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RESEARCH ARTICLE

Prognostic Effect of Albumin-to-Globulin Ratio in Patients with Advanced Epithelial Ovarian Cancer Receiving Neoadjuvant Chemotherapy

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Abstract

Background: Advanced epithelial ovarian cancer (EOC) is frequently diagnosed at an advanced stage and remains associated with poor survival despite multimodal treatment. The albumin-to-globulin ratio (AGR), a composite marker reflecting nutritional and systemic inflammatory status, has emerged as a potential prognostic biomarker in several malignancies. This study evaluated the prognostic significance of pretreatment AGR in patients with advanced EOC receiving neoadjuvant chemotherapy. **Materials and Methods:** This retrospective cohort study included patients with FIGO stage II–IV epithelial ovarian carcinoma treated at Dr. B. Borooah Cancer Institute between January 2019 and June 2023. All patients received at least two cycles of platinum-based neoadjuvant chemotherapy. Pretreatment AGR was calculated by dividing serum albumin by serum globulin concentrations. The optimal AGR cut-off value was determined using receiver operating characteristic (ROC) curve analysis. Progression-free survival (PFS) and overall survival (OS) were analyzed using the Kaplan–Meier method and Cox proportional hazards regression models. **Results:** A total of 284 patients were included, with a median age of 52 years. Most patients had FIGO stage III disease, and high-grade serous carcinoma was the predominant histological subtype. Low pretreatment AGR (<1.00) was observed in 128 patients, whereas 156 patients had an AGR ≥1.00. Patients with AGR ≥1.00 demonstrated significantly longer median PFS than those with AGR <1.00 (16.1 vs. 13.2 months; p=0.042). Median OS was also significantly longer in the high-AGR group (30.8 vs. 26.3 months; p=0.038). On multivariable Cox regression analysis, AGR <1.00 remained independently associated with poorer PFS (HR, 1.34; 95% CI, 1.01–1.89; p=0.046) and OS (HR, 1.41; 95% CI, 1.02–2.06; p=0.039). **Conclusion:** Pretreatment AGR appears to be an inexpensive and readily available prognostic biomarker in patients with advanced epithelial ovarian cancer undergoing neoadjuvant chemotherapy. A low AGR was independently associated with shorter progression-free and overall survival; however, its prognostic discrimination was modest. Larger prospective studies are warranted to validate these findings before AGR can be incorporated into routine clinical risk stratification.

Keywords: epithelial ovarian cancer, albumin-to-globulin ratio, neoadjuvant chemotherapy, prognosis, survival

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Introduction

Epithelial ovarian cancer remains one of the most lethal gynecological malignancies worldwide, largely because most patients are diagnosed at an advanced stage. According to GLOBOCAN 2022, more than 324,000 new ovarian cancer cases and over 200,000 deaths were reported globally, underscoring the substantial mortality associated with this disease [1].

Standard treatment for advanced epithelial ovarian cancer includes cytoreductive surgery and platinum-based chemotherapy. In patients with extensive disease

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burden, poor performance status, or a low likelihood of achieving optimal upfront cytoreduction, neoadjuvant chemotherapy followed by interval debulking surgery is an accepted treatment strategy. Randomized trials, including EORTC 55971 and CHORUS, demonstrated that neoadjuvant chemotherapy followed by interval debulking surgery is non-inferior to primary debulking surgery in appropriately selected patients with advanced disease [2, 3]. Current international guidelines continue to recommend individualized treatment selection based on disease distribution, surgical resectability, patient fitness, and multidisciplinary team assessment [4].

Despite advances in surgery, chemotherapy, maintenance therapy, and molecularly guided treatment, outcomes in advanced ovarian cancer remain heterogeneous. Established prognostic factors include FIGO stage, residual disease after cytoreduction, age, tumor grade, performance status, and molecular characteristics such as BRCA mutation and homologous recombination deficiency (HRD) status. Among these, residual disease after cytoreductive surgery remains one of the strongest potentially modifiable prognostic factors.[5]

In recent years, systemic inflammatory and nutritional biomarkers have gained increasing attention as inexpensive and readily available prognostic tools in oncology. Biomarkers such as the neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio have demonstrated prognostic value in ovarian cancer [6. 7]. However, these indices primarily reflect systemic inflammation and may not adequately capture the nutritional component of the host response to cancer.

