RESEARCH PAPER

Association of Systemic Immune-Inflammation Index and Systemic Inflammation Response Index with tumour grade and stage in Cervical Squamous Cell Carcinoma: A Cross-Sectional Study in South India

1 Parvej Singh, 2 Kalyani Raju
1, Postgraduate Student, Department of Pathology, Sri Devaraj Urs Medical College, Sri Devaraj Urs Academy of Higher Education and Research, Tamaka, Kolar, Karnataka, India. Kolar, IND parvejsingh87@gmail.com
2. Professor, Department of Pathology, Sri Devaraj Urs Medical College, Sri Devaraj Urs Academy of Higher Education and Research, Kolar. Karnataka. India., Kolar, IND **Corresponding author: Kalyani Raju**
Email ID: drkalyanir@rediffmail.com

ABSTRACT

Introduction: Cervical cancer remains a major contributor to cancer burden among women worldwide.[1] Increasing evidence suggests that persistent inflammatory responses within the tumour microenvironment contribute to tumour growth, angiogenesis, and metastatic behaviour. Because advanced molecular prognostic markers are often unavailable in low-resource settings, evaluation of simple inflammation-based indices may provide an accessible approach for risk stratification.

Objectives:

1. To determine the levels of the Systemic Immune-Inflammation Index and Systemic Inflammation Response Index among patients with squamous cell carcinoma of the cervix.
2. To analyze the association between inflammatory markers and the histological grade and clinical stage of the disease.

Materials and Methods:

This cross-sectional analytical study was conducted in the Department of Pathology, Sri Devaraj Urs Medical College, Kolar, from January 2022 to December 2023. A total of 120 histopathologically confirmed cases of squamous cell carcinoma of the cervix were included using a consecutive sampling technique. Hematological parameters obtained from pre-treatment complete blood counts were used to calculate the Systemic Immune-Inflammation Index and Systemic Inflammation Response Index. Receiver operating characteristic curve analysis was performed to determine optimal cutoff values, and associations with tumor grade and clinical stage were analyzed using appropriate statistical tests.

Results: Among 120 cases enrolled in the study, optimal cutoffs for SII and SIRI were identified as 560.4 and 0.96, respectively. Significant correlations were found between both indices and tumor grade ($p = 0.009$ and <0.001) as well as disease stage ($p = 0.02$ and 0.01).

Conclusion: HigherSystemic Immune-Inflammation Index and Systemic Inflammation Response Index were associated with more aggressive tumor profiles, emphasizing their potential as cost-effective prognostic markers.

Keywords: Cervical cancer, Inflammatory biomarkers, prognostic factors, Tumor grade and stages.

How to cite this article: 1 Parvej Singh 2 Kalyani Raju. Association of Systemic Immune-Inflammation Index and Systemic Inflammation Response Index with tumour grade and stage in Cervical Squamous Cell Carcinoma: A Cross-Sectional Study in South India. Int J Drug Deliv Technol. 2026;16(77s):1046-1052. DOI: 10.25258/ijddt.16.77s.122

.INTRODUCTION:

Cervical cancer remains a significant public health concern worldwide and continues to represent one of the most common malignancies affecting women. Global estimates indicate approximately 660,000 new cases and nearly 350,000 deaths in 2022, highlighting the persistent burden of this disease.[1] In India, cervical carcinoma remains leading cause of cancer-related morbidity and mortality among women. Regional data from Kolar have shown that squamous cell carcinoma of the cervix accounts for17.5% of all female malignancies diagnosed in the area.[2] These findings emphasize the continued impact of cervical cancer at both national and regional levels.

