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Relationship Between Albumin to Fibrinogen Ratio and Different Stages of Cervical Cancer in a Tertiary Care Center

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Abstract

Introduction: Cervical cancer is a significant global health concern, being the fourth most common cancer and leading cause of cancer death in women. Therefore, the purpose of this study was to determine the relationship of albumin-to-fibrinogen ratio in different stages of cervical cancer.

Aim of the study: The aim of the study was to assess the relationship between pretreatment albumin-to-fibrinogen ratio (AFR) and the stages of cervical cancer in a tertiary care center.

Methods: This cross-sectional analytical study, conducted at the Department of Gynecological Oncology, BSMMU, Dhaka, from July 2022 to June 2023, included 70 women with biopsy-confirmed cervical cancer, categorized into early-stage (IA-IIA) and advanced-stage (IIB-IV) groups. Data were collected using a semi-structured questionnaire and included socio-demographic and clinical variables, with analyses performed using SPSS version 27.0 to evaluate the relationship between cervical cancer stages and various factors.

Result: Nearly half (47.1%) of respondents were aged 30–44, with a mean age of 45.37 ± 9.54 years; 84.3% were housewives. About 44.3% were in FIGO stage I, and 50% had advanced-stage cancer. The mean AFR was 10.26 ± 1.47, decreasing significantly with higher stages. A negative correlation (r_s = -0.421, $p < 0.001$) showed AFR < 10.7 raised the odds of advanced cancer by 10.2 times (OR = 10.154, $p < 0.001$).

Conclusion: AFR decreases with advancing cervical cancer stages, showing potential as a predictive biomarker, with patients having AFR <10.7 being 10.2 times more likely to present with advanced-stage disease.

Keywords: Cervical cancer; Albumin-to-fibrinogen ratio; Staging; Prognosis; Tertiary care center

Introduction

Cervical cancer is a significant global health concern, being the fourth most common cancer diagnosed and the fourth leading cause of cancer death in women, with an estimated 604,000 new cases and 342,000 deaths worldwide in 2020 [1]. In Bangladesh, the GLOBOCAN 2020 database reports crude incidence and mortality rates for cervical cancer are 10.2 and 6.1 per 100,000, respectively [2]. Alarmingly, 84% of new cases and between 87 and 90% of deaths occur in low- and middle-income countries [3] underscoring the critical need for studies assessing the relationship between pretreatment factors, such as the albumin-to-fibrinogen ratio (AFR), and the stages of cervical cancer.

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The high incidence of cervical cancer in developing countries is due to the ineffectiveness of a comprehensive population-based early detection of cervical precancerous lesions, along with low awareness, education levels, and public knowledge about the occurrence of this cancer [4]. In 2020, Southeast Asia was ranked seventh for cervical cancer incidence and sixth for mortality compared to other regions of the world [5].

The International Federation of Gynecology and Obstetrics (FIGO) classification system is widely used for staging cervical cancer, based on clinical examination of the anatomical extent of the disease. In 2018, the FIGO cancer committee modified the staging to incorporate imaging findings for tumor size measurement and evaluation of lymph node metastasis [6].

Inflammation is a hallmark of cancer and contributes to various aspects of tumor progression, including angiogenesis, immune evasion, and metastasis. Consequently, systemic inflammatory markers have gained attention as potential prognostic indicators in cancer patients [7]. Low serum albumin levels are often observed in cancer patients and are associated with poor outcomes due to factors such as malnutrition, inflammation, and cancer-induced alterations in protein metabolism [8,9].

Fibrinogen, on the other hand, is a glycoprotein involved in blood clotting and wound healing. Elevated fibrinogen levels have been associated with a pro-inflammatory state and linked to cancer progression and metastasis [10]. The prognosis and survival rates of cervical cancer are closely related to the stage at which the disease is diagnosed [11]. Five-year survival rates range from over 90% if diagnosed at an early, localized stage to less than 20% if diagnosed as distant or metastatic [12] Early-stage cervical cancer typically includes stages IA, IB, and IIA, while advanced cervical cancer includes stages IIB, III, and IVA and IVB [13].

