

Diagnosis-specific systemic inflammatory responses to narrowband UVB phototherapy: evidence from hemogram-derived biomarkers

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Abstract

Introduction: Narrowband ultraviolet B (NB-UVB) phototherapy is widely used for inflammatory dermatoses and selected cutaneous lymphomas. Beyond its local skin effects, NB-UVB may also induce systemic immunomodulatory changes. Hemogram-derived indices, including the systemic inflammatory index (SII) and neutrophil-to-lymphocyte ratio (NLR), are practical markers of systemic inflammation.

Methods: This multicenter retrospective cohort study included 46 patients treated with NB-UVB phototherapy for psoriasis, mycosis fungoides (MF), prurigo nodularis, or other inflammatory dermatoses. Complete blood count parameters obtained before treatment and after 8 to 10 weeks were used to calculate SII and NLR. Biomarker changes were analyzed in the overall cohort and diagnostic subgroups.

Results: Overall, NB-UVB did not significantly change SII or NLR ($p = 0.409$ and $p = 0.756$, respectively). Subgroup analyses demonstrated numerical differences among diagnostic groups. MF demonstrated the greatest numerical reductions in mean SII and NLR, decreasing by 26.05% and 18.58%, respectively, although without statistical significance ($p = 0.138$ and $p = 0.345$). Psoriasis showed modest non-significant reductions, whereas prurigo nodularis showed non-significant increases. Percentage changes in SII and NLR were strongly correlated (Spearman's $\rho = 0.869$, $p < 0.001$). CRP remained stable ($p = 0.939$).

Conclusions: NB-UVB did not significantly alter systemic inflammatory indices overall, but subgroup-specific response patterns, particularly in MF, suggest possible diagnosis-specific numerical trends.

Keywords: lymphoma, mycosis fungoides, phototherapy, psoriasis, T cells

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Introduction

Phototherapy remains a cornerstone treatment for numerous dermatological diseases, including psoriasis, vitiligo, prurigo nodularis, and cutaneous T-cell lymphomas such as mycosis fungoides (MF). Among available modalities, narrowband ultraviolet B (NB-UVB) has become the preferred option due to its favorable efficacy and safety profile compared to broadband UVB and psoralen-UVA photochemotherapy (1–7).

Although NB-UVB primarily targets cutaneous immune responses, accumulating evidence indicates that ultraviolet radiation may induce broader immunological alterations extending beyond the skin. Experimental studies have demonstrated that NB-UVB exposure can influence systemic cytokine networks, modulate dendritic cell activity, and alter T-cell subset distribution (8, 9). These findings raise the possibility that phototherapy may induce systemic inflammatory changes that could be detectable through peripheral blood biomarkers.

Hemogram-derived indices, including the systemic inflammatory index (SII) and neutrophil-to-lymphocyte ratio (NLR), have emerged as practical markers of systemic inflammatory activity across multiple medical disciplines (10–13). In dermatology, these parameters have been investigated in conditions such as psoriasis, hidradenitis suppurativa, and cutaneous lymphomas (14, 15). However, data evaluating their dynamics during NB-UVB phototherapy remain limited.

Furthermore, systemic responses to phototherapy may vary

according to the underlying disease mechanism. For example, psoriasis is primarily driven by interleukin (IL)-23/Th17-mediated inflammation, whereas MF represents a cutaneous T-cell lymphoma with complex immune dysregulation (16, 17). Whether NB-UVB induces distinct systemic inflammatory patterns across these diagnostic groups remains unclear.

Therefore, this multicenter retrospective cohort study evaluates systemic inflammatory responses to NB-UVB phototherapy using SII and NLR derived from routine complete blood counts to determine whether these responses differ among common dermatological indications for phototherapy.

Methods

Study design and settings

This is a multicenter retrospective observational study; the data were collected at two dermatology clinics from January 2022 to May 2025. The objective of this study was to assess the systemic inflammatory response to NB-UVB phototherapy by using routine hematological indices. This study was approved by the Afyonkarahisar Health Sciences University Ethics Committee (meeting no. 2025/8; approval date: June 13th, 2025). Because this was a retrospective study using anonymized patient data, obtaining individual informed consent was not required, and the committee granted a waiver of informed consent. All procedures were conducted in accordance with the Declaration of Helsinki.

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Data sources and patient identification

Electronic medical records, phototherapy treatment logs, and laboratory databases were systematically reviewed across both institutions. Patients were included if they initiated a new NB-UVB treatment course and had complete blood count (CBC) results available at baseline and again 8 to 10 weeks after treatment initiation.