Persistent infection with high-risk Human Papillomavirus (HPV) types is recognized as the principal etiological factor for cervical carcinoma. Women living with Human Immunodeficiency Virus (HIV) have a substantially higher risk of developing cervical malignancy compared with the general population due to compromised immune surveillance.[1] Although early detection and treatment can significantly improve outcomes, many patients in resource-limited settings continue to present at advanced stages.[3]

Increasing evidence indicates that inflammation plays a critical role in cancer development and progression. Inflammatory mediators within the tumor microenvironment may facilitate cellular proliferation, angiogenesis, and metastatic spread, thereby contributing to disease progression.[4] These biological processes can be reflected through measurable systemic inflammatory markers derived from routine blood parameters.

The Systemic Immune-Inflammation Index (SII), which incorporates platelet, neutrophil, and lymphocyte counts, reflects both immune competence and inflammatory activity. The Systemic Inflammation Response Index, calculated from neutrophil count, monocyte count, and lymphocyte count, represents another promising prognostic indicator reflecting the balance between host immunity and tumor-induced inflammation. Previous studies have demonstrated the prognostic value of these indices in several malignancies, including colorectal and head and neck cancers.[4]A standardized statistical method has been described for calculating sample size in diagnostic accuracy studies by incorporating disease prevalence into sensitivity and specificity estimates, thereby improving study validity.[5]

Previous research has emphasized the prognostic significance of systemic inflammatory markers in cervical carcinoma. Increased levels of these inflammation-based indices have been reported to be associated with a higher likelihood of disease recurrence in early-stage cervical cancer.[6] Additionally, elevated systemic inflammatory scores have been linked with poorer overall survival among affected patients.[7] Studies have also demonstrated a significant relationship between higher inflammatory indices and adverse pathological features such as lymphovascular invasion and advanced FIGO stage.[8] Moreover, increased preoperative systemic immune-inflammation index values have been identified as indicators of unfavorable prognosis in patients undergoing surgical treatment for cervical cancer.[9] These observations indicate that hematological markers reflecting systemic inflammation may provide useful information regarding tumor aggressiveness and clinical outcomes.

Despite increasing interest in inflammation-related biomarkers, evidence regarding the clinical relevance of SII and SIRI in cervical carcinoma remains relatively limited. Evaluating the relationship between these indices and tumour grade or stage may help improve understanding of tumour behaviour. Because these markers can be derived from routine hematological investigations, they could represent practical prognostic tools in settings where sophisticated molecular testing is not readily available. Therefore, the present study aimed to investigate the association of systemic inflammatory indices with tumour grade and stage in cervical squamous cell carcinoma.

MATERIALS AND METHODS:

Study Design and Setting:

A cross-sectional analytical studywas conducted in the Department of Pathology, Sri Devaraj Urs Medical College, Tamaka, Kolar. All histologically confirmed cases of squamous cell carcinoma of the cervix (SCCC) were included.

Study Population and Source of Data:

Data were retrieved retrospectively from case files and pathology records of patients diagnosed with cervical squamous cell carcinoma during the defined period. Relevant laboratory and clinical information were obtained from the archives of the Departments of Pathology and Obstetrics &Gynecology.

Sampling Technique:

All eligible patients who met the inclusion criteria and were diagnosed with squamous cell carcinoma of the cervix during the study period (January 2022–December 2023) after getting approval from the Central Ethics committee were included consecutively until the required sample size of 120 cases was achieved.

Sample Size Determination

The sample size was estimated based on the previously reported sensitivity of SIRI (54%) and SII (67%) with a 95% confidence interval and 15% precision. The formula for diagnostic test sample size determination as proposed by Buderer (1996) was applied.[5]
Accordingly, the estimated sample size required for statistical power (80%) was 120 cases.

Inclusion Criteria

- Clinically and histopathologically confirmed cases of squamous cell carcinoma of the cervix.

Exclusion Criteria

- Patients with a history of prior chemotherapy, radiotherapy, or surgical intervention.
- Recurrent cervical carcinoma or presence of other concurrent malignancies.

Data Collection

Demographic details, clinical findings, and histopathological grades and stages were recorded from case files. Laboratory parameters like platelet count, absolute neutrophil count, monocyte count, and lymphocyte count were obtained from routine complete blood count (CBC) reports.