The albumin-to-fibrinogen ratio (AFR) combines two markers, offering insights into the balance between the body's immune response and the acute-phase reaction during cancer. The diagnostic efficacy of the albumin-to-fibrinogen ratio has been exhibited in several types of human cancers [14,15]. but the role of AFR in predicting stages of cervical cancer remains a topic of conflicting findings within the existing literature. Therefore, the purpose of this study was to determine the relationship of albumin-to-fibrinogen ratio in different stages of cervical cancer.

Objectives

- The aim of the study was to assess the relationship between pretreatment albumin-to-fibrinogen ratio (AFR) and the stages of cervical cancer in a tertiary care center.

Methodology & Materials

This cross-sectional analytical 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 70 participants were recruited, divided into two groups: early-stage (IA-IIA) and advanced-stage (IIB-IV).

Inclusion Criteria:

- Women diagnosed with cervical cancer confirmed by histopathology report obtained from biopsy.
- Had given consent to participate in the study.

Exclusion Criteria:

- Women with a history of previous surgery, chemotherapy, or radiation treatment for cervical disease or neoplasia.
- Women with known HIV infection.
- 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 and clinical examinations were conducted. Staging of cervical cancer was performed based on FIGO 2018 classifications, categorizing the stages into early stage (IA-IIA) and advanced stage (IIB-IV). Serum albumin and fibrinogen levels were measured to calculate the albumin to fibrinogen ratio (AFR), an inflammatory index. 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 between early-stage and advanced-stage cervical cancer groups used t-tests or chi-square tests, with a significance level set at $p < 0.05$. Univariate and multivariate logistic regression models assessed 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 relationship between cervical cancer stages and various demographic and clinical factors in women diagnosed with cervical cancer.

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Result

Table 1 shows that 47.1% of the patients were within the 30–44 years age group, and the average age was 45.37 ± 9.54 years. A total of 68.6% were educated up to the primary level, 85.7% were married, 84.3% were housewives, and 64.3% belonged to the lower-middle-class social status, with a monthly family income between 7,379 and 28,810 Tk.

Figure 1 depicts the distribution of study subjects across different stages of cervical cancer. Out of 70 subjects, 31 (44.3%) were in FIGO stage I (IA1 4.29%, IA2 5.71%, IB1 8.57%, IB2 21.43%, and IB3 4.29%), 17 (24.3%) in stage II (IIA1 4.29%, IIA2 1.43%, and IIB 18.57%), 19 (27.1%) in stage III (IIIA 7.1%, IIIB 15.7%, IIIC1 2.9%, and IIIC2 1.4%), and 3 (4.3%) in stage IV (IVA 4.29%).

Figure 2 shows that 35 (50.0%) of the respondents had advanced-stage cervical cancer, while the remaining 35 (50.0%) were identified at an early stage.

Figure 3 illustrates the distribution of the pretreatment albumin-to-fibrinogen ratio (AFR) among the respondents with cervical cancer. The overall mean AFR was 10.26 ± 1.47, with a median value of 10.23.

Table 1: Distribution of respondents according to their socio-demographic characteristics (n=70).

Socio-demographic characteristics		Frequency (N)	Percentage (%)
Age (in years)	30 – 44	33	47.1
	45 – 59	29	41.4
	≥ 60	8	11.4
	Mean ± SD	45.37 ± 9.54	
Educational Qualification	Up to Primary	48	68.6
	S.S.C./equivalent	19	27.1
	H.S.C. and above	3	4.3
Marital Status	Married	60	85.7
	Widowed	9	12.9
	Divorced/separated	1	1.4
Occupation	Housewife	59	84.3
	Service holder	7	10
	Household worker	4	5.7
Monthly family income (in BDT)	Lower class (≤7,378 Tk.)	13	18.6
	Lower middle class (7,379-28,810 Tk.)	45	64.3
	Upper middle class (28,811-89,280Tk.)	12	35.1