The albumin-to-globulin ratio (AGR) is a composite biomarker derived from routine biochemical parameters. Serum albumin reflects nutritional status, hepatic synthetic function, and the systemic inflammatory response, whereas serum globulin comprises immunoglobulins and other inflammatory proteins. Consequently, a low AGR may indicate the coexistence of malnutrition and heightened systemic inflammation. Meta-analyses across multiple solid tumors have consistently shown that a low AGR is associated with poorer survival outcomes [8, 9].Furthermore, serum albumin alone has previously been associated with prognosis in epithelial ovarian cancer, supporting the biological rationale for evaluating AGR in this disease [10].

However, evidence regarding the prognostic significance of AGR specifically among patients with advanced epithelial ovarian cancer receiving neoadjuvant chemotherapy remains limited. Therefore, the present study aimed to evaluate the association between pretreatment AGR and survival outcomes in patients with advanced epithelial ovarian carcinoma treated with neoadjuvant chemotherapy at a tertiary cancer center.

Materials and Methods

Study Design and Patients

This retrospective cohort study was conducted at Dr. B. Borooah Cancer Institute, Guwahati, India. Patients diagnosed with FIGO stage II–IV epithelial ovarian carcinoma between January 1, 2019 and June 30, 2023 were eligible for inclusion.

Eligibility Criteria

Eligible patients had histologically confirmed epithelial ovarian carcinoma, FIGO stage II–IV disease, received at least two cycles of platinum-based neoadjuvant chemotherapy, and had available pretreatment laboratory data, including serum albumin and globulin levels. Patients who subsequently underwent interval debulking surgery, completion surgery, or surgical assessment following neoadjuvant chemotherapy were included.

Data Collection

Clinical, demographic, pathological, treatment, and follow-up data were extracted retrospectively from institutional medical records. Pretreatment serum albumin and globulin concentrations were recorded before initiation of neoadjuvant chemotherapy.

Albumin-to-Globulin Ratio

The albumin-to-globulin ratio (AGR) was calculated as:

AGR = Serum albumin / Serum globulin

Receiver operating characteristic (ROC) curve analysis was performed to determine the optimal AGR cut-off for survival prediction. An AGR value of 1.00 was identified as the optimal threshold, and patients were categorized into a low-AGR group (<1.00) and a high-AGR group (≥1.00).

Outcome Measures

The primary study endpoints were progression-free survival (PFS) and overall survival (OS). PFS was defined as the interval from initiation of treatment to documented disease progression, recurrence, or death from any cause, whichever occurred first. OS was defined as the interval from initiation of treatment to death from any cause or the date of the last follow-up.

Statistical Analysis

Continuous variables are presented as the mean ± standard deviation or median (range), as appropriate. Categorical variables are presented as frequencies and percentages. Survival curves were estimated using the Kaplan–Meier method and compared using the log-rank test. Univariate and multivariate Cox proportional hazards regression analyses were performed to identify independent prognostic factors. Variables entered into the multivariate model included age, FIGO stage, tumor grade, cytoreductive status, surgical status, and AGR. Hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated. A two-sided P value <0.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics version 29.

Baseline Characteristics

A total of 284 patients with FIGO stage II–IV epithelial ovarian carcinoma were included in the analysis. The baseline demographic and clinical characteristics are summarized in Table 1.

The median age was 52 years (range, 26–82 years),

and the mean age was 52.33 ± 9.21 years. Most patients (39.8%) were between 51 and 60 years of age. The majority were postmenopausal (62.7%), while 35.9% were premenopausal. Most women had one or two previous deliveries (43.0%).

Stage III disease was the most common presentation (59.2%), followed by stage IV disease (37.7%). High-grade serous carcinoma was the predominant histological subtype (76.0%). After completion of neoadjuvant chemotherapy, 90 patients (31.7%) did not undergo interval debulking surgery because of disease progression, persistent unresectability, or poor performance status.

Baseline Laboratory Parameters

Baseline laboratory findings are presented in Table 2.

The mean hemoglobin concentration was 10.63 ± 1.54 g/dL. Mean serum albumin and globulin concentrations were 3.78 ± 0.57 g/dL and 3.80 ± 0.64 g/dL, respectively. The mean pretreatment albumin-to-globulin ratio (AGR) was 1.02 ± 0.20, with a median value of 1.00 (range, 0.46–1.96).