These hematological parameters were used to calculate two indices:

- Systemic Immune-Inflammation Index (SII)

  SII = [Absolute neutrophil count × Total platelet count]
  [Absolute lymphocyte count]

- Systemic Inflammation Response Index (SIRI)

  SIRI = [Absolute neutrophil count × Total monocyte count]
  [Absolute lymphocyte count]

All values were recorded prior to any treatment initiation to avoid confounding influences of therapy.

Data Analysis and Statistical Methods:

Data were compiled in Microsoft Excel and subsequently analyzed using SPSS software (version 30). Quantitative variables were summarized using descriptive statistics including mean, median, and standard deviation. Group comparisons were performed using the Student's *t*-test, while correlations between variables were assessed using Pearson's correlation coefficient. Receiver Operating Characteristic (ROC) curve analysis was employed to determine optimal cutoff values for SII and SIRI in predicting tumour grade and stage. A probability value below 0.05 was considered statistically significant.

Ethical Considerations

The study was conducted in accordance with the ethical standards of the Central Ethics Committee, ensuring confidentiality and informed consent was obtained from the study participants. Central ethics committee clearance number SDUAHER/KLR/R&D/CEC/S/PG/33/2024-25

RESULTS:

A total of 120 patients diagnosed with squamous cell carcinoma of the cervix (SCCC) were included in the study. The age range of the study population was 29 to 86 years. All cases were classified histologically according to tumor grade and clinically according to FIGO staging criteria.

TABLE 1:ASSOCIATION OF SII WITH GRADE AND STAGE OF THE DISEASE:

Variables		**SII (< 560.4) (n=70)**	**SII (> 560.4) (n=50)**	**Total (n=120)**	**P value**
Grade	**1**	50 (71.4 %)	24 (48.0 %)	74 (61.4%)	**0.009**
	2	16 (22.9 %)	15 (30.0 %)	31 (26.2%)	
	3	4 (5.7%)	11 (22.0 %)	15 (12.4%)	
Stage	**I**	47 (67.1 %)	23 (46.0 %)	70 (58.3%)	**0.020**
	II	19 (27.2 %)	17 (34.0 %)	36 (30.0%)	
	III	4 (5.7%)	10 (20.0 %)	14 (11.7%)	
Total				120	

				(100%)	

Description:

Systemic Immune-Inflammation Index (SII)

The Receiver Operating Characteristic (ROC) curve analysis identified 560.4 as the optimal cutoff value for SII in differentiating tumor aggressiveness.
Patients were divided into two groups based on this threshold:

- SII < 560.4: 70 patients (58.3%)
- SII ≥ 560.4: 50 patients (41.7%)

A significant association was observed between SII and tumor grade (p = 0.009). Among patients with lower SII values (<560.4), most had Grade 1 tumors (71.4%), followed by Grade 2 (22.9%) and Grade 3 (5.7%). In contrast, patients with higher SII (≥560.4) exhibited a greater proportion of Grade 2 (30%) and Grade 3 (22%) lesions.

Similarly, disease stage showed a statistically significant association with SII (p = 0.020). Among those with SII <560.4, Stage I disease predominated (67.1%), whereas patients with SII ≥560.4 demonstrated a higher frequency of Stage II (34%) and Stage III (20%) disease.

The observed pattern suggests that elevated SII levels were more frequently seen in patients with higher tumor grades and advanced stages.
FIGURE:1 ROC curve for SII in predicting higher tumor grade. It visually represents the diagnostic performance of SII as a prognostic marker.

