



DIAGNOSTIC UTILITY OF PRE TREATMENT NLR, PLR & MPV/PC IN CERVICAL CANCER STAGING

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Abstract

Background: Cervical cancer remains a significant public health issue, especially in developing countries. Early-stage identification is essential for initiating timely treatment and improving patient outcomes. Recent evidence suggests that systemic inflammatory markers such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and mean platelet volume to platelet count ratio (MPV/PC) may aid in predicting cancer progression.

Objective: To evaluate the diagnostic utility of pretreatment NLR, PLR, and MPV/PC ratios in differentiating early (Stage I–II) and late (Stage III–IV) cervical cancer patients.

Methods: A prospective study was conducted on 100 newly diagnosed, treatment-naïve cervical cancer patients. NLR, PLR, and MPV/PC ratios were calculated using pretreatment complete blood counts. Receiver operating characteristic (ROC) curve analysis was employed to determine cut-off values. Statistical significance was assessed using t-tests and chi-square tests, with p-values <0.05 considered significant.

Results: NLR (cutoff 4): Sensitivity 64.5%, Specificity 78.3%, p <0.0001

PLR (cutoff 150): Sensitivity 74.2%, Specificity 71%, p <0.0001

MPV/PC (cutoff 4.8): Sensitivity 58.1%, Specificity 56.5%, p 0.134

PLR demonstrated the highest diagnostic sensitivity and strongest statistical association with late-stage disease, followed by NLR. MPV/PC showed a lower sensitivity and lacked statistical significance.

Conclusion: Pretreatment inflammatory markers, particularly PLR and NLR, are significantly associated with the stage of cervical cancer and can serve as cost-effective, non-invasive tools for

clinical risk stratification. Incorporating these parameters into routine pre-treatment evaluation may assist in early-stage identification and individualized treatment planning.

Keywords: Cervical cancer, Neutrophil-to-lymphocyte ratio (NLR), Platelet-to-lymphocyte ratio (PLR), Mean platelet volume (MPV), Platelet count, Hematologic biomarker Cervical cancer, Neutrophil-to-lymphocyte ratio (NLR), Platelet-to-lymphocyte ratio (PLR), Mean platelet volume (MPV), Platelet count, Hematologic biomarkers, Cancer Staging, Inflammatory markers.

1. Introduction

Globally, cervical cancer is the fourth most common cancer in women, with around 660 000 new cases in 2022. In the same year, about 94% of the 350000 deaths caused by cervical cancer occurred in low- and middle-income countries. (1,2)

The incidence and mortality rate of cervical cancer are much higher in less developed countries, on part because of poor sanitation, insufficient medical infrastructure and economic conditions. HPV infection is the most important causative factor in cervical carcinogenesis (3).

Presently many tumor specific parameters are identified as prognostic factors for cervical cancer, and most of these factors are based on post operative pathological findings such as tumor size, lymph nodes status, depth of invasion and histological grade are identified as prognostic factors of cervical cancer (4-7).

Several studies has been established that systemic inflammation is involved in the progression of cancer at different stages such as initiation, promotion, invasion, and metastasis. (8-10) The systemic inflammation can be manifested as neutrophilia, thrombocytosis and relative lymphocytopenia detected in a complete blood count (CBC) examination (8-10). Hematological biomarkers classified as routine laboratory tests are easily available and affordable. Biopsy, as a gold standard, also needs a special facilities rarely established in remote areas. Therefore, CBC has a potential to be a hematological biomarkers in predicting the cancer progression. (10) Neutrophils and platelets supply the required bioactive molecules in neoplastic progression by providing angiogenic, epithelial, and stromal growth factors, as well as matrix-remodeling enzymes (11). In addition, the imbalance in the innate and adaptive immune systems, as reflects by lymphocytopenia and an impaired T lymphocytic response compromises the effectiveness of host-tumor immune responses (12). The progression of the malignancies to the advanced stage are marked with neutrophilia, thrombocytosis and lymphocytopenia (10). Therefore, the purpose of this study is to investigate NLR and PLR as the hematological markers in predicting the staging of the cervical cancer.

Recent studies have shown that both inflammatory reaction and immune status are prognostic factors of tumor formation. (13,14,17) Tumor-associated inflammatory responses consist of inflammatory cells and a series of inflammatory mediators. Together, these generate a tumor-related inflammatory microenvironment and play vital roles in the pathogenesis and progression of tumors. (14,17) On the other hand, tumor-induced inflammatory responses can lead to changes in hematological components such as neutrophils, lymphocytes, monocytes, and platelets. (15,16,17)

The aim of this study is to investigate whether pretreatment NLR, PLR, & MPV/ PC could be used in predicting the severity of cervical cancer patients.

