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Preoperative Platelet-to-Lymphocyte Ratio and Serum Albumin as Predictors of Clinicopathological Outcomes in Cervical Cancer

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Abstract

***Background*:** Cervical cancer remains one of the most prevalent cancers globally and a leading cause of cancer-related deaths among women. Early detection and precise prognostic assessment are vital for enhancing outcomes in cervical cancer patients. The purpose of this study is to evaluate the predictive value of preoperative PLR and serum albumin levels for clinicopathological outcomes in cervical cancer. ***Aim of the Study*:** The aim of the study was to evaluate the predictive value of preoperative Platelet-to-Lymphocyte Ratio and Serum Albumin levels on clinicopathological outcomes in patients with cervical cancer. ***Methods*:** This cross-sectional study, conducted at the Department of Gynecological Oncology, BSMMU, Dhaka (July 2022–June 2023), analyzed 120 women with early-stage (IA-IIA) cervical cancer to assess the association of PLR, S.Albumin for clinicopathological outcome using SPSS 27.0. Data included socio-demographics, clinical details, and serum markers. ***Results*:** The majority of participants were aged 30-44 years (46.7%) and married before 18 years of age (83.3%). Most had a PLR <128.3 (62.2%) and SA ≥3.5 (57.8%). Larger tumors (2-4 cm), higher prevalence of lymphovascular space invasion (LVSI), and deeper stromal invasion (≥½ thickness) were significantly associated with higher PLR (≥128.3) and lower SA (<3.5) ($p < 0.001$, $p = 0.006$). ***Conclusion*:** Preoperative Platelet-to-Lymphocyte Ratio and Serum Albumin levels can serve as valuable predictors of clinicopathological outcomes in cervical cancer, aiding in personalized treatment strategies.

Keywords: Preoperative, Platelet-to-Lymphocyte Ratio, Serum Albumin, Predictors, Cervical Cancer.

INTRODUCTION

Cervical cancer remains one of the most prevalent cancers globally and a leading cause of cancer-related deaths among women [1]. It ranks as the third most frequently diagnosed cancer and the second major cause of cancer mortality in women, with approximately 500,000 new cases and 250,000 deaths annually [2]. In 2022, an estimated 6,60,000 new cases and 3,50,000 deaths were reported worldwide [3]. It is also the fourth leading cause of cancer death among women, with morbidity and mortality rates surpassed only by breast cancer [4]. These figures highlight the substantial global impact of cervical cancer, emphasizing its significance as a critical public health concern.

Early detection and precise prognostic assessment are vital not only for enhancing outcomes but also individualizing treatment in cervical cancer patients. Prognostic factors such as tumor size, lymph node involvement, depth of invasion, and histologic grade,

and lymphovascular space invasion (LVSI) play a crucial role in guiding treatment decisions [5-7]. For patients with early stage cervical cancer though surgery is more suitable than CCRT but both are equally effective [8]. However, tumor recurrence significantly worsens prognosis due to limited treatment options [9, 10]. Monotherapy therapy is the treatment of choice to avoid any gynecological complications. Currently, aside from the squamous cell carcinoma antigen, no robust laboratory biomarkers exist to reliably predict recurrence or clinical outcomes [11]. This underscores the urgent need for identifying reliable preoperative prognostic markers to enable personalized treatment approaches and improve survival rates.

The systemic inflammatory response is pivotal in cancer progression and the facilitation of metastatic spread [12, 13]. Growing evidence highlights the significant interplay between inflammation, nutrition, and the initiation and advancement of various cancers, including renal cell carcinoma (RCC) [14]. Host inflammatory reactions have been identified as key drivers of tumor development and progression, underscoring the critical role of inflammation-related factors in unraveling cancer biology [15].

Several hematological markers have gained prominence as indicators of systemic inflammation and nutritional status, with increasing importance in cancer prognosis. Key among these are the platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-albumin ratio (PAR), which serve as significant clinical markers of inflammation [16]. Serum albumin and PLR, in particular, have been extensively studied, with recent research demonstrating a association between preoperative PLR and prognosis in pancreatic cancer [17, 18]. These markers offer a convenient and clinically applicable method for outcome prediction.

Despite advancements in the management of cervical cancer, the lack of reliable, cost-effective prognostic biomarkers remains a significant challenge in improving personalized treatment approaches. Current prognostic factors, such as tumor size, lymph node involvement, and histologic grade, provide valuable insights but fail to capture the systemic factors contributing to disease progression and recurrence. Emerging evidence suggests that systemic inflammatory and nutritional markers, such as platelet-to-lymphocyte ratio (PLR) and serum albumin, hold promise as accessible and clinically relevant tools for predicting cancer outcomes. However, their prognostic utility in cervical cancer remains underexplored and inconsistent across studies. The purpose of this study is to evaluate the predictive value of preoperative PLR and serum albumin levels for clinicopathological outcomes in cervical cancer.