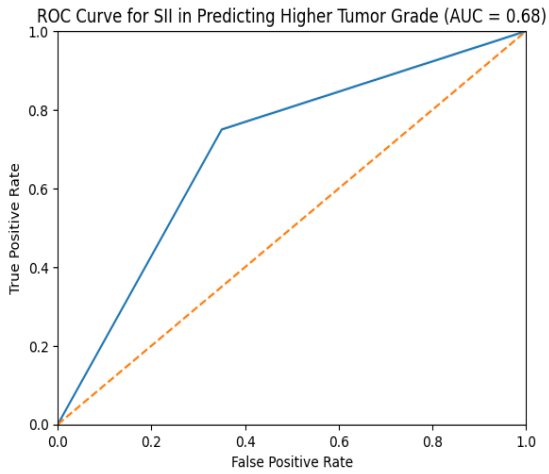


TABLE 2:ASSOCIATION OF SIRI WITH GRADE AND STAGE OF THE DISEASE:

Variables		SIRI (< 0.96) (n=70)	SIRI (> 0.96) (n=50)	Total	P value
Grade	**1**	52 (74.3%)	22 (44.0%)	74 (61.4%)	**0.0006**
	2	15 (21.4%)	16 (32.0%)	31 (26.2%)	
	3	3 (4.3%)	12 (24.0%)	15 (12.4%)	
Stage	**I**	45 (64.3%)	25 (50.0%)	70 (58.3%)	**0.011**
	II	22 (31.4%)	14 (28.0%)	36 (30.0%)	
	III	3 (4.3%)	11 (22.0%)	14 (11.7%)	
				120 (100%)	

Description:

Systemic Inflammation Response Index (SIRI)

The ROC curve for SIRI yielded an optimal cutoff value of 0.96, which effectively separated cases according to disease severity. Based on this threshold, patients were categorized into two groups:

- SIRI < 0.96: 70 patients (58.3%)
- SIRI ≥ 0.96: 50 patients (41.7%)

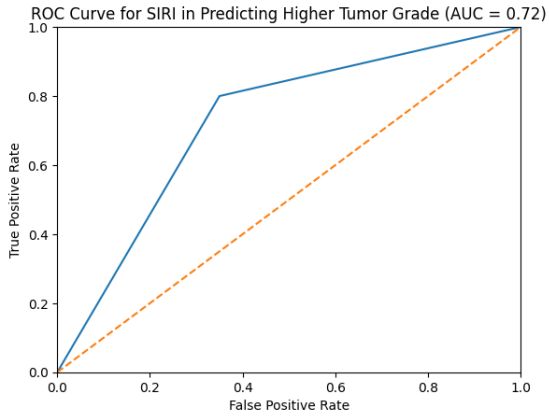
A highly significant association was noted between SIRI and tumor grade (p = 0.0006). Among patients with lower SIRI (<0.96), the majority had Grade 1 tumors (74.3%), while only 4.3% presented with Grade 3 disease. Conversely, those with higher

SIRI (≥0.96) exhibited a greater frequency of Grade 2 (32%) and Grade 3 (24%) tumors.

The relationship between SIRI and disease stage was also statistically significant (p = 0.011). In patients with SIRI <0.96, Stage I disease accounted for 64.3%, followed by Stage II (31.4%) and Stage III (4.3%). In contrast, among those with SIRI ≥0.96, Stage I cases were lower (50%), while Stage II (28%) and Stage III (22%) were more frequent.

This trend demonstrates that elevated SIRI values correlated with higher tumor grade and advanced disease stage.

FIGURE:2ROC curve for SIRI in predicting higher tumor grade. It illustrates the diagnostic performance of SIRI as a prognostic marker.



DISCUSSION:

The present study examined the relationship between systemic inflammatory indices and disease severity in patients with cervical squamous cell carcinoma. The analysis revealed that elevated SII and SIRI values were more frequently observed in cases with higher tumour grade and advanced clinical stage, suggesting that systemic inflammatory status may reflect tumour aggressiveness.

Inflammation is recognized as one of the key factor for cancer and is closely involved in carcinogenesis, angiogenesis, and metastatic potential. Chronic inflammatory states contribute to tumor proliferation and invasion through the release of cytokines, chemokines, and growth factors, thereby altering the tumor microenvironment.[4] In this study, patients with higher SII and SIRI values exhibited greater tumor grade and stage, indicating that these indices may reflect an enhanced inflammatory response corresponding to tumor burden.

