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RESEARCH ARTICLE

Comparison of Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio Before and After Chemotherapy on the Prognosis of Nasopharyngeal Carcinoma Patients

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Abstract

Background: The neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) have emerged as reliable systemic inflammatory markers associated with cancer progression and prognosis. Their prognostic role in nasopharyngeal carcinoma (NPC) remains of significant clinical interest, particularly in evaluating treatment response to chemotherapy. This study aimed to compare NLR and PLR values before and after chemotherapy and to analyze their relationship with prognosis in patients with NPC. **Methods:** A total of 100 NPC patients who met the inclusion criteria were enrolled. NLR and PLR values were calculated from peripheral blood samples obtained before and after three cycles of chemotherapy. Statistical analyses were performed using the Wilcoxon signed-rank test to compare pre- and post-treatment values and the Chi-square test to assess their association with prognosis. **Results:** Median NLR decreased significantly from 3.2 (0.2–16.4) pre-treatment to 1.9 (0.5–8.3) post-treatment ($p < 0.001$), and median PLR decreased from 185.9 (23.1–741.7) to 150.4 (67.8–270.2) ($p < 0.001$). Stage-stratified analysis revealed significant reductions in NLR and PLR in patients with stage II–IVA disease ($p < 0.05$), whereas stage IVB patients showed non-significant decreases. Patients with lower post-treatment NLR and PLR values were more likely to have a favorable prognosis, with 72.7–73.7% of stage II–III patients classified as good prognosis versus only 16.7–20.0% in stage IVB. **Conclusion:** Three cycles of chemotherapy significantly reduced systemic inflammation markers NLR and PLR in stage II–IVA NPC, with reductions correlating with improved short-term prognosis. Persistently elevated NLR and PLR in stage IVB patients suggest ongoing systemic inflammation and potential chemoresistance. NLR and PLR are practical, cost-effective biomarkers for monitoring treatment response and predicting prognosis in NPC.

Keywords: Neutrophil-Lymphocyte Ratio- Platelet-Lymphocyte Ratio- Prognosis- Chemotherapy

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Introduction

Nasopharyngeal carcinoma (NPC) is a malignant epithelial tumor of the nasopharynx, classified as a squamous cell carcinoma (SCC) [1]. According to the GLOBOCAN 2022 report, there were 120,434 new cases of NPC globally, resulting in 73,482 deaths [2]. Based on data from Dr. Wahidin Sudirohusodo General Hospital, Makassar, South Sulawesi, 1,096 cases of NPC were recorded between 2011 and 2021, with the highest prevalence among patients aged 46–60 years (41.2%) [3, 4].

Inflammation and immunological mechanisms play essential roles in tumor initiation, progression, and metastasis. Systemic inflammation can promote tumorigenesis by suppressing apoptosis, stimulating angiogenesis, and inducing DNA damage [5]. Elevated neutrophil, lymphocyte, and monocyte counts in peripheral blood have been identified as prognostic markers for poor survival among cancer patients undergoing therapy [5]. Bahremani et al. (2019), in a study involving 46 patients with head and neck carcinoma, demonstrated that pre-treatment Neutrophil-Lymphocyte Ratio (NLR)

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values could predict chemotherapy response in epithelial head and neck cancers [6]. Furthermore, platelets play a crucial role in tumor progression and metastasis. Activated platelets promote tumor cell proliferation, angiogenesis, and invasion through aggregation with tumor cells, enhancing their survival in circulation. Platelet-related indices, such as platelet count, have been correlated with cancer prognosis [7]. A meta-analysis revealed that an elevated Platelet-Lymphocyte Ratio (PLR) is associated with poorer survival and higher nodal stage (N stage) in NPC patients [8].

Although previous studies have reported that elevated NLR and PLR are associated with poorer survival in NPC, most existing data are retrospective and primarily focus on pre-treatment values. To date, limited evidence is available regarding dynamic changes in NLR and PLR following chemotherapy across specific clinical stages, particularly within Southeast Asian populations where NPC burden is high. To our knowledge, no prior study in Indonesia has prospectively evaluated dynamic changes in NLR and PLR before and after a standardized paclitaxel–cisplatin regimen across AJCC stages II–IVB. Therefore, this study addresses a critical gap by providing stage-specific evidence from a Southeast Asian population, offering insights into early systemic inflammatory changes in response to chemotherapy.

Therefore, this study was conducted to compare pre- and post-chemotherapy NLR and PLR values and to analyze their association with prognosis in patients with NPC.