Due to variability in laboratory availability over time, especially for older phototherapy courses, patients without full paired CBC information were excluded.

Study population

Patients age 12 and older that underwent NB-UVB phototherapy during the study period and had complete paired CBC measurements available before treatment initiation and after 8 to 10 weeks of therapy were eligible for inclusion. Only patients with baseline and follow-up CBC results obtained from the same institution where phototherapy was administered and that attended phototherapy sessions regularly (typically 2 to 3 times per week) were included in the analysis.

Patients with incomplete laboratory data, irregular phototherapy attendance, recent acute infection, recent trauma, surgery within 4 weeks of either CBC assessment, or medical conditions known to substantially affect hematologic parameters were excluded. These criteria were selected to minimize potential confounding factors that could influence hemogram-derived inflammatory indices, which are sensitive to intercurrent systemic processes independently of phototherapy.

Phototherapy protocol

NB-UVB phototherapy was administered two to three times weekly at the participating centers. At Afyonkarahisar Health Sciences University’s Health Research and Application Center, treatments were performed using a Waldmann NB-UVB phototherapy system (Waldmann Medizintechnik, Villingen-Schwenningen, Germany). At Ankara Training and Research Hospital, treatments were administered using a Waldmann UV5040K narrowband UVB phototherapy unit (Waldmann Medizintechnik, Villingen-Schwenningen, Germany).

Initial irradiation doses and subsequent dose increments were determined according to Fitzpatrick skin phototype and institutional phototherapy protocols. Treatment was delivered for 8 to 10 weeks as part of routine clinical practice.

The treatment protocol was based on established phototherapy recommendations and current clinical guidelines (3, 18).

Laboratory measurements and inflammatory indices

CBC parameters, including absolute neutrophil, lymphocyte, and platelet counts, were recorded at baseline, within 10 days before the initiation of phototherapy, and after approximately 8 to 10 weeks of NB-UVB treatment. Hemogram-derived inflammatory indices were calculated using previously validated formulas. NLR was defined as the absolute neutrophil count divided by the absolute lymphocyte count (19). SII was calculated as platelet count multiplied by neutrophil count and divided by lymphocyte count (20). The primary outcomes were the changes in SII and NLR between baseline and post-treatment measurements. Secondary

outcomes included subgroup analyses according to diagnostic categories.

Statistical analysis

The statistical analysis was conducted using SPSS software (version 22.0, IBM Corp., Armonk, NY, USA). The Shapiro–Wilk test assessed normality of distribution. Because SII and NLR typically exhibit non-normal distribution, the Wilcoxon signed-rank test was used for pre–post comparisons, the Kruskal–Wallis test evaluated differences across diagnostic groups, and Spearman’s rank correlation coefficient (ρ) assessed relationships between percentage changes in inflammatory indices.

Descriptive statistics were reported as mean $\pm$ standard deviation for normally distributed variables, and median (interquartile range) for non-normally distributed variables. Missing laboratory values were handled using complete-case analysis. A two-tailed p -value < 0.05 was considered statistically significant.

Results

Study cohort and baseline characteristics

A total of 46 patients met the eligibility criteria and had complete paired CBC measurements available for analysis (Fig. 1). The mean age of the cohort was 51 ± 12 years, and the female-to-male ratio was 1.7:1. The largest diagnostic subgroup consisted of patients with other inflammatory dermatoses ($n = 24$, 52%), followed by psoriasis ($n = 12$, 26%), MF ($n = 5$, 11%), and prurigo nodularis ($n = 5$, 11%; Table 1).

Table 1 | Baseline demographic and clinical characteristics of the study cohort.

Variable	Value
Number of patients	46
Mean age, years (SD)	51 $\pm$ 12
Female: male	1.7:1
Diagnosis distribution*	
Psoriasis	12 (26%)
Mycosis fungoides	5 (11%)
Prurigo nodularis	5 (11%)
Other inflammatory dermatoses†	24 (52%)

*Diagnostic categories were defined based on clinical and histopathologic evaluation. †Includes vitiligo, perforating dermatoses, pityriasis rosea, lichen sclerosus, granuloma annulare, atopic dermatitis, and pityriasis lichenoides chronica. SD = standard deviation.

Changes in systemic inflammatory indices after phototherapy

No statistically significant changes were observed in SII or NLR when the entire cohort was analyzed as a single group (SII: $p = 0.409$; NLR: $p = 0.756$). Subgroup analyses suggested diagnosis-specific numerical trends. Patients with MF showed the most prominent non-significant reductions in both SII and NLR following NB-UVB phototherapy. Psoriasis demonstrated modest non-significant reductions, whereas prurigo nodularis showed non-significant increases. Other inflammatory dermatoses showed no statistically significant changes in either NLR or SII following treatment (Table 2). Percentage changes in SII and NLR did not differ significantly among diagnostic groups (Kruskal–Wallis test, $p > 0.05$ for both).