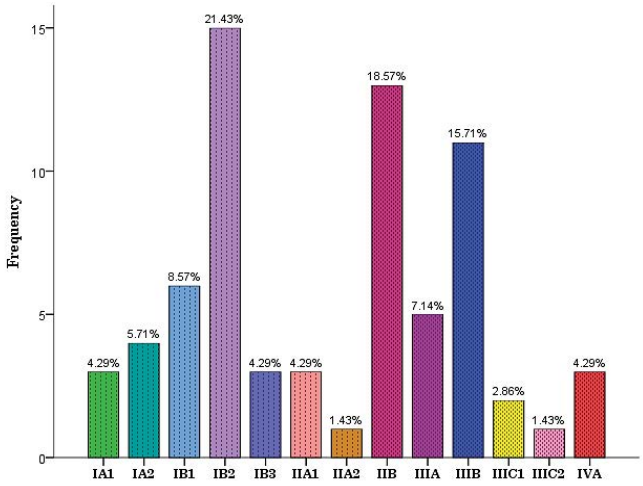

Figure 1: Bar diagram showing the distribution of respondents according to clinical staging (FIGO stages) of cervical cancer (n=70)

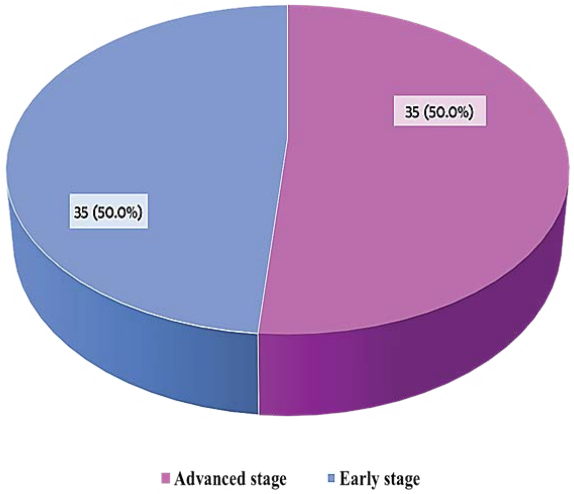

Figure 2: Pie diagram showing the distribution of respondents in advanced and early stages of cervical cancer (n=70)

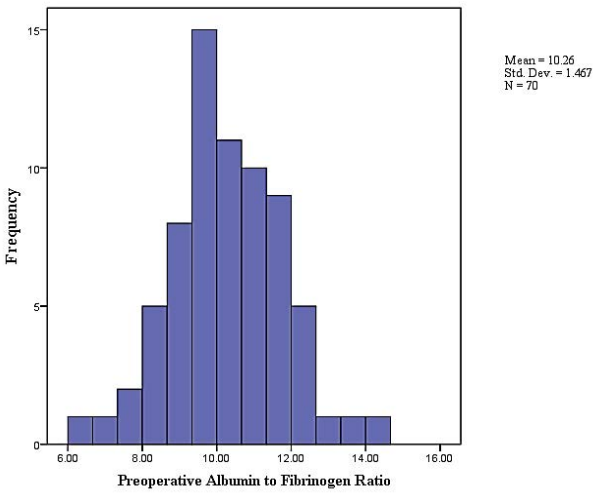

Figure 3: Histogram showing the distribution of pretreatment AFR among respondents with cervical cancer

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Table 2: Comparison of respondents' albumin-to-fibrinogen ratio across different stages of cervical cancer (n=70).

Albumin to fibrinogen ratio	Stage I (n = 31)	Stage II (n = 16)	*p*-value
Mean ± SD	10.69 ± 1.63	10.56 ± 1.31	0.784[b]
	Stage I (n = 31)	Stage III (n = 20)	
Mean ± SD	10.69 ± 1.63	9.63 ± 0.97	0.012[b]
	Stage I (n = 31)	Stage IV (n = 3)	
Mean ± SD	10.69 ± 1.63	8.41 ± 0.33	0.023[b]
	Stage II (n = 16)	Stage III (n = 20)	
Mean ± SD	10.56 ± 1.31	9.63 ± 0.97	0.020[b]
	Stage II (n = 16)	Stage IV (n = 3)	
Mean ± SD	10.56 ± 1.31	8.41 ± 0.33	0.013[b]
	Stage III (n = 20)	Stage IV (n = 3)	
Mean ± SD	9.63 ± 0.97	8.41 ± 0.33	0.046[b]

Table 2 shows no statistically significant difference in AFR between stage I and stage II cervical cancer ($p > 0.05$). However, significant differences were observed between stage I and stage III ($p = 0.012$), stage I and stage IV ($p = 0.023$), stage II and stage III ($p = 0.02$), stage II and stage IV ($p = 0.013$), and stage III and stage IV ($p = 0.046$).