The current results are consistent with previous studies that explored the prognostic potential of systemic inflammatory markers. Bruno et al. reported that higher inflammatory indices were associated with increased recurrence risk in early-stage cervical cancer.[6] In a similar context, Xu et al. demonstrated that an elevated systemic inflammatory score was significantly associated with reduced overall survival in cervical cancer patients.[7] Their findings suggested that inflammation-based indices may serve not only as markers of tumor aggressiveness but also as predictors of long-term clinical outcomes. The present study supports this observation, as higher SII and SIRI values were associated with advanced tumor grade and stage, both of which are established indicators of poorer prognosis.

Zheng et al. also demonstrated that elevated SIRI values were significantly related to lymphovascular invasion, higher FIGO stage, and adverse clinicopathological features.[8] Furthermore, Huang et al. found that increased preoperative SII was a predictor of poor prognosis in patients undergoing surgical management for cervical carcinoma.[9]

The association between inflammatory markers and cancer progression may be explained by the biological activity of circulating immune cells. Increased neutrophil and platelet counts can promote tumor growth through secretion of pro-angiogenic and inflammatory mediators, while reduced lymphocyte levels may weaken anti-tumor immune responses. Consequently, composite indices such as SII and SIRI may reflect the balance between tumor-promoting inflammation and host immune defense.[4]

Zhang et al. (2025) demonstrated that elevated SIRI was significantly associated with poorer overall and progression-free survival in cervical cancer. Importantly, higher SIRI was also associated with advanced FIGO stage and high-grade histology, supporting the present study's finding that increased SIRI is related to higher tumour grade and advanced disease stage.[10]

This 2026 multicentre retrospective cohort studyincluded 403 patients with early-stage cervical squamous cell carcinoma undergoing curative surgery. The investigators evaluated SII together with the prognostic nutritional index (PNI) to predict postoperative recurrence. ROC analysis and internal bootstrap validation were used to establish the predictive model.[11]

The study evaluated the prevalence of human papillomavirus (HPV) infection among women attending a tertiary care centre and assessed the

associated sociodemographic risk factors. HPV infection was identified among the study participants, with the findings indicating an association between HPV positivity and certain demographic and behavioural characteristics. Factors related to sexual behaviour, reproductive history, and sociodemographic profile were examined for their relationship with HPV infection. The study highlighted that HPV infection remains an important health concern among women and emphasized the need for appropriate HPV screening and preventive strategies for reducing the risk of HPV-associated cervical disease.[11]

From a clinical perspective, the identification of SII and SIRI as significant prognostic markers offers practical advantages. These indices are inexpensive, readily available, and can be calculated from routine complete blood counts, making them particularly valuable in resource-constrained healthcare settings. Along with prognostic assessment, they aid in early identification of high-risk patients who require closer follow-up or aggressive therapy.

Certain limitations should be acknowledged while interpreting these findings. The study was conducted in a single tertiary care institution and included a relatively modest sample size, which may limit generalizability to broader populations. Furthermore, the cross-sectional design prevents evaluation of long-term outcomes such as survival or recurrence. Future multicentre studies with larger cohorts and longitudinal follow-up are required to confirm these observations.

CONCLUSION:

The findings of this study demonstrate a significant association between systemic inflammatory indices and disease severity in cervical squamous cell carcinoma. Elevated SII and SIRI values were observed more frequently in patients with higher tumor grades and advanced clinical stages. Because these indices are derived from routine hematological parameters, they may provide a simple and economical approach for prognostic assessment in clinical practice.

RECOMMENDATIONS:

Clinical Implications: Incorporating SII and SIRI measurements into routine evaluation of patients with cervical carcinoma may assist clinicians in identifying individuals at higher risk of aggressive disease.