Correlation and secondary analyses

Across the overall cohort, percentage changes in SII and NLR af-

ter NB-UVB phototherapy were strongly and positively correlated (Spearman's $\rho = 0.869$, $p < 0.001$). This finding indicates that both hemogram-derived inflammatory indices changed in parallel between baseline and post-treatment measurements.

Among patients with available paired CRP measurements, CRP levels remained stable throughout treatment, with no statistically significant change observed between baseline and month 2 ($p = 0.939$).

A more variable response was found in female patients, but there were no statistically significant differences between males and females. Differences in NLR before or after NB-UVB phototherapy were not significantly different between male and female patients (Table 3).

Discussion

This multicenter retrospective study investigated changes in hemogram-derived inflammatory markers following NB-UVB phototherapy in patients with various dermatological diseases. Although no statistically significant changes were observed when all patients were analyzed collectively, subgroup analyses suggested diagnosis-specific numerical patterns. Most notably, patients with MF showed the most pronounced numerical reductions in both SII and NLR following treatment; however, these changes did not reach statistical significance. This finding is clinically relevant because phototherapy is an established treatment modality for MF (21), and NLR has previously been evaluated as a simple

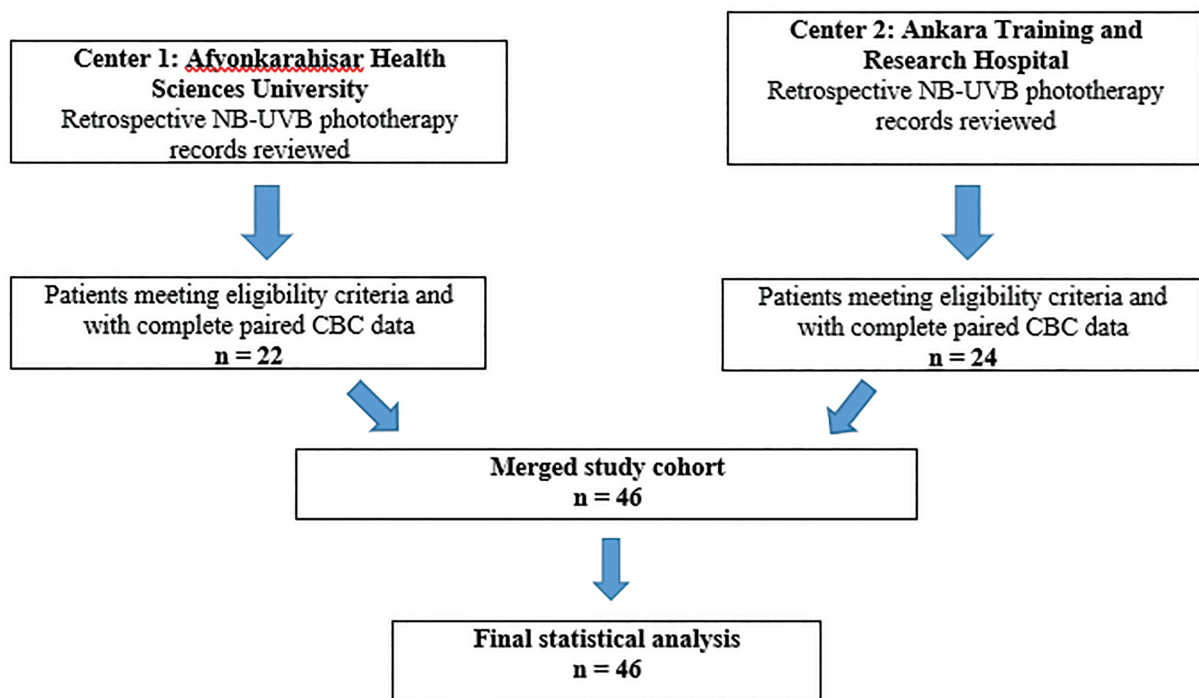


Figure 1 | Patient selection flowchart. The final cohort included 22 patients from Afyonkarahisar Health Sciences University and 24 patients from Ankara Training and Research Hospital, totaling 46 patients with complete paired complete blood count measurements before and after narrowband ultraviolet B phototherapy. Because the study was retrospective and screening logs were not prospectively maintained, only the number of eligible patients with complete paired laboratory data could be reliably reported.