Determination of the Optimal AGR Cut-off

Receiver operating characteristic (ROC) curve analysis was performed to determine the optimal pretreatment AGR threshold for survival prediction. As shown in Figure 1, the optimal cut-off value was 1.00.

The area under the ROC curve (AUC) was 0.58 (95% CI, 0.51–0.65; p = 0.045), corresponding to a sensitivity of 55.3% and a specificity of 57.1%. Although the discriminatory performance was modest, the ROC analysis identified AGR = 1.00 as the optimal threshold for subsequent survival analyses (Table 3).

Table 1. Baseline Demographic Characteristics of the Study Population (N = 284).

Characteristic	Value
Age (years)	
Mean ± SD	52.33 ± 9.21
Median (Range)	52 (26–82)
Age group, n (%)	
<40	26 (9.2)
40–50	84 (29.6)
51–60	113 (39.8)
>60	61 (21.5)
Menopausal status, n (%)	
Premenopausal	102 (35.9)
Postmenopausal	178 (62.7)
Unknown	4 (1.4)
Parity, n (%)	
Nulliparous (P0)	24 (8.5)
P1–P2	122 (43.0)
P3–P4	86 (30.3)
≥P5	15 (5.3)
Missing*	37 (13.0)

Table 2. Baseline Laboratory Characteristics of the Study Population.

Parameter	Mean ± SD	Median (Range)
Hemoglobin (g/dL)	10.63 ± 1.54	10.65 (6.0–16.6)
Albumin (g/dL)	3.78 ± 0.57	3.80 (1.8–5.5)
Globulin (g/dL)	3.80 ± 0.64	3.70 (2.3–6.1)
Albumin-to-globulin ratio (AGR)	1.02 ± 0.20	1.00 (0.46–1.96)

Survival According to Pretreatment AGR

Patients were stratified according to the optimal pretreatment AGR cut-off value of 1.00. Of the 284 patients, 156 (54.9%) had an AGR ≥1.00 and 128 (45.1%) had an AGR <1.00. Patients with an AGR ≥1.00 had significantly longer median progression-free survival than those with an AGR <1.00 (16.1 vs. 13.2 months; log-rank P = 0.042) (Figure 2). Similarly, median overall survival was significantly longer in the high-AGR group (30.8 vs. 26.3 months; log-rank P = 0.038) (Figure 3). The 1-year and 2-year PFS rates were 59.6% and 25.0% in the high-AGR group compared with 47.7% and 18.8% in the low-AGR group, respectively. Likewise, the 1-year and 2-year OS rates were 84.6% and 55.8% versus 78.1% and 47.7%, respectively.

Multivariable Cox Regression Analysis

Variables associated with survival were further evaluated using multivariable Cox proportional hazards regression analysis.

For progression-free survival (PFS), age >60 years, FIGO stage IV disease, suboptimal cytoreduction, absence of surgery, and an AGR <1.00 were independently associated with poorer outcomes. Low AGR remained an independent predictor of shorter PFS (hazard ratio [HR] 1.34, 95% confidence interval [CI] 1.01–1.89; P = 0.046) (Table 4) and Figure 4.

For overall survival (OS), age >60 years, FIGO stage IV disease, suboptimal cytoreduction, absence of surgery, and an AGR <1.00 also remained independently associated with inferior survival. Patients with an AGR <1.00 had a 41% higher risk of death than those with an AGR ≥1.00

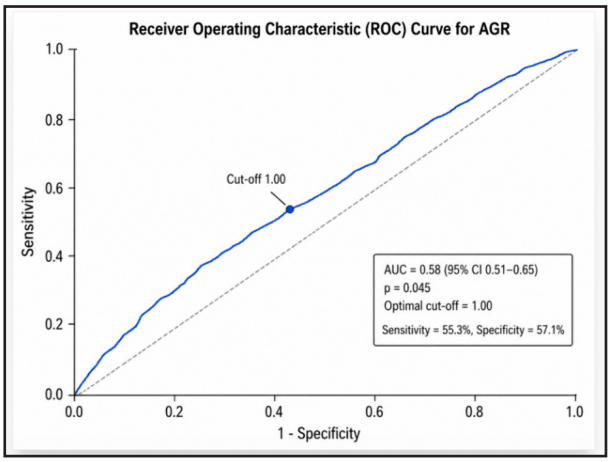

Figure 1. Graph Representing ROC Analysis for Calculation of Optimal Cut-off of AGR.