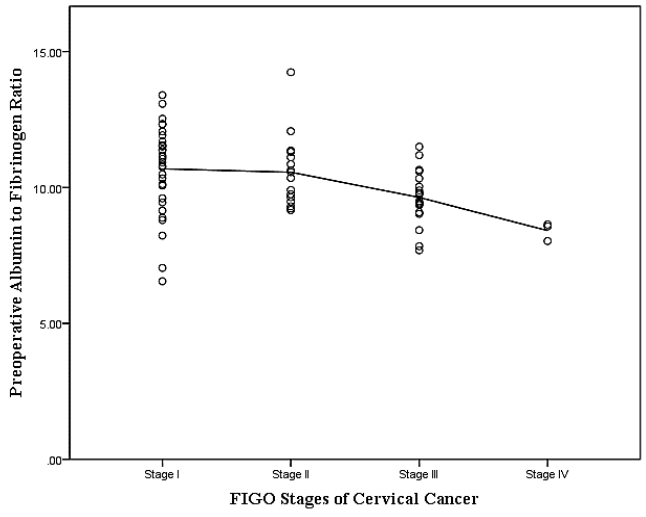

Figure 4: Scatterplot showing the correlation between pretreatment AFR and stages of cervical cancer ($rs = -0.421$, $p < 0.001$)

Figure 4 demonstrates the correlation between the pretreatment albumin-to-fibrinogen ratio and the clinical stages of cervical cancer. A significant negative correlation was observed ($rs = -0.421$, $p < 0.001$).

Table 3 reveals a significant difference in pretreatment AFR between advanced and early-stage cervical cancer groups ($p < 0.001$). Respondents with an AFR < 10.7 had a 10.2-fold higher chance of developing advanced-stage cervical cancer compared to those with an AFR ≥ 10.7 (OR = 10.154; 95% CI = 3.155–32.681).

Table 3: Odds ratios (OR) and 95% confidence intervals (CI) for stages based on pretreatment AFR in cervical cancer patients (Group A = 35, Group B = 35).

AFR	Groups		*p*-value	Odds Ratio (95% CI)
	Group A (Stage IIB-IV) N (%)	Group B (Stage IA-IIA) N (%)		
< 10.7	30 (85.7)	13 (37.1)	<0.001[c]	10.154
≥ 10.7	5 (14.3)	22 (62.9)		(3.155-32.681)

Discussion

Cervical cancer is a significant health concern in Bangladesh, with high incidence rates primarily due to limited access to screening and healthcare services, emphasizing the need for improved awareness and prevention efforts. Early detection through proper staging is crucial for effective treatment and positive patient outcomes. The albumin-to-fibrinogen ratio (AFR) reflects inflammatory and nutritional status as well as coagulation function, which can aid in assessing the severity of cervical cancer. In this cross-sectional study, a total of 70 histopathologically diagnosed women with cervical cancer were consecutively included and evaluated for their AFR and clinical stages. Respondents with advanced-stage cancer (stage IIB-IV) were categorized into group A (n=35), while those with early-stage cancer (stage IA-IIA) were categorized into group B (n=35).

In the present study, 47.1% of the patients were within the 30-44 years age group, and in the advanced cervical cancer group, the mean age was slightly higher at 46.93±10.62 years compared to the early-stage group at 43.91±8.22 years (p=0.203). Nearly two-thirds (68.6%) of the participants were educated up to the primary level. The majority (85.7%) were married, 84.3% were housewives, and 64.3% belonged to the lower middle-class social status, with a monthly family income ranging from 7,379 to 28,810 Tk. In a similar study by Khanam et al. (2018), comparable findings were reported, with 96.3% of respondents being housewives, 0.2% laborers, 2.3% in service, 0.6% business owners, and 0.6% teachers. They also reported that two-thirds of the families belonged to low- and middle-class income groups [16].