Objective

The aim of the study was to evaluate the predictive value of preoperative Platelet-to-Lymphocyte Ratio and Serum Albumin levels on clinicopathological outcomes in patients with cervical cancer.

METHODOLOGY & MATERIALS

This cross-sectional study was conducted at the Department of Gynecological Oncology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, between July 2022 and June 2023, focusing on women with biopsy-confirmed cervical cancer. A total of 120 participants were recruited, all in early stages (IA-IIA) of cervical cancer.

Inclusion Criteria:

- Women diagnosed with cervical cancer confirmed by histopathology report obtained from biopsy.
- Clinical staging suggestive of early-stage cervical cancer, who underwent radical hysterectomy and bilateral pelvic lymphadenectomy.
- Had given consent to participate in the study.

Exclusion Criteria:

- Known cases of acute or chronic infection.
- Undergoing fertility-saving surgery.
- Received neoadjuvant chemotherapy.
- Received preoperative radiotherapy or corticosteroids.
- Women with known hematological diseases, autoimmune diseases, infectious diseases, or concomitant malignant tumors.
- Women with any other cancer.
- Women receiving any anticoagulant drugs before enrollment.

Informed consent was obtained from all participants, ensuring confidentiality and voluntary participation. A thorough medical history was taken, and clinical examinations were conducted. Cervical cancer staging was performed based on the FIGO 2018 classification, categorizing stages into early stage (IA–IIA). Serum albumin and platelet-to-lymphocyte ratio (PLR) levels were measured, with a PLR value of 128.3 used as the cut-off to categorize PLR as high or low, and serum albumin levels categorized using a cut-off of 3.5 g/dL. Data were collected using a pre-designed, semi-structured questionnaire, capturing socio-demographic details, clinical variables (age at first sexual intercourse, age at first childbirth, parity, BMI, and history of oral contraceptive use), and laboratory results. Analyses were performed using SPSS version 27.0, with continuous variables presented as means with standard deviations and categorical variables as counts with percentages. Comparisons of various clinicopathological outcomes were conducted using t-tests or chi-square tests, with a significance level set at $p < 0.05$. Univariate and multivariate logistic regression models were used to

assess associations while adjusting for potential confounding variables. The study was approved by the Institutional Review Board (IRB) of Bangabandhu Sheikh Mujib Medical University (BSMMU), ensuring compliance with ethical guidelines and patient confidentiality. The primary outcome variables included the association of PLR and serum albumin with various clinicopathological outcomes, such as tumor size, lymphovascular space invasion (LVSI) and cervical stromal invasion, in women diagnosed with cervical cancer.

RESULTS

Table 1: Demographic Characteristics of the Study Participants (n = 120)

Variables		Frequency (n)	Percentage (%)
Patient's Age (yrs)	30 – 44	56	46.7
	45 – 59	51	42.5
	≥ 60	13	10.8
	Mean ± SD	45.14 ± 9.03	
Age at Marriage	<18 years	100	83.3
	≥ 18 years	20	16.7
Age at First Delivery	<18 years	75	62.5
	≥ 18 years	45	37.5
Parity	1 – 2	28	23.3
	3 – 4	76	63.3
	≥5	16	13.3
Oral Contraceptive Pills Use	Yes	79	65.8
	No	41	34.2
Duration of OCP Use	≥5 years	58	73.4
	<5 years	21	26.6
BMI (kg/m²)	Underweight (<18.5)	35	29.2
	Normal (18.5 – 24.9)	75	62.5
	Overweight (25.0 – 29.9)	10	8.3
	Mean ± SD	20.54 ± 2.82	

Table 1 shows the distribution of respondents according to socio-demographic parameters. Nearly half (46.7%) of the respondents were aged between 30-44 years, with an average age of 45.14 ± 9.03 years. The majority (83.3%) of respondents married before the age of 18 years, while 62.5% had their first delivery before the age of 18 years. In terms of parity, most respondents (63.3%) had 3-4 children. Regarding oral contraceptive use, 65.8% of respondents used oral contraceptive pills, with 73.4% using them for more than 5 years. As for Body Mass Index (BMI), the majority (62.5%) of respondents had a normal BMI (18.5 – 24.9 kg/m²), with 29.2% being underweight and 8.3% overweight.

Table 2: Hematological Characteristics of the Study Participants (n = 120)

Parameters		Frequency (n)	Percentage (%)
Platelet to Lymphocyte Ratio (PLR)	≥128.3	45	37.8
	<128.3	75	62.2
	Mean ± SD	139.46 ± 104.61	
Serum Albumin Level	≥3.5	69	57.8
	<3.5	51	42.2
	Mean ± SD	3.60 ± 0.60	

Table 2 shows the distribution of respondents according to Platelet to Lymphocyte Ratio (PLR) and Serum Albumin Level. PLR was classified into two categories: ≥128.3 and <128.3. A majority (62.2%) of respondents had a PLR less than 128.3, while 37.8% had a PLR of 128.3 or greater. The mean PLR across the sample was 139.46 ± 104.61. Regarding Serum Albumin Level, 57.8% of respondents had a level of ≥3.5g/dl, while 42.2% had a level of less than 3.5 g/dL. The mean Serum Albumin Level was 3.60 ± 0.60.