Table 3. Receiver Operating Characteristic (ROC) Analysis for Determination of the Optimal Albumin-to-globulin Ratio (AGR) Cut-off.

Parameter	AUC	95% CI	P value	Optimal cut-off	Sensitivity (%)	Specificity (%)
Albumin-to-globulin ratio (AGR)	0.58	0.51–0.65	0.045	1.00	55.3	57.1

Table 4. Multivariable Cox Proportional Hazards Regression Analysis for Progression-free Survival.

Variable	HR	95% CI	P value
Age >60 years	1.52	1.04–2.23	0.031
FIGO stage IV	1.86	1.29–2.68	0.001
AGR <1.00	1.34	1.01–1.89	0.046
Grade 3	1.47	0.83–2.61	0.189
Suboptimal cytoreduction	1.95	1.30–2.91	0.001
No surgery	2.38	1.61–3.51	<0.001

(HR 1.41, 95% CI 1.02–2.06; P = 0.039) (Table 5) and Figure 5.

Discussion

In this retrospective cohort study of patients with advanced epithelial ovarian cancer treated with platinum-based neoadjuvant chemotherapy, pretreatment albumin-to-globulin ratio (AGR) was significantly associated with both progression-free survival (PFS) and overall survival (OS). Patients with an AGR <1.00 experienced significantly shorter survival than those with an AGR ≥1.00. Importantly, this association remained significant after adjustment for established prognostic factors, including age, FIGO stage, tumor grade, cytoreduction status, and surgical management, suggesting that AGR provides prognostic information beyond conventional clinicopathological variables.

These findings support the growing recognition that host-related factors contribute substantially to cancer outcomes alongside tumor biology and treatment-related characteristics. AGR is biologically plausible as a prognostic biomarker because it integrates two complementary components of the systemic host response. Serum albumin reflects nutritional status, hepatic synthetic function, and the severity of systemic inflammation, whereas serum globulin largely represents inflammatory and immune-related proteins. Consequently, a low AGR may indicate the coexistence of malnutrition and persistent systemic inflammation, both of which have been associated with impaired treatment tolerance, reduced physiological reserve, and poorer survival outcomes in patients with advanced malignancies.

Systemic inflammatory biomarkers have received considerable attention as prognostic indicators in epithelial ovarian cancer. Meta-analyses have demonstrated that elevated neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are associated with inferior survival. However, unlike these hematologic indices, AGR simultaneously reflects inflammatory activity and nutritional status through routinely available biochemical parameters. This integrated assessment may be particularly relevant in advanced ovarian cancer, where cachexia, hypoalbuminemia, malignant ascites, and chronic inflammation frequently coexist and collectively influence prognosis.

Our findings are consistent with evidence from the broader oncology literature. In a systematic review and meta-analysis including 13,890 patients with solid tumors, He et al. demonstrated that a higher AGR was associated with improved overall survival, disease-free survival, and cancer-specific survival. Similarly, Chi et al [9]. reported that a low AGR correlated with poorer survival and more aggressive clinicopathological characteristics across multiple malignancies. Although these studies support AGR as a broadly applicable prognostic biomarker, disease-specific validation remains essential because the biological behavior and treatment response of different cancers vary considerably.

Within ovarian cancer, serum albumin has long been recognized as an independent prognostic indicator.

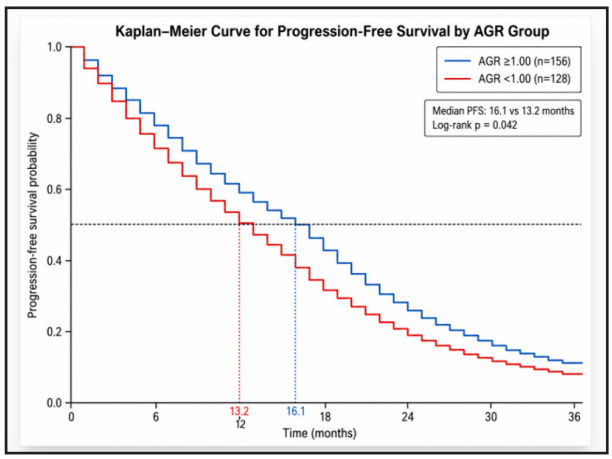

Figure 2. Kaplan Meier Curve for PFS with Respect to AGR.