In ammation has an important role in the initiation and progression of many cancers [2,3]. Various in ammatory mediators promote tumour growth, invasion, metastasis and angiogenesis [4]. In ammatory blood parameters like neutrophil- lymphocyte ratio and platelet lymphocyte ratio have been extensively studied in various cancers [5,6 In ammation has an important role in the initiation and progression of many cancers [2,3]. Various in ammatory mediators promote tumour growth, invasion, metastasis and angiogenesis [4]. In ammatory blood parameters like neutrophil- lymphocyte ratio and platelet lymphocyte ratio have been extensively studied in various cancers [5,6]

2. Materials And Methods

This prospective study included 100 newly diagnosed cases of cervical cancer enrolled at Shyam Shah Medical College, Rewa, over a one-year period (October 2023 to September 2024). Only treatment-naïve patients were included. Patients aged over 70 years, those with acute or chronic infections, autoimmune or cardiovascular diseases, or those who were pregnant were excluded. Individuals with a prior history of immunosuppressive therapy, radiotherapy, or chemotherapy were also excluded.

Cancer staging was performed according to the FIGO classification (Stages I–

IV). Based on this, patients were categorized into two groups: early stage (Stages I and II) and late stage (Stages III and IV). Blood samples were collected from all patients for complete blood count (CBC) analysis. From the CBC data, inflammatory markers including the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and mean platelet volume to platelet count ratio (MPV/PC) were calculated. These parameters were then correlated with the clinical stage of the disease to assess their potential role as predictive markers in cervical cancer progression. Biomarkers Measured

- Neutrophil-to-Lymphocyte Ratio (NLR): ANC / ALC
- Platelet-to-Lymphocyte Ratio (PLR): $Platelet\ count / ALC$
- Mean Platelet Volume to Platelet Count Ratio (MPV/PC): $MPV \div Platelet\ count$

Statistical Analysis:

Data analysis was done using SPSS. Normality was assessed using the Shapiro-Wilk test. Independent t-tests or Mann-Whitney U tests were used to compare NLR, PLR, and MPV between groups. Correlations with PANSS scores

were analyzed using Pearson's or Spearman's tests. A p-value <0.05 was considered statistically significant.

3. Results

Comparative Statistical Analysis of NLR, PLR, and MPV/PC to differentiate early (Stages I–II) and late (Stages III–IV) cervical cancer:

Parameter	NLR (cutoff 4)	PLR (Cutoff 150)	MPV/PC (Cutoff 4.8)
Sensitivity	64.5%	74.2%	58.1%
Specificity	78.3	71.0%	56.5%
Positive Predictive Value	57.1%	53.5%	37.5%
Negative Predictive Value	83.1%	86.0%	75.0%
Odd Ratio	6.545	7.044	1.800
Positive Likelihood Ratio (LR+)	2.972	2.559	1.336
Negative Likelihood ratio (LR-)	0.453	0.363	0.742
Accuracy	74.0%	72.0%	57.0%
Youden's Index (J)	0.428	0.452	0.146
Diagnostic Odd Ratio	6.562	7.050	1.800
Correlation Coefficient (r) with FIGO Stage	0.52 (p<0.0001)	0.49 (p<0.0001)	-0.15 (p=0.134)

A comparative statistical analysis was performed to evaluate the diagnostic performance of Neutrophil-to-Lymphocyte Ratio (NLR), Platelet-to-Lymphocyte Ratio (PLR), and Mean Platelet Volume-to-Platelet Count ratio (MPV/PC) in differentiating early (Stage I–II) from late (Stage III–IV) cervical cancer.

The NLR, with a cutoff value of 4, demonstrated a sensitivity of 64.5% and specificity of 78.3%, yielding a positive predictive value (PPV) of 57.1% and a negative predictive value (NPV) of 83.1%. The overall accuracy was 74.0%, with a Youden's Index of 0.428 and a diagnostic odds ratio (DOR) of 6.562. The positive likelihood ratio (LR+) and negative likelihood ratio (LR–) were 2.972 and 0.453, respectively. A moderate positive correlation was observed between NLR and FIGO stage ($r = 0.52$, $p < 0.0001$).