Table 3: Comparison of Tumor Size Across Preoperative Platelet-to-Lymphocyte Ratio (PLR) and Serum Albumin (SA) Levels (n = 120)

Tumor Size	PLR		SA		p-value
	≥128.3 (n=45)	<128.3 (n=75)	≥3.5 (n=69)	<3.5 (n=51)	
2-4 cm	10 (22.2%)	25 (33.3%)	20 (29.0%)	15 (29.4%)	
< 2 cm	35 (77.8%)	50 (66.7%)	49 (71.0%)	36 (70.6%)	
Mean ± SD	1.45 ± 0.78	2.01 ± 0.85	1.88 ± 0.80	2.35 ± 0.82	< 0.001

Table 3 shows the comparison of tumor size among the study participants, stratified by their preoperative Platelet-to-Lymphocyte Ratio (PLR) and Serum Albumin (SA) levels. Participants with PLR ≥128.3 predominantly had tumors smaller than 2 cm (77.8%), whereas those with PLR <128.3 had a higher proportion of larger tumors between 2–4 cm (33.3%). Similarly, participants with SA ≥3.5g/dl had a higher percentage of smaller tumors (<2 cm, 71.0%), while those with SA <3.5g/dl were more likely to have larger tumors (2–4 cm, 29.4%). The mean tumor size increased with elevated PLR and decreased SA levels, with significant differences observed across groups ($p < 0.001$).

Table 4: Association of Lymphovascular Space Invasion (LVSI) with Preoperative Platelet-to-Lymphocyte Ratio (PLR) and Serum Albumin (SA) Levels (n = 120)

LVSI	PLR		SA		p-value
	≥128.3 (n=45)	<128.3 (n=75)	≥3.5 (n=69)	<3.5 (n=51)	
Present (n=17)	3 (6.7%)	14 (18.7%)	8 (11.6%)	9 (17.6%)	0.006
Absent (n=103)	42 (93.3%)	61 (81.3%)	61 (88.4%)	42 (82.4%)	

Table 4 presents the association between lymphovascular space invasion (LVSI) and preoperative Platelet-to-Lymphocyte Ratio (PLR) and Serum Albumin (SA) levels in the study participants. A significantly higher proportion of participants with LVSI present had PLR <128.3 (18.7%) and SA <3.5g/dl (17.6%), compared to those without LVSI, where the majority had PLR ≥128.3 (93.3%) and SA ≥3.5g/dl (88.4%). The p-value of 0.006 indicates a statistically significant association between LVSI and both PLR and SA levels.

Table 5: Association of Depth of Stromal Invasion with Preoperative Platelet-to-Lymphocyte Ratio (PLR) and Serum Albumin (SA) Levels (n = 120)

Depth of Stromal Invasion	PLR		SA		p-value
	≥128.3 (n=45)	<128.3 (n=75)	≥3.5 (n=69)	<3.5 (n=51)	
≥ ½ Thickness (n=71)	22 (48.9%)	49 (65.3%)	30 (43.5%)	41 (80.4%)	0.006
< ½ Thickness (n=49)	23 (51.1%)	26 (34.7%)	39 (56.5%)	10 (19.6%)	

Table 5 shows the association between the depth of stromal invasion (≥½ thickness vs. <½ thickness) and preoperative Platelet-to-Lymphocyte Ratio (PLR) and Serum Albumin (SA) levels. Among patients with stromal invasion of ≥½ thickness, a higher proportion had PLR values <128.3 (65.3%) and SA levels <3.5 (80.4%). In contrast, patients with stromal invasion of <½ thickness had a significantly higher proportion with PLR values ≥128.3 (51.1%) and SA levels ≥3.5 (56.5%). The association between stromal invasion depth and both PLR and SA levels was statistically significant ($p = 0.006$).

DISCUSSION

Surgical intervention is a key approach in managing early-stage cervical cancer, complemented by radiotherapy or concurrent chemoradiotherapy (CCRT) in more advanced stages. These treatment modalities aim to optimize outcomes while minimizing treatment-associated morbidity. Recently, systemic inflammation markers have gained attention for their potential role in predicting cancer progression and tailoring therapeutic strategies. Against this backdrop, the present study was conducted among 120 cervical cancer patients to assess the predictive value of preoperative Platelet-to-Lymphocyte Ratio (PLR) and Serum Albumin levels, examining their predictive value with clinicopathological outcome.