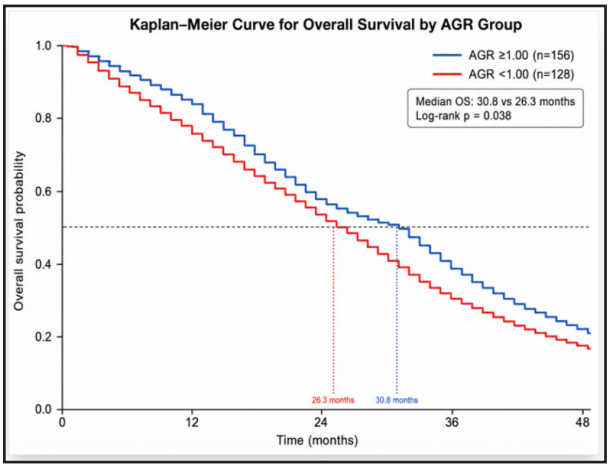

Figure 3. Kaplan Meier Curve for OS with Respect to AGR.

Table 5. Multivariable Cox Proportional Hazards Regression Analysis for Overall Survival.

Variable	HR	95% CI	P value
Age >60 years	1.83	1.17–2.87	0.008
FIGO stage IV	2.14	1.39–3.29	<0.001
AGR <1.00	1.41	1.02–2.06	0.039
Grade 3	1.69	0.85–3.35	0.135
Suboptimal cytoreduction	2.32	1.45–3.72	<0.001
No surgery	3.15	2.01–4.93	<0.001

Parker et al [10]. identified pretreatment serum albumin, together with CA-125, as a strong predictor of survival, particularly among patients with advanced-stage disease. Likewise, a subsequent meta-analysis confirmed that low preoperative serum albumin is associated with inferior overall survival in epithelial ovarian cancer. Our study extends these observations by demonstrating that AGR, which incorporates both nutritional and inflammatory components, may provide additional prognostic information beyond serum albumin alone.

Although AGR remained an independent prognostic factor in multivariable analysis, its discriminatory performance was modest (AUC = 0.58). Therefore, AGR should not be considered a standalone prognostic tool but rather an adjunct to established clinical and pathological prognostic factors. Its principal advantages are its low cost, universal availability, and ease of calculation from routine laboratory investigations, making it particularly attractive for resource-limited clinical settings.

In this retrospective cohort study of patients with advanced epithelial ovarian cancer treated with neoadjuvant chemotherapy, pretreatment AGR was significantly associated with both progression-free survival (PFS) and overall survival (OS). Patients with an AGR <1.00 experienced significantly shorter PFS and OS than those with an AGR ≥1.00. Moreover, low AGR remained an independent prognostic factor after adjustment for established clinical variables, including age, FIGO stage, tumor grade, cytoreduction status, and surgical treatment.

These findings support the growing recognition that host-related factors, particularly systemic inflammation and nutritional status, contribute substantially to outcomes in advanced ovarian cancer alongside tumor-related characteristics. AGR is biologically plausible as a prognostic biomarker because it integrates two complementary physiological domains. Serum albumin reflects nutritional reserve, hepatic synthetic function, and the systemic inflammatory response, whereas serum globulin represents circulating immunoglobulins and other inflammatory proteins. Consequently, a low AGR may indicate the coexistence of malnutrition and persistent systemic inflammation, both of which are associated with impaired treatment tolerance and poorer survival.

Inflammation-based biomarkers have attracted considerable attention in ovarian cancer. Previous studies have shown that elevated neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are associated with adverse clinical outcomes [6, 7]. Unlike these hematologic indices, AGR incorporates both inflammatory and nutritional status, potentially providing a more comprehensive reflection of the host response. This may be particularly relevant in advanced ovarian cancer, where ascites, cachexia, reduced oral intake, and chronic inflammation frequently coexist.