The PLR, with a cutoff of 150, showed the highest sensitivity among the three parameters (74.2%), with a specificity of 71.0%. The PPV and NPV were 53.5% and 86.0%, respectively. PLR had an accuracy of 72.0%, Youden's Index of 0.452, and a DOR of 7.050. The LR+ and LR– were 2.559 and 0.363, respectively. PLR also showed a moderate positive correlation with FIGO stage ($r = 0.49$, $p < 0.0001$).

The MPV/PC ratio, using a cutoff value of 4.8, demonstrated the lowest diagnostic performance, with a sensitivity of 58.1%, specificity of 56.5%, PPV of 37.5%, and NPV of 75.0%. The diagnostic accuracy was 57.0%, with a Youden's Index of 0.146, a DOR of 1.800, LR+ of 1.336, and LR– of 0.742. The correlation between MPV/PC and FIGO stage was weak and statistically insignificant ($r = -0.15$, $p = 0.134$).

Among the three markers, PLR exhibited the highest diagnostic odds ratio and Youden's index, indicating slightly superior overall performance, while NLR showed better specificity and accuracy. MPV/PC had limited utility in staging differentiation due to lower diagnostic indices and a lack of significant correlation with FIGO stage.

Both NLR and PLR showed a statistically significant positive correlation with FIGO stage, with correlation coefficients of 0.52 and 0.49, respectively ($p < 0.0001$ for both), suggesting a moderately strong association with disease advancement. These findings are consistent with existing literature. I Putu Yuda Prabawa et al. (2019)¹⁰ reported even stronger correlations of NLR ($r = 0.638$) and PLR ($r = 0.668$) with FIGO stage ($p < 0.001$), supporting their clinical relevance in disease stratification. Conversely, Justina Omoikhefe Alegbeleye et al. (2023)¹⁸ reported weaker, non-significant correlations for NLR (r

$= 0.195$, $p = 0.096$) and PLR ($r = 0.078$, $p = 0.511$), possibly due to a

smaller sample size, different population characteristics, or methodological variations.

In contrast, MPV/PC ratio did not show any significant correlation with FIGO stage in our study ($r = -0.15$, $p = 0.134$), and similar data are lacking in previous studies for comparison. This suggests that while platelet activation indices may reflect systemic inflammation, they may not directly mirror tumor burden or stage progression in cervical cancer.

Comparison of NLR

	Cut off	Sensitivity	Specificity	Area under curve	P-value
Present Study	4.0	64.5%	78.3%	0.78	<0.0001
I Putu Yuda Prabawa et al., 2019 ¹⁰	3.38	82%	71%	0.803	<0.001
Lin Wang et al., 2017 ²²	2.27	38.64%	82.48%	0.570	<0.0007
Justina Omoikhefe Alegbeleye et al., 2023 ¹⁸	1.38	81%	82%	0.456	0.60

In the present study, a neutrophil-to-lymphocyte ratio (NLR) cut-off of 4.0 demonstrated a sensitivity of 64.5% and specificity of 78.3%, with an area under the curve (AUC) of 0.78 ($p < 0.0001$), indicating good discriminatory power in differentiating early and late stages of cervical cancer. These findings are comparable to the study by I Putu Yuda Prabawa et al. (2019)¹⁰, who reported an NLR cut-off of 3.38 with higher sensitivity (82%) and slightly lower specificity (71%), and an AUC of 0.803 ($p < 0.001$).

Lin Wang et al. (2017) reported a lower cut-off value of 2.27, with modest sensitivity (38.64%) and higher specificity (82.48%), but a comparatively lower AUC (0.570), suggesting limited overall diagnostic utility.

Similarly, studies by Lekha Madhavan Nair et al. (2021)¹⁹, Mingxia Cheng et al. (2022)²⁰, and Qicheng Deng et al.²¹ reported elevated NLR values in cervical cancer patients, though detailed diagnostic metrics were not available. Interestingly, Justina Omoikhefe Alegbeleye et al. (2023)¹⁸ used a notably low cut-off (1.38) and reported high sensitivity (81%) and specificity (82%), yet with an AUC of only 0.456 and a non-significant p-value (0.60), indicating questionable diagnostic value. These variations in NLR cut-off values and diagnostic performance across studies may be attributed to differences in study design, population characteristics, and disease stage distribution. Nonetheless, the consistent statistical significance of elevated NLR in cervical cancer patients supports its potential as a simple, cost-effective inflammatory biomarker. Our study adds to this growing body of evidence, suggesting that an NLR cut-off of 4.0 may provide reliable discrimination between early and late-stage cervical cancer.