Materials and Methods

Study Design

This study was a prospective cohort study conducted from March to July 2025 at Dr. Wahidin Sudirohusodo General Hospital, Hasanuddin University Hospital, and Pelamonia Hospital, Makassar.

Study Participants

The study included newly diagnosed NPC patients classified as stage II, III, or IV based on histopathological examination, who received three cycles of paclitaxel–cisplatin chemotherapy. Patients with malignancies in other organs, autoimmune diseases, active infections, leukemia, or those undergoing radiotherapy were excluded.

Staging was determined using the 2018 AJCC classification, based on chest X-ray, abdominal ultrasound, bone survey, and nasopharyngeal biopsy results.

Chemotherapy Administration

All patients received three cycles of chemotherapy with paclitaxel (175 mg/m² BSA) and cisplatin (100 mg/m² BSA), administered every 21 days. No cycles were extended beyond this interval in our cohort.

Dose Modifications

Standard dosing based on body surface area was applied. Dose reductions were implemented only in cases of clinically significant toxicity, according to institutional protocols.

Treatment Delays: There were no planned delays. Any transient toxicity-related postponements were documented but did not exceed the 21-day cycle schedule in the analyzed cohort.

NLR and PLR Assessment

Routine hematological tests were performed to determine NLR and PLR values before and after three chemotherapy cycles. NLR was calculated as the ratio of neutrophil count to lymphocyte count [9,10]. PLR was calculated as the ratio of platelet count to lymphocyte count [11, 12].

Prognosis Classification

Prognosis in this study was defined using dynamic changes in systemic inflammatory markers specifically NLR and PLR measured after three cycles of paclitaxel–cisplatin chemotherapy compared with baseline (pre-chemotherapy) values.

• Good prognosis was assigned to patients whose NLR and PLR values decreased following three chemotherapy cycles.

• Poor prognosis was assigned when NLR and/or PLR values increased after the third chemotherapy cycle.

This definition was based on the established evidence that decreasing inflammatory biomarker levels correlate with better treatment response and survival outcomes in head and neck cancer, as supported by previous literature [13, 14]

For the prognostic analysis, patients were classified as having high or low NLR and PLR values using standard cut-offs from the literature: NLR $\geq$ 3 was considered high, and PLR $\geq$ 150 was considered high, while values below these thresholds were considered low [13-17]. These cut-offs have been widely validated in head and neck squamous cell carcinoma (HNSCC) as prognostic markers. Due to the limited sample size of this study, ROC curve analysis was not performed; the adopted thresholds allow comparability with previous studies.

Data Analysis

All analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Normality of continuous variables was assessed using the Shapiro-Wilk test. Continuous data with non-normal distribution were presented as medians with interquartile ranges and compared using the Mann-Whitney U test (two groups) or Kruskal-Wallis test (more than two groups). Categorical variables were analyzed using the Chi-square test; however, for comparisons with small expected cell counts ($n < 5$), Fisher's exact test was applied to ensure accuracy. Statistical significance was defined as $p < 0.05$.

Ethical Considerations

All procedures in this study were conducted in accordance with the ethical standards of the Declaration of Helsinki. Informed consent was obtained from all participants prior to enrollment. The research protocol

was reviewed and approved by the Human Biomedical Research Ethics Commission, Faculty of Medicine, Hasanuddin University (Approval No. 239/UN.4.64.5.31/PP.36/2025), issued on April 21, 2025.

Results

Characteristics of Study Participants

A total of 100 patients met the inclusion criteria, with a mean age of 45.7 ± 14.2 years (range: 13–76). Most patients were male (71%) and diagnosed at stage III (57%) (Table 1).

Comparison of NLR and PLR Before and After Chemotherapy

Median NLR and PLR values decreased significantly after chemotherapy in stages II, III, and IVA ($p < 0.05$), whereas reductions in stage IVB were not statistically significant (Table 2). In stage IVA, the PLR reduction (241.8 to 228.5) was statistically significant but modest, suggesting limited clinical impact despite the p-value. Clinically, this modest reduction may reflect only a limited improvement in systemic inflammatory status following chemotherapy, which may not translate into a meaningful effect on patient outcomes. This distinction highlights the importance of interpreting statistical significance alongside clinical relevance.

Prognosis Based on Post-Chemotherapy NLR and PLR Values

Post-treatment NLR and PLR were strongly associated with disease stage, with early-stage patients (II–III) showing better prognoses than advanced-stage patients (IVA–IVB) (Table 3).