NB-UVB = narrowband ultraviolet B, CBC = complete blood count.

Table 2 | Changes in hemogram-derived inflammatory indices following narrowband ultraviolet B phototherapy.

Measure	Diagnosis (n)			
	Psoriasis (12)	Mycosis fungoides (5)	Prurigo nodularis (5)	Other dermatoses (24)*
Baseline NLR	2.18	3.39	2.88	3.20
Post-treatment NLR	1.91	2.76	3.99	3.03
Δ NLR	-0.28	-0.63	1.11	-0.17
% change	-12.68	-18.58	38.60	-5.31
<i>p</i> -value	0.388	0.345	0.500	0.587
Baseline SII	604.71	878.83	836.98	1040.42
Post-treatment SII	532.44	649.87	1241.11	862.42
Δ SII	-72.27	-228.96	404.13	-178.00
% change	-11.95	-26.05	48.28	-17.11
<i>p</i> -value	0.117	0.138	0.686	0.627

Δ values were calculated as post-treatment minus baseline. Percentage change was calculated relative to baseline. *P*-values were calculated using the Wilcoxon signed-rank test. *Other dermatoses include vitiligo, perforating dermatoses, pityriasis rosea, lichen sclerosus, granuloma annulare, atopic dermatitis, and pityriasis lichenoides chronica.

NLR = neutrophil-to-lymphocyte ratio, SII = systemic inflammatory index, *n* = number of patients.

Table 3 | Sex-based comparison of percentage changes in inflammatory indices after narrowband ultraviolet B phototherapy.

Variable	Female, <i>n</i> = 29	Male, <i>n</i> = 17	<i>p</i> -value
SII percentage change, mean rank	24.10	22.47	0.690
NLR percentage change, mean rank	24.17	22.35	0.657

NLR = neutrophil-to-lymphocyte ratio, SII = systemic inflammatory index.

inflammatory biomarker in patients with early-stage MF (22). In contrast, no statistically significant changes were observed in psoriasis, prurigo nodularis, or other inflammatory dermatoses. These findings suggest that systemic inflammatory responses to NB-UVB phototherapy may vary according to the underlying disease process, although the results should be interpreted cautiously because of limited subgroup sample sizes.

NB-UVB phototherapy is widely recognized as an effective treatment modality for inflammatory and lymphoproliferative skin diseases. Although its primary therapeutic effects occur within the skin, increasing evidence suggests that ultraviolet radiation may also induce broader immunological changes. Experimental studies have demonstrated that NB-UVB exposure can influence cytokine production, alter dendritic cell function, induce T-cell apoptosis, and modify immune cell trafficking beyond the irradiated skin (9). Current phototherapy guidelines also emphasize that NB-UVB exerts immunomodulatory effects extending beyond local cutaneous inflammation (3). Consequently, systemic inflammatory markers derived from routine blood tests may provide indirect insight into these immunological effects.

NLR has emerged as a practical and inexpensive marker of systemic inflammation in numerous dermatological disorders. Elevated NLR values have been reported in psoriasis, hidradenitis suppurativa, atopic dermatitis, and cutaneous lymphomas, reflecting increased inflammatory burden and immune dysregulation (14). Asahina et al. demonstrated that successful biologic treatment in psoriasis was associated with reductions in NLR, supporting its potential role as a treatment-response biomarker (23). Similarly, SII, which incorporates neutrophil, lymphocyte, and platelet counts, has been proposed as a comprehensive marker of systemic inflammatory status and prognosis in inflammatory conditions (12). However, studies evaluating changes in these parameters during phototherapy remain relatively limited.

Psoriasis was the second largest subgroup in this study. Several previous investigations have demonstrated elevated NLR and SII values in patients with psoriasis compared to healthy controls (14, 23). Moreover, successful systemic treatment has been associated with reductions in these markers, supporting their potential utility as indicators of inflammatory activity (23). In this study's cohort, psoriasis patients demonstrated numerical reductions in both SII and NLR following NB-UVB phototherapy, corresponding to decreases of 11.95% and 12.68%, respectively; however, these changes did not reach statistical significance. This finding may reflect the relatively small sample size, variability in disease severity, or the possibility that peripheral blood inflammatory markers are less sensitive to treatment-related changes than clinical severity scores. It is also possible that the systemic inflammatory burden in psoriasis is more effectively modified by biologic or systemic therapies than by skin-directed phototherapy alone (23).