Comparison of PLR

Cut off	Sensitivity	Specificity	Area under curve	P-value
Present 150	74.2% Study	71%	0.80	<0.0001
I Putu Yuda Prabawa et al., 2019 ¹⁰	172.050 72%	70%	0.716	<0.001
Lin Wang et al., 2017 ²²	148.9 32.04%	88.54%	0.566	<0.0013
Justina Omoikhefe Alegbeleya et al. 2023	3.91 88%	94%	0.406	0.26

In the present study, a PLR cut-off of 150 demonstrated good diagnostic performance in differentiating early and late-stage cervical cancer, with a sensitivity of 74.2%, specificity of 71%, and an AUC of 0.80 ($p < 0.0001$). This is comparable to the findings by I Putu yuda Prabawa et al. (2019)¹⁰, who reported a cut-off of 172.05 with similar sensitivity (72%) and specificity (70%).

In contrast, Lin Wang et al. (2017) found lower sensitivity (32.04%) but higher specificity (88.54%) at a cut-off of 148.9, with a modest AUC (0.566). Other studies, such as those by Lekha madhvan Nair et al. (2021)¹⁹, Cheng et al. (2022)²⁰, and Quicheng Deng et al.²¹, reported elevated PLR values but lacked complete diagnostic metrics. An outlier was the study by Justina omoikhefe Alegbeleye et al. (2023), which reported a low AUC (0.406) despite high sensitivity and specificity, suggesting inconsistency.

Overall, PLR appears to be a useful and accessible inflammatory marker with potential to support staging in cervical cancer, though optimal cut-off values may vary by population.

The MPV/PC ratio shows a slight difference, with a cutoff of <4.8 , indicating that this parameter does not exhibit as strong distinction between early and late stages as NLR and PLR.

In a similar study performed by Qicheng Deng et al, 2021²¹, the cut of value of MPV/PC was found to be ≤ 4.1 , and discussed about the overall survival of the patients.

Notably, the MPV/PC ratio in the current study showed a non-significant inverse correlation with FIGO stage, which aligns with the limited data available on this parameter. Its potential role remains unclear and warrants further investigation in larger cohorts.

4. Conclusion

In conclusion, NLR and PLR are valuable, non-invasive biomarkers for predicting cervical cancer progression and distinguishing early from late stages,

with recommended cutoffs of ≥ 4 for NLR and ≥ 150 for PLR. These markers can aid early detection and treatment decisions, especially where advanced diagnostics are limited. Although MPV/PC showed limited relevance, incorporating NLR and PLR into clinical practice can improve patient risk stratification and personalized care.