In our study, the demographic profile of participants revealed a mean age of 45.14 ± 9.03 years, with nearly half (46.7%) of the respondents falling within the age range of 30–44 years. This aligns closely with findings from another study, which reported a mean age of 41.8 ± 11.5 years in a similar cohort [19]. Additionally, the majority (83.3%) of our participants married before the age of 18, a trend reflective of early marriage practices common in certain regions. This is further supported by the observation that 62.5% of participants had their first delivery before the age of 18. Regarding parity, most participants (63.3%) had 3–4 children, emphasizing the high parity often associated with cervical cancer. Oral contraceptive use was reported by 65.8% of participants, with 73.4% of these using it for over five years, highlighting its potential influence as a risk factor in this population. Finally, the majority (62.5%) of participants had a normal BMI, comparable to standard population distributions, though a notable

proportion (29.2%) were underweight. The relatively low average BMI among Bangladeshi women does not offer protection against cervical cancer, with persistent HPV infection being the primary causal factor. These findings underscore the multifactorial nature of demographic influences on cervical cancer outcomes.

In our study, the majority of respondents (62.2%) had a Platelet to Lymphocyte Ratio (PLR) below 128.3, with a mean PLR of 139.46 ± 104.61, indicating variability in inflammatory status. Regarding Serum Albumin Levels, 57.8% had levels above 3.5g/dl, suggesting adequate nutritional status, while 42.2% had levels below 3.5g/dl, which may reflect underlying nutritional deficiencies or inflammatory conditions that could adversely affect prognosis. This variation in serum albumin levels emphasizes the need to monitor nutritional and inflammatory markers in patients for better disease management and outcome prediction.

Our study revealed a significant association between tumor size and preoperative inflammatory and nutritional markers, specifically the Platelet-to-Lymphocyte Ratio (PLR) and Serum Albumin (SA) levels. Participants with a PLR ≥128.3 predominantly had tumors smaller than 2 cm (77.8%), whereas those with a PLR <128.3 showed a higher proportion of tumors measuring between 2–4 cm (33.3%). Similarly, participants with an SA level ≥3.5g/dl were more likely to have smaller tumors (<2 cm, 71.0%), while those with an SA level <3.5g/dl had a higher likelihood of larger tumors (2–4 cm, 29.4%). The mean tumor size increased significantly with elevated PLR and decreased SA levels ($p < 0.001$). These findings align with the study by Gemer *et al*., [20], which reported that larger tumor sizes, particularly those exceeding 2 cm, were associated with more aggressive treatment approaches, including radiotherapy. Our results underscore the potential role of systemic inflammation and nutritional status in influencing tumor progression and shaping clinical management strategies.

A clear association was also observed between lymphovascular space invasion (LVSI) and preoperative PLR and SA levels. Participants with PLR <128.3 had a significantly higher prevalence of LVSI (18.7%) compared to those with PLR ≥128.3 (6.7%). Similarly, LVSI was more common in participants with SA <3.5 (17.6%) than in those with SA ≥3.5g/dl (11.6%). The statistically significant association ($p = 0.006$) underscores the potential role of inflammation and nutritional status in influencing the presence of LVSI.

The depth of stromal invasion also showed significant differences based on PLR and SA levels. Participants with stromal invasion ≥ ½ thickness were predominantly those with higher PLR (<128.3, 65.3%) and lower SA (<3.5g/dl, 80.4%). Conversely, participants with stromal invasion < ½ thickness had a higher proportion with lower PLR (≥128.3, 51.1%) and higher SA (≥3.5, 56.5%). These associations ($p = 0.006$) further suggest that elevated PLR and reduced SA levels may contribute to more extensive stromal invasion, highlighting the role of inflammation and nutritional status in tumor invasiveness.

Limitations of the Study

This study had some limitations:

- The study was conducted at a single institution, which may limit the generalizability of the results.
- The sample was not randomly selected, potentially introducing selection bias.
- The sample size was relatively small (120 patients), which may affect the statistical power of the findings.
- The study period was short, limiting the ability to assess long-term outcomes.
- The follow-up period was brief, and longer follow-up could provide more insight into the prognostic value of preoperative Platelet-to-Lymphocyte Ratio and Serum Albumin on overall survival and progression-free survival.

CONCLUSION

The study findings highlight a significant association between preoperative Platelet-to-Lymphocyte Ratio (PLR) and Serum Albumin levels with clinicopathological outcomes in cervical cancer. Elevated PLR was linked to larger tumor size, deeper stromal invasion while low serum albumin levels were associated with the presence of lymphovascular space invasion (LVSI). These results suggest that both PLR and serum albumin levels could serve as important predictors of tumor aggressiveness and prognosis, aiding in the identification of patients who may require more selective treatment based on their individual risk profiles.

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