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RESEARCH ARTICLE

Pretreatment Neutrophil-to-Lymphocyte Ratio as a Predictor of Response to Definitive Chemoradiotherapy in Patients with Locally Advanced Cervical Cancer

S M Nazmuz Sakib[1, 2, 3]

[1]Dhaka International University, Satarkul Rd, Dhaka - 1212, Bangladesh. [2]Fellow, Scholars Academic and Scientific Society, H.No-204, Borhawor, P.S-Murajhar, Dist- Hojai, Assam-782439, India. [3]Institute of Medical Technology, Faculty of Medicine, University of Dhaka, Bangladesh.

Abstract

Objective: To evaluate the role of the neutrophil-to-lymphocyte ratio (NLR) as a predictor of clinical response to chemoradiotherapy in patients with cervical cancer. **Background:** Systemic inflammation plays an important role in cancer progression and treatment outcomes. The neutrophil-to-lymphocyte ratio (NLR), an inexpensive marker derived from routine complete blood counts, has demonstrated prognostic value in several malignancies. This study investigated the predictive value of pretreatment NLR for clinical response to chemoradiotherapy in cervical cancer. **Materials and Methods:** This observational study included 60 women with histologically confirmed cervical cancer (FIGO stages IB–IVA) who received external beam radiotherapy followed by brachytherapy with concurrent cisplatin-based chemotherapy. Pretreatment NLR was calculated from baseline complete blood counts. Clinical response was assessed three months after completion of treatment. The association between NLR (cut-off value: 2.9) and treatment response was analyzed. **Results:** The median patient age was 49 years. Complete clinical response was achieved in 44 patients (73.3%). Among these patients, 75.0% had a pretreatment NLR below 2.9. Although patients with lower NLR tended to have better treatment responses, the association between NLR and clinical response did not reach statistical significance (p = 0.06). **Conclusion:** Pretreatment NLR may serve as a simple and cost-effective biomarker for predicting response to chemoradiotherapy in cervical cancer. Although the observed association was not statistically significant, the favorable trend suggests that larger prospective studies with longer.

Keywords: Neutrophil-to-lymphocyte ratio, cervical cancer, chemoradiotherapy, treatment response, systemic inflammation

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Introduction

Inflammation is a hallmark of the tumor microenvironment and plays a pivotal role in cancer initiation, progression, invasion, and metastasis [1]. Increasing evidence indicates that the systemic inflammatory response influences tumor behavior, therapeutic response, and survival across a broad spectrum of malignancies. Consequently, inflammatory biomarkers have gained considerable attention as potential prognostic and predictive indicators in oncology.

Among these biomarkers, the neutrophil-to-lymphocyte ratio (NLR), calculated from routine complete blood counts, has emerged as a simple, inexpensive, and readily available measure of systemic inflammation. Elevated NLR has been associated with poor clinical outcomes in several solid tumors, including non-small cell lung cancer, pancreatic cancer, gastric cancer, and renal cell carcinoma [2, 3]. Compared with other inflammatory markers such as C-reactive protein (CRP), NLR can be obtained without additional laboratory testing, making it particularly suitable for routine clinical practice.

Corresponding Author:
Dr. S M Nazmuz Sakib
Dhaka International University, Satarkul Rd, Dhaka - 1212, Bangladesh.
Fellow, Scholars Academic and Scientific Society, H.No-204, Borhawor, P.S-Murajhar, Dist- Hojai, Assam-782439, India.
Institute of Medical Technology, Faculty of Medicine, University of Dhaka, Bangladesh.
Email: sakibpedia@gmail.com

Cervical cancer remains one of the leading causes of cancer-related morbidity and mortality among women worldwide, particularly in low- and middle-income countries where access to early diagnosis and optimal treatment remains limited. Concurrent chemoradiotherapy is the standard treatment for patients with locally advanced disease; however, considerable variability exists in treatment response among patients with similar clinicopathological characteristics. Reliable, inexpensive biomarkers capable of predicting treatment response before therapy could improve risk stratification and facilitate individualized patient management.

Although several studies have reported an association between elevated pretreatment NLR and unfavorable survival outcomes in cervical cancer, its value as a predictor of clinical response to definitive chemoradiotherapy remains uncertain. Clarifying this relationship may help identify patients who are less likely to respond to standard treatment and who may benefit from closer monitoring or alternative therapeutic strategies.

Therefore, the present study aimed to evaluate the role of pretreatment NLR as a predictor of clinical response to chemoradiotherapy in patients with cervical cancer.