References

1. Stelze, Dominik et al. Estimates of the global burden of cervical cancer associated with HIV. *The Lancet*. 2020. [https://doi.org/10.1016/S2214-109X\(20\)30459-9](https://doi.org/10.1016/S2214-109X(20)30459-9)
2. Beas-Lozano EL, Contreras S, Mac Donald-Jaramillo MA, Frayde-Aguilar C, CarrilloVidales J, Jaime-Casas S, Martinez-Cannon BA. Current management of cervical cancer in women living with HIV. *Critical Reviews in Oncology/Hematology*. 2024 Sep 24;104519.
3. Hull R, Mbele M, Makhafa T, Hicks C, Wang SM, Reis RM, Mehrotra R, MkhizeKwitshana Z, Kibiki G, Bates DO, Dlamini Z. Cervical cancer in low and middle-income countries. *Oncol Lett*. 2020 Sep;20(3):2058-2074.
4. Joo J, Shin HJ, Park B, et al. Integration pattern of human papillomavirus is a strong prognostic factor for disease-free survival after radiation therapy in cervical cancer patients. *Int J Radiat Oncol Biol Phys* 2017;98:654–61. [DOI] [PubMed] [GoogleScholar]
5. Chen L, Zhang F, Sheng XG, et al. Peripheral platelet/lymphocyte ratio predicts lymph node metastasis and acts as a superior prognostic factor for cervical cancer when combined with neutrophil: lymphocyte. *Medicine (Baltimore)* 2016;95:e4381. [DOI] [PMC free article] [PubMed] [Google Scholar]
6. Mao S, Dong J, Li S, et al. Prognostic significance of number of nodes removed in patients with node-negative early cervical cancer. *J Obstet Gynaecol Res* 2016;42:1317–25. [DOI] [PubMed] [Google Scholar]
7. Ma JY, Ke LC, Liu Q. The pretreatment platelet-to-lymphocyte ratio predicts clinical outcomes in patients with cervical cancer: A meta-analysis. *Medicine (Baltimore)*. 2018 Oct;97(43):e12897. doi: 10.1097/MD.00000000000012897. PMID: 30412089; PMCID: PMC6221620.
8. Grivennikov SI, Greten FR, Karin M. Immunity, inflammation, and cancer. *Cell*.2010;140:883–9. doi: 10.1016/j.cell.2010.01.025. [DOI] [PMC free article] [PubMed] [Google Scholar]
9. Grivennikov SI, Greten FR, Karin M. Immunity, inflammation, and cancer. *Cell*.2010;140:883–9. doi: 10.1016/j.cell.2010.01.025. [DOI] [PMC free article] [PubMed] [Google Scholar]
10. Prabawa IPY, Bhargah A, Liwang F, Tandio DA, Tandio AL, Lestari AAW, Budiana NG, Manuaba IBAP. Pretreatment Neutrophil-to-Lymphocyte ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) as a Predictive Value of Hematological Markers in Cervical Cancer. *Asian Pac J Cancer Prev*. 2019 Mar 26;20(3):863-868. doi: 10.31557/APJCP.2019.20.3.863. PMID: 30912405; PMCID: PMC6825764
11. Hanahan D, Weinberg RA. Hallmarks of cancer: The next generation. *Cell*. 2011;144:646–74. doi: 10.1016/j.cell.2011.02.013. [DOI] [PubMed] [Google Scholar]
12. Canna K, McArdle PA, McMillan DC, et al. The relationship between tumour Tlymphocyte infiltration, the systemic inflammatory response and survival in patients undergoing curative resection for colorectal cancer. *Br J Cancer*. 2005;92:651–4. doi: 10.1038/sj.bjc.6602419. [DOI] [PMC free article] [PubMed] [Google Scholar]
13. Del Prete A, Allavena P, Santoro G, et al. Molecular pathways in cancer-related inflammation. *Biochimica Medica* 2011; 21:264–275. [DOI] [PubMed] [Google Scholar]
14. Mantovani A, Allavena P, Sica A, et al. Cancer-related inflammation. *Nature* 2008; 454:436–444. [DOI] [PubMed] [Google Scholar]
15. Mizunuma M, Yokoyama Y, Futagami M, et al. The pretreatment neutrophil-to-lymphocyte ratio predicts therapeutic response to radiation therapy and concurrent chemoradiation therapy in uterine cervical cancer. *Int J ClinOncol* 2015; 20:989–996. [DOI] [PubMed] [Google Scholar]

16. Feng JF, Huang Y, Liu JS. Combination of neutrophil lymphocyte ratio and platelet lymphocyte ratio is a useful predictor of postoperative survival in patients with esophageal squamous cell carcinoma. *OncoTargets Ther* 2013; 6:1605–1612. [DOI] [PMC free article] [PubMed] [Google Scholar]
17. Chen L, Zhang F, Sheng XG, Zhang SQ, Chen YT, Liu BW. Peripheral platelet/ lymphocyte ratio predicts lymph node metastasis and acts as a superior prognostic factor for cervical cancer when combined with neutrophil: Lymphocyte. *Medicine (Baltimore)*. 2016 Aug;95(32):e4381. doi: 10.1097/MD.0000000000004381. PMID: 27512849; PMCID: PMC4985304.
18. Alegbeleye JO, John OC. A multicentre review of gynaecological cancer services in the South-South and South-East regions of Nigeria. *JMSCR*. 2023;11:1-7.
19. Nair LM, Babu A, KM JK, Kumar A, Mathews S, Joseph J, James FV. Prognostic Significance of Pre-treatment Serum Inflammatory Biomarkers on Survival in Patients with Carcinoma Cervix Treated by Radical Radiotherapy or Chemo-radiation. *Asian Pacific Journal of Cancer Care*. 2021 Oct 27;6(4):417-23.
20. Cheng M, Li G, Liu Z, Yang Q, Jiang Y. Pretreatment Neutrophil-to-Lymphocyte Ratio and Lactate Dehydrogenase Predict the Prognosis of Metastatic Cervical Cancer Treated with Combination Immunotherapy. *J Oncol*. 2022 Oct 18;2022:1828473.
21. Deng Q, Hou Y, Zhang X, Zan H. A systematic review of the predictive value of radiomics for nasopharyngeal carcinoma prognosis. *Medicine*. 2024 Aug 30;103(35):e39302.
22. Wang J, Zhou X, Liu Y, Li Z, Li X. Prognostic significance of neutrophil-to-lymphocyte ratio in diffuse large B-cell lymphoma: a meta-analysis. *PLoS One*. 2017 Apr 25;12(4):e0176008.