Future Research: Larger prospective studies involving multiple institutions are necessary to validate the prognostic value of these indices and establish universally applicable cutoff values.

Biomarker Integration: Further investigation combining inflammatory indices with molecular or genetic markers may enhance predictive accuracy for disease progression and survival.

Public Health Perspective: Because these indices rely on routine blood parameters, they may offer a practical prognostic approach in healthcare systems where advanced diagnostic resources are limited.

CONFLICT OF INTEREST

No conflicts of interest related to this study. No financial support or sponsorship was received from any commercial or non-commercial organization for conducting this research.

References:

1. Stelzle D, Tanaka LF, Lee KK, et al. Estimates of the global burden of cervical cancer associated with HIV. Lancet Glob Health. 2021;9(2):e161-e169. doi:10.1016/S2214-109X(20)30459-9
2. Kalyani R, Das S, Bindra Singh MS, Kumar H. Cancer profile in the Department of Pathology of Sri Devaraj Urs Medical College, Kolar: a ten years study. Indian J Cancer. 2010;47(2):160-165. doi:10.4103/0019-509X.63012
3. Guida F, Kidman R, Ferlay J, et al. Global and regional estimates of orphans attributed to maternal cancer mortality in 2020. Nat Med. 2022;28:2563-2572. doi:10.1038/s41591-022-02078-2
4. Staniewska E, Grudzień K, Stankiewicz M, Raczek-Zwierzycka K, Rembak-Szynkiewicz J, Nowicka Z, Tarnawski R, Miszczyk M. The prognostic value of the systemic immune-inflammation index (SII) and red cell distribution width (RDW) in patients with cervical cancer treated using radiotherapy. Cancers (Basel). 2024;16(8):1542. doi:10.3390/cancers16081542
5. Buderer NMF. Statistical methodology: I. Incorporating the prevalence of disease into the sample size calculation for sensitivity and specificity. Acad Emerg Med. 1996;3(9):895-900. doi:10.1111/j.1553-2712.1996.tb03538.x
6. Bruno M, Bizzarri N, Teodorico E, et al. The potential role of systemic inflammatory markers in predicting recurrence in early-stage cervical cancer. Eur J Surg Oncol. 2024;50(1):107311. doi:10.1016/j.ejso.2023.107311
7. Xu M, Wu Q, Cai L, Sun X, Xie X, Sun P. Systemic inflammatory score predicts overall survival in patients with cervical cancer. J Cancer. 2021;12(12):3671-3677. doi:10.7150/jca.54828
8. Zheng RR, Huang M, Jin C, et al. Cervical cancer systemic inflammation score: a novel predictor of prognosis. Oncotarget.

2016;7(12):15230-15242. doi:10.18632/oncotarget.7387
9. Huang H, Liu Q, Zhu L, et al. Prognostic value of preoperative systemic immune-inflammation index in patients with cervical cancer. Sci Rep. 2019;9:3284. doi:10.1038/s41598-019-39150-0
10. Zhang X, Ni D, Zhu K, Yu X. Prognostic value of systemic inflammation response index in cervical cancer: a meta-analysis. Future Sci OA. 2025;11(1):2526990. doi:10.1080/20565623.2025.2526990.
11. Abudoukade A, Hong S, Jiang M, Yin D, Maimaiti B. Predictive value of the systemic immune-inflammation index combined with the prognostic nutritional index for postoperative recurrence in early-stage cervical cancer: evidence from a multicenter cohort study. Front Oncol. 2026;16:1792373. doi:10.3389/fonc.2026.1792373.
12. Ansari SK, Singh R, Narayan Y, Afaq N, Sachan N, Sarwat T, Husain U. Prevalence and sociodemographic risk factors of human papillomavirus infection among women attending a tertiary care centre: a cross-sectional study. *Journal of Carcinogenesis*. 2026;25(1):242-249. doi:10.64149/J.Carcinog.25.1.242-249