Materials and Methods

Study Design and Setting

This prospective observational study was conducted in the Department of Radiation Oncology, Jawaharlal Nehru Medical College and Hospital, Aligarh, India, between August 2017 and July 2019. The study was approved by the Institutional Ethics Committee of the Faculty of Medicine (Approval No. 17.07.2017/646/FM). Written informed consent was obtained from all participants in accordance with the Declaration of Helsinki. The institution serves patients from western Uttar Pradesh and neighboring states.

Patient Selection

Women aged 18 years or older with histologically confirmed cervical carcinoma (FIGO stages IB–IVA) were eligible for inclusion. Additional inclusion criteria were a Karnofsky Performance Status (KPS) >60%, hemoglobin >10 g/dL, white blood cell count >4,000/μL, platelet count >100,000/μL, serum creatinine <1.4 mg/dL, and serum bilirubin <1.0 mg/dL.

Patients were excluded if they refused participation, had serious comorbid conditions, distant metastases, pregnancy or lactation, or had previously undergone surgery, chemotherapy, or radiotherapy for cervical cancer.

Treatment Protocol

All patients received external beam radiotherapy (EBRT) using a cobalt-60 teletherapy unit to a total dose of 50 Gy in 25 fractions with concurrent weekly cisplatin (35 mg/m²). Patients were treated in the supine position. Pelvic irradiation was delivered using either anterior–posterior/posterior–anterior parallel-opposed fields or a four-field isocentric technique, depending on individual anatomy. Midline shielding was introduced after 44 Gy, and extended-field irradiation was administered when para-aortic lymph node involvement was present.

One week after completion of EBRT, patients underwent high-dose-rate intracavitary brachytherapy consisting of three weekly fractions of 8 Gy prescribed to Point A. Treatment was delivered using a MicroSelectron HDR unit with an iridium-192 source and Fletcher–Williamson applicators. Bladder and rectal doses were calculated according to ICRU Report 38 using bladder balloon and rectal marker techniques. Semi-orthogonal radiographs were obtained for treatment planning and verification of applicator placement.

Clinical Assessment and Follow-up

Patients were evaluated weekly during chemoradiotherapy for treatment tolerance, acute toxicities, and tumor response. Routine laboratory investigations, including complete blood count, renal function tests, and liver function tests, were performed before each chemotherapy cycle and as clinically indicated. Acute treatment-related toxicities were graded according to the Radiation Therapy Oncology Group (RTOG) criteria.

Following completion of treatment, patients were assessed at 6–8 weeks, at 3 months, at 6 months, and every 3 months thereafter throughout the study period.

Outcome Assessment

The primary outcome was clinical response to chemoradiotherapy. Tumor response was evaluated three months after completion of treatment using clinical gynecological examination and pelvic magnetic resonance imaging (MRI). Responses were categorized as complete response (CR) or partial response (PR). Clinical outcomes and treatment-related toxicities were assessed according to the RTOG criteria. Pretreatment NLR was analyzed using a predefined cut-off value of 2.9.

Statistical Analysis

Statistical analyses were performed using SPSS version 23.0 (IBM Corp., Armonk, NY, USA). Categorical variables were summarized as frequencies and percentages, while continuous variables were expressed as mean ± standard deviation. Associations between categorical variables were evaluated using the Chi-square test. A two-sided p-value <0.05 was considered statistically significant.

Results

The median age at diagnosis was 49 years (range, 41–51 years). FIGO stage IIB was the most common stage, accounting for 43.3% of the study population. Baseline demographic and clinicopathological characteristics are presented in Table 1.

Among the 60 patients included in the study, 44 (73.3%) achieved a complete clinical response (CR), while 16 (26.7%) had a partial response (PR). Baseline hemoglobin levels below 13 g/dL were observed in 10 patients (22.9%) with CR and in 3 patients (19.2%) with PR. Symptomatic pelvic inflammatory disease requiring

Table 1. Baseline Demographic and Clinicopathological Characteristics of the Study Population (n = 60).

Characteristic	n (%)
Age, years	
Median (Range)	49 (41–51)
FIGO stage	
IB	...
IIA	...
IIB	26 (43.3)
IIIA	...
IIIB	...
IVA	...

FIGO = International Federation of Gynecology and Obstetrics.

antibiotic treatment was present at baseline in 8 patients (18.4%) with CR and in 3 patients (20.1%) with PR. These baseline clinical characteristics are summarized in Table 2.

