- and long-term adverse outcomes in sepsis. Therefore, assess-

ing patient status using CALLY and HALP may help improve sepsis prognosis. In DNIs, integrating inflammatory, nutritional, and immunological markers into clinical decision-making enhances early prognostic assessment of sepsis secondary to infection.[31,34]

The etiological source of infection and predisposing conditions from patients' comorbidities may increase the severity of the clinical course in DNI, affecting the need for surgical drainage, complication development, and hospital stay duration. No association was found between the CALLY index, HALP score, and inflammatory biomarkers with the need for surgical drainage in DNI patients. An assessment was attempted for complications in the DNI patients we followed; however, since complications occurred in only three patients (one with mediastinitis, one with necrotizing fasciitis, and one with airway obstruction), statistical evaluation of the relationship between these biomarkers and complication development was not possible. Assessment of the relationship between the length of hospital stay and the CALLY index and HALP score revealed that patients with prolonged hospitalization had lower CALLY index values. This suggests that patients with poor nutritional and immunological status and higher inflammation levels tend to remain hospitalized longer.

It should be noted that our study has certain limitations. First, the study was designed retrospectively and conducted at a single center. In addition, the sample size is relatively small, and the number of complications is insufficient for statistical evaluation. We are aware that inflammatory parameters such as the CALLY index, HALP score, SII, SIRI, and NLPR may require dynamic monitoring. In our study, assessment was based on laboratory values obtained at patients' initial presentation and during hospitalization. Therefore, we acknowledge important limitations, such as monitoring all laboratory parameters and biomarkers throughout hospitalization. It was determined that the CALLY index and HALP score were affected by the etiological cause, presence of comorbidities, and number of these predisposing conditions in DNI patients; however, their relationship with surgical drainage need and complications could not be established. To validate the predictive efficacy of biomarkers regarding DNI patients' clinical course, prospective studies with larger sample sizes and multiple centers are required.

CONCLUSION

In patients with DNI, the presence of an etiological infection source and predisposing conditions such as concomitant systemic diseases may influence the clinical course of the disease, the treatment approach, and the development of complications. The use of biomarkers to predict the effect of such a large number of interrelated and interacting predictive variables on DNI may lead to meaningful improvements in the clinical and prognostic follow-up and treatment of DNI patients. Multifactorial biomarkers such as the CALLY index and HALP score allow for the assessment of not only inflammation and immunological status but also hematological and nutritional status in complex diseases such as DNI, thereby providing insights into disease severity and progression.

DECLARATIONS

Ethics Committee Approval: The study was approved by Antalya Training and Research Hospital Ethics Committee (No: 16/9, Date: 24/10/2024).

Informed Consent: This was a retrospective study; thus, informed consent was not obtained.

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