The absence of significant changes in patients with prurigo nodularis is also noteworthy. Prurigo nodularis is characterized by chronic itch, neural sensitization, and complex immune dysregulation involving Th2-associated cytokines, including IL-4, IL-13, and IL-31 (24). Although NB-UVB phototherapy has demonstrated clinical efficacy in many patients with prurigo nodularis, relatively little is known regarding its effects on systemic inflammatory biomarkers. In this study, SII and NLR showed non-significant numerical increases in this subgroup. This may suggest that these indices do not adequately reflect the immunological pathways driving disease activity in prurigo nodularis. Alternatively, the limited sample size may have reduced the ability to detect

subtle treatment-related changes. Additional studies evaluating cytokine profiles and immune biomarkers in prurigo nodularis are needed to better understand the systemic effects of phototherapy.

One of the most interesting observations of the study was the prominent numerical reduction in inflammatory indices among patients with MF. Previous studies have reported associations between elevated NLR values and advanced disease stage, poorer prognosis, and increased disease activity in cutaneous T-cell lymphomas (25). Eren et al. further demonstrated that elevated NLR values may correlate with disease severity in patients with MF and proposed NLR as a simple biomarker for disease monitoring (22). Consequently, NLR has been proposed as a potential prognostic biomarker in MF (22, 25).

NB-UVB phototherapy is known to induce apoptosis of malignant T lymphocytes, suppress epidermotropic lymphocytic infiltrates, and modify local cytokine networks. These mechanisms may contribute to reductions in inflammatory activity and could explain the numerical decline in SII and NLR observed in the MF subgroup. Hart and Norval highlighted the ability of ultraviolet radiation to regulate immune responses through effects on cytokine signaling and immune cell function (9). Similarly, phototherapy guidelines published by Elmetts et al. emphasized the broad immunomodulatory effects of NB-UVB therapy in inflammatory skin diseases (3). Therefore, the numerical reductions observed in MF are biologically plausible and may reflect treatment-associated modulation of inflammatory pathways.

Nevertheless, because only five MF patients were included, this finding should be interpreted cautiously. The reductions in SII and NLR did not reach statistical significance, and small subgroup sizes increase the possibility of statistical error and limit generalizability. Therefore, the pattern observed should be considered hypothesis-generating rather than definitive evidence of systemic immunomodulation.

The findings of this study are generally consistent with the concept that phototherapy-induced systemic effects are likely disease-specific rather than universal. Psoriasis, MF, and prurigo nodularis involve distinct immunological pathways, cellular targets, and inflammatory mediators. Therefore, identical responses in peripheral inflammatory markers should not necessarily be expected across these conditions. In this study, percentage changes in SII and NLR were strongly and positively correlated after phototherapy, suggesting that both hemogram-derived inflammatory indices changed in parallel. This finding is biologically expected, given that both indices share neutrophil and lymphocyte components. CRP values, measured in a subset of patients, remained stable throughout treatment, supporting the interpretation that broad systemic inflammatory changes were not detected in the overall cohort.

Several strengths of this study should be acknowledged. First, the study reflects real-world clinical practice and includes patients from two independent centers. Second, readily available and inexpensive biomarkers were evaluated, increasing the potential clinical applicability of the findings. Third, different dermatological indications for phototherapy were analyzed simultaneously, allowing direct comparison of biomarker responses among disease groups.

The study also has important limitations. The retrospective design introduces the possibility of selection bias and limits control over confounding factors. The overall sample size was modest, and subgroup numbers were particularly small for MF and prurigo nodularis. Information regarding cumulative UVB dose and

exact treatment session numbers was not consistently available. Furthermore, clinical response scores were not consistently available because of the retrospective design; therefore, associations between clinical improvement and changes in inflammatory biomarkers could not be evaluated. Finally, NLR and SII are indirect measures of systemic inflammation and may be influenced by factors unrelated to dermatological disease activity (12, 14).

Conclusions

NB-UVB phototherapy was not associated with statistically significant changes in SII or NLR in the overall cohort. However, subgroup analyses demonstrated numerical trends, with the most notable non-significant numerical reductions observed in patients with MF. These findings suggest that hemogram-derived indices such as SII and NLR may serve as readily available exploratory

markers for evaluating systemic inflammatory responses during phototherapy.

Given the retrospective design, modest sample size, and particularly small number of patients in some diagnostic subgroups, these findings should be interpreted cautiously. Larger prospective studies with standardized phototherapy protocols, clinical response assessments, and comprehensive immunological profiling are needed to clarify the systemic immunomodulatory effects of NB-UVB therapy and to determine whether hemogram-derived biomarkers have clinical utility in monitoring treatment responses.

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