Discussion

This study investigated the dynamic changes in NLR and PLR in NPC patients undergoing chemotherapy and their relationship with disease stage and short-term prognosis. Our results show that NLR and PLR significantly decreased after chemotherapy in stage II–IVA patients, whereas stage IVB patients exhibited no statistically significant reductions. Furthermore, lower post-treatment NLR and PLR were strongly associated with favorable short-term outcomes, suggesting that these inflammatory markers may serve as practical, non-invasive indicators of treatment response.

Table 1. Characteristics of Study Participants

Characteristics	n (%) /Mean ± SD
Age (years)	45.70 ± 14.24
Sex	
Male	71 (71.0)
Female	29 (29.0)
Stage	
II	11 (11.0)
III	57 (57.0)
IVA	20 (20.0)
IVB	12 (12.0)

The observed reduction in NLR and PLR in early- to mid-stage NPC aligns with previous reports linking decreased systemic inflammation with better therapeutic outcomes. Chen et al. (2017) and Wang et al. (2023) reported that patients demonstrating post-treatment reductions in NLR had improved disease control and overall survival (OS) [18, 19]. Locally, Kurnianda et al. (2021) observed longer median OS among patients with decreased NLR after chemotherapy at Dr. Sardjito General Hospital, highlighting the clinical relevance of monitoring these markers in routine practice [20]. Similarly, Yamada et al. (2023) reported that patients with reduced post-treatment NLR showed higher lymphocyte recovery and faster tumor regression [21]. Yudistira et al. (2024) also found that PLR reductions correlated with improved clinical response, reinforcing the role of systemic inflammation in disease progression and therapeutic efficacy [22].

Compared to previous studies that evaluated NLR and PLR at a single time point, the strength of this study lies in its prospective, stage-stratified evaluation, allowing a more nuanced understanding of the impact of chemotherapy on systemic inflammation across disease stages. Notably, the lack of significant changes in stage IVB patients suggests persistent systemic inflammation, which may reflect chemoresistance, higher tumor burden, or immune dysregulation, a distinction that is rarely addressed in prior literature.

The decrease in NLR and PLR after chemotherapy likely reflects the dual impact of cytotoxic treatment on tumor cells and inflammatory pathways. Neutrophils, through the secretion of cytokines, proteolytic enzymes, and growth factors, promote angiogenesis, tumor proliferation, and immune evasion [23]. Lymphocytes, particularly cytotoxic T cells, play a pivotal role in tumor surveillance and apoptosis induction [24]. Therefore, a reduction in NLR reflects a shift toward improved immune homeostasis and enhanced anti-tumor activity. Similarly, platelets support tumor growth and metastasis through shielding circulating tumor cells and releasing pro-angiogenic factors; a decrease in PLR may signify reduced platelet-mediated tumor facilitation [25].

It is important to note that both NLR and PLR are influenced by lymphocyte counts, which are particularly susceptible to chemotherapy-induced cytotoxicity. In our cohort, the post-treatment reductions in NLR and PLR were predominantly associated with relative recovery of lymphocytes rather than major declines in neutrophils or platelets. This suggests that dynamic changes in these inflammatory markers reflect restoration of immune homeostasis in response to chemotherapy, supporting their utility as early indicators of treatment response.

The modest reduction in PLR observed in stage IVA (241.8 to 228.5) despite statistical significance illustrates the distinction between statistical and clinical significance. This suggests that while chemotherapy can partially modulate systemic inflammation, the effect may not be sufficient to meaningfully alter patient outcomes in

Table 2. Comparison of NLR and PLR in Nasopharyngeal Carcinoma Patients

Stage	Variable	Before (Median, min–max)	After (Median, min–max)	p-value
II	NLR	2.5 (1.2–11.6)	1.3 (0.5–2.4)	0.01
	PLR	125.7 (71.7–658.3)	92.7 (53.8–197.4)	0.033
III	NLR	3.2 (0.2–16.4)	1.9 (0.5–8.3)	< 0.001
	PLR	185.9 (23.1–741.7)	150.4 (67.8–270.2)	< 0.001
IVA	NLR	4.3 (1.5–14.9)	2.6 (0.3–15.5)	< 0.001
	PLR	241.8 (123.4–615.0)	228.5 (45.1–402.2)	< 0.001
IVB	NLR	10.3 (1.7–22.7)	5.1 (2.4–50.2)	0.814
	PLR	521.8 (110.8–1312.0)	357.7 (179.3–1127.1)	0.639

Note: Statistical analysis was conducted using the Wilcoxon signed-rank test.