Among women with cervical cancer, 42.9% of those in the advanced group and 51.4% in the early-stage group reported using oral contraceptive pills (OCPs) for contraception. Notably, a substantial proportion in both groups had a history of using OCPs for five or more years (group A: 80.0% vs. group B: 72.2%), with a p-value of 0.699, indicating no

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statistically significant difference in the duration of OCP use between the two groups. Song et al. (2017) revealed that the average age at menarche was 16.2±1.8 years, and the average age for sexual debut was 21.1±2.1 years. The vast majority (92.0%) of the women employed contraception measures, and 79.7% of them had undergone sterilization [17].

In this study, over a quarter (25.7%) of the overweight women developed advanced cervical cancer compared to 14.3% of women with early-stage cervical cancer. The average body mass index (BMI) of the women was higher in group A compared to group B (22.98±2.44 vs. 21.94±2.19 kg/m²). None of these differences were statistically significant ($p>0.05$). In a study by Lee et al.18, compared to women with a normal BMI (18.5–23 kg/m²), the odds ratios (ORs) for cervical cancer were 1.25 for overweight (23–25 kg/m²) and 1.70 for mild obesity (≥25 kg/m²), suggesting that obesity may increase cervical cancer risk [18]. This disparity was likely due to the difference in the comparison group.

In the present study, there were notable differences in the mean (±SD) of the albumin-to-fibrinogen ratio (AFR) among different stages of cervical cancer ($p<0.05$). Stage IV cancer exhibited the lowest mean AFR of 8.41±0.33, while stage I had the highest mean AFR at 10.69±1.63. Furthermore, the average AFR was significantly lower among respondents in group A compared to group B (9.77±1.21 vs. 10.74±1.54; $p=0.005$). The correlation analysis in this study revealed a statistically significant negative correlation between pretreatment AFR and the stages of cervical cancer, with a Spearman correlation coefficient (rs) of -0.421 and a p-value of less than 0.001. This negative correlation implies that as AFR decreases, the stage of cervical cancer increases. In other words, lower AFR values are associated with more advanced stages of the disease. Respondents with an AFR <10.7 were found to have a 10.2 times higher risk of developing advanced-stage cervical cancer compared to patients with an AFR value ≥10.7 (OR=10.154; 95% CI=3.155-32.681).

Sun et al [19]. assessed the correlation of AFR with cancer prognosis. Pooled univariate and multivariate analyses indicated significant correlations of low AFR with poor overall survival (HR 2.18, 95% CI 1.87–2.55 and HR 1.75, 95% CI 1.54–2.00, respectively), poor disease-free survival (HR 1.89, 95% CI 1.54–2.32 and HR 1.51, 95% CI 1.29–1.76, respectively), and poor progression-free survival (HR 1.68, 95% CI 1.42–1.99 and HR 1.48, 95% CI 1.16–1.88, respectively). They recommended that AFR might be a promising prognostic marker for cancers [19].

Therefore, proper staging is vital for effective treatment and patient outcomes. The albumin-to-fibrinogen ratio (AFR) emerges as a promising prognostic marker, demonstrating a significant negative correlation with disease stage. Moreover, AFR's ability to differentiate between advanced and early-stage cases could aid in clinical decision-making.

Limitations of the study

This study had some limitations:

- The study was conducted in a selected tertiary-level hospital.
- The sample was not randomly selected.
- The sample size was inadequate.

Therefore, the findings of this study cannot be generalized to the entire population.

Conclusion

The relationship between the albumin-to-fibrinogen ratio (AFR) and different stages of cervical cancer, the results indicate that AFR decreases significantly with advancing stages. A mean AFR of 10.26 ± 1.47 was observed overall, with significant differences between later stages (III and IV) compared to early stages (I and II). A negative correlation ($rs = -0.421$, $p < 0.001$) was found between AFR and cancer stage. Patients with AFR <10.7 were 10.2 times more likely to present with advanced-stage cervical cancer, demonstrating the potential of AFR as a predictive biomarker for disease progression.

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