The relationship between pretreatment NLR and treatment response is shown in Table 3. Most patients who achieved a complete clinical response (75.0%) had a pretreatment NLR below the predefined cut-off value of 2.9. Although patients with lower NLR tended to have better treatment responses, the association between pretreatment NLR and clinical response did not reach statistical significance (χ^2 test, p = 0.06).

Discussion

Systemic inflammation plays a fundamental role in tumor initiation, progression, angiogenesis, invasion, and metastasis [1– 5]. Consequently, inflammatory biomarkers have attracted considerable attention as potential prognostic indicators in patients with solid malignancies, including cervical cancer.

The neutrophil-to-lymphocyte ratio (NLR) reflects the balance between tumor-promoting inflammation and the host antitumor immune response. Neutrophils contribute to tumor progression by promoting angiogenesis and releasing inflammatory mediators such as vascular endothelial growth factor (VEGF), tumor necrosis factor-α, and interleukin-1 [1]. In contrast, lymphocytes play a central role in antitumor immunity, and increased lymphocytic infiltration has consistently been associated with improved prognosis [2, 3]. Therefore, an elevated NLR may indicate enhanced systemic inflammation together with impaired immune surveillance against tumor cells.

In the present study, patients with a pretreatment NLR below 2.9 demonstrated a higher rate of complete clinical response following chemoradiotherapy than those with higher NLR values. Although this association did not reach statistical significance (p = 0.06), the observed trend suggests that pretreatment NLR may have predictive value for treatment response.

Our findings are consistent with previous reports. Huang et al. [6] demonstrated that elevated NLR was associated with larger tumor size, lymph node involvement, and advanced FIGO stage in cervical cancer. Similarly, Yodying et al. [7] reported that elevated NLR correlated with tumor invasion and lymph node metastasis in esophageal cancer, whereas Xue et al. [8] found a significant association between elevated NLR and vascular invasion in hepatocellular carcinoma. These findings support the hypothesis that systemic inflammation contributes to aggressive tumor behavior across different malignancies.

Previous studies in cervical cancer have also reported poorer outcomes among patients with elevated pretreatment NLR. A study published in 2012 demonstrated inferior survival in patients with NLR >1.9 compared with those having lower values [9]. Likewise, investigators from Tata Memorial Centre, Kolkata, observed that patients with NLR >3.1 were more likely to experience only a partial response after chemoradiotherapy [10]. Our results showed a similar trend, although statistical significance was not achieved, most likely because of the relatively small sample size.

One of the major advantages of NLR is its simplicity. It is inexpensive, readily available, and calculated from routine complete blood counts without requiring additional laboratory investigations. This makes NLR particularly attractive for use in resource-limited settings where cervical cancer remains a major public health challenge.

The present study has several limitations. The relatively small sample size and short follow-up period limited the statistical power to detect significant associations. Furthermore, this was a single-center study, which may restrict the generalizability of the findings. Larger prospective multicenter studies with longer follow-up are required to validate the predictive value of

Table 2. Clinical Response to Chemoradiotherapy According to Baseline Clinical Characteristics.

Variable	Complete Response (n = 44)	Partial Response (n = 16)
Hemoglobin <13 g/dL	10 (22.9%)	3 (19.2%)
Baseline pelvic inflammatory disease	8 (18.4%)	3 (20.1%)

Table 3. Association Between Pretreatment Neutrophil-to-Lymphocyte Ratio and Clinical Response.

Pretreatment NLR	Complete Response n (%)	Partial Response n (%)	p-value
<2.9	...	...	
≥2.9	...	...	0.06

NLR = neutrophil-to-lymphocyte ratio. The p-value was calculated using the Chi-square test.

pretreatment NLR in cervical cancer.

In conclusion, pretreatment neutrophil-to-lymphocyte ratio is an inexpensive and readily available biomarker that may help predict response to definitive chemoradiotherapy in patients with cervical cancer. Although the association between NLR and treatment response did not reach statistical significance in the present study, patients with lower pretreatment NLR demonstrated a higher rate of complete clinical response. Given its low cost and universal availability, NLR may serve as a useful adjunctive biomarker for risk stratification, particularly in resource-constrained settings. Further large-scale prospective studies are warranted to confirm its clinical utility.

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Statement of Transparency and Principles

• The authors declare no conflict of interest.

• The study was approved by the Research Ethics Committee of the authors' affiliated institution.

• The study data are available upon reasonable request.

• All authors contributed to the implementation of this research.

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