Table 3. Associations between NLR and PLR Categories and Clinicopathologic Characteristics

Prognosis	Stage II n (%)	Stage III n (%)	Stage IVA n (%)	Stage IVB n (%)	p-value
NLR					0.002
Good	8 (72.7)	42 (73.7)	11 (55.0)	2 (16.7)	
Poor	3 (27.3)	15 (26.3)	9 (45.0)	10 (83.3)	
PLR					< 0.001
Good	7 (63.6)	50 (87.7)	4 (20.0)	2 (16.7)	
Poor	4 (36.4)	7 (12.3)	16 (80.0)	10 (83.3)	

Note: Chi-square test was used for most comparisons; Fisher's exact test applied for categories with small expected frequencies (Stage II and IVB).

advanced disease stages. Such observations underscore the importance of interpreting inflammatory biomarkers within the broader clinical context rather than relying solely on p-values.

Our findings suggest that NLR and PLR are practical, cost-effective biomarkers that can complement traditional staging systems to monitor therapeutic response and predict prognosis. Regular monitoring of these indices may identify high-risk patients who might benefit from intensified surveillance or adjunctive therapies, particularly when imaging or molecular diagnostics are limited. Additionally, the combination of NLR and PLR appears to enhance prognostic accuracy, with patients displaying concurrent reductions in both markers experiencing the most favorable outcomes [18, 26].

Furthermore, dynamic changes in these hematologic parameters may serve as early indicators of treatment efficacy. For example, patients with persistently elevated NLR or PLR post-therapy may require early intervention, closer monitoring, or enrollment in clinical trials for novel therapies. Integrating these markers into routine clinical workflows could improve individualized care, particularly in resource-limited settings.

Several limitations of this study should be noted. First, the single-center design and relatively small sample size may limit the generalizability of findings. Second, the follow-up period was insufficient to evaluate long-term outcomes, such as OS and progression-free survival (PFS). Third, potential confounders including infections, nutritional status, comorbidities, and use of anti-inflammatory medications were not fully controlled, which could affect hematologic parameters. Lastly, the study did not evaluate other immune or inflammatory biomarkers (e.g., CRP, IL-6) that could complement NLR and PLR in prognostication.

Therefore, future research should aim to validate optimal cut-off values for NLR and PLR in larger, multicenter cohorts and correlate dynamic changes in these markers with long-term clinical outcomes such as PFS and OS. Prospective studies could also assess the integration of NLR and PLR monitoring with imaging and molecular biomarkers to refine risk stratification and therapeutic decision-making. Additionally, investigations into adjunctive strategies such as immunotherapy or anti-inflammatory agents for patients with persistently elevated NLR/PLR may provide new avenues to improve outcomes in advanced-stage NPC.

In conclusion, this study highlights the prognostic relevance of NLR and PLR as dynamic, stage-stratified biomarkers in NPC. Significant post-chemotherapy reductions in NLR and PLR were associated with favorable short-term outcomes in stage II–IVA patients, whereas stage IVB patients exhibited persistent systemic inflammation. These findings support the use of NLR and PLR as accessible, cost-effective tools to guide patient management, complement staging systems, and inform individualized therapeutic strategies.

Declarations

Clinical trial registration

Not applicable

Conflicts of interest/Competing interests

Authors declare that they have no conflicts of interest.

Availability of data and material

The data sets used and/or analyzed during the current study are available from the corresponding authors per reasonable request.

Authors' contributions

RR (Concept, Design, Resources, Materials, Data Collection and Processing, Analysis and Interpretation, Literature Search, Writing Manuscript), NID (Concept, Design, Supervision, Analysis and Interpretation, Literature Search), RD (Concept, Design, Supervision, Analysis and Interpretation, Literature Search), and AQ (Concept, Design, Analysis and Interpretation, Critical Review). All authors read and approved the final version of the manuscript.

Ethics approval

This study was approved by Ethics Committee of Dr Wahidin Sudirohusodo Hospital Faculty of Medicine, Hasanuddin University (approval no. 239/UN4.6.4.5.31/PP36/2025).

Consent for publication

Written informed consent was obtained from all participants, and the trial was conducted in accordance with the Declaration of Helsinki.

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Declaration on generative AI and AI-assisted technologies in the writing process

None

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