Our findings are consistent with evidence from the broader oncology literature. In a systematic review and meta-analysis including 13,890 patients with various solid tumors, He et al. demonstrated that a higher AGR was significantly associated with improved overall, disease-free, and cancer-specific survival [8]. Similarly, Chi et al. reported that low AGR correlated with poorer overall survival and more aggressive clinicopathological characteristics across multiple malignancies [9]. Although these studies were not specific to ovarian cancer, they support the concept that AGR reflects fundamental aspects of cancer-related host biology that influence prognosis across tumor types.

Within ovarian cancer, serum albumin has long been recognized as an independent prognostic marker. Parker et al. identified pretreatment serum albumin, together with CA-125, as a strong predictor of survival in epithelial ovarian cancer, particularly in patients with advanced disease [10]. A subsequent meta-analysis likewise confirmed that hypoalbuminemia is associated with significantly worse overall survival [11]. Our findings extend these observations by demonstrating that AGR, which incorporates both albumin and globulin concentrations, may provide additional prognostic information by simultaneously reflecting nutritional status and systemic inflammatory activity.

Although statistically significant, the prognostic effect

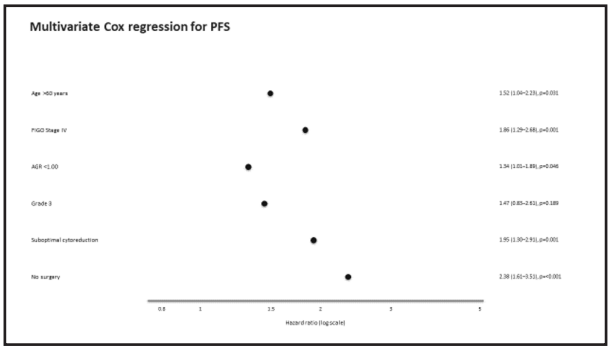

Figure 4. Multivariate Cox Regression for PFS.

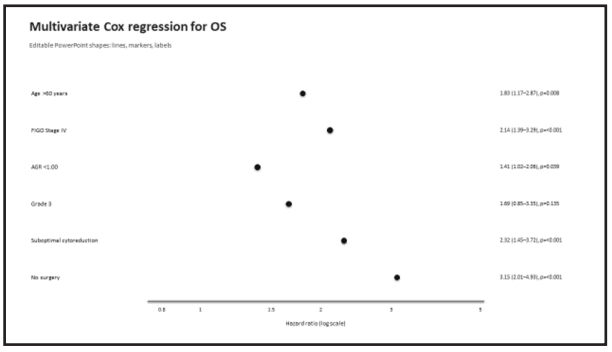

Figure 5. Multivariate Cox Regression for OS.

of AGR in the present study was modest. The receiver operating characteristic analysis yielded an AUC of only 0.58, indicating limited discriminatory performance when AGR is used in isolation. Therefore, AGR should not be considered a standalone prognostic tool but rather an adjunct to established clinical and pathological factors, including FIGO stage, response to neoadjuvant chemotherapy, surgical resectability, residual disease after cytoreduction, and patient performance status. Incorporating AGR into multifactorial prognostic models may provide greater clinical value than relying on the marker alone.

Consistent with previous evidence, cytoreduction status remained one of the strongest prognostic determinants in this cohort, reinforcing the well-established survival benefit of maximal cytoreductive surgery in advanced epithelial ovarian cancer [5]. Likewise, patients who remained unsuitable for surgery after neoadjuvant chemotherapy experienced substantially poorer outcomes, likely reflecting more aggressive tumor biology and poorer overall clinical condition.

From a practical perspective, AGR offers several advantages. It is inexpensive, reproducible, and readily calculated from routine biochemical tests that are universally available in clinical practice. These characteristics make AGR particularly attractive in resource-limited settings where access to molecular profiling or advanced prognostic assays may be restricted. Patients with a low pretreatment AGR may warrant closer surveillance, early nutritional assessment, supportive care interventions, and careful evaluation of treatment response throughout neoadjuvant chemotherapy.

Several limitations should be acknowledged. First, the retrospective single-center design introduces the potential for selection bias and limits the generalizability of the findings. Second, serum albumin and globulin concentrations may be influenced by comorbid conditions such as chronic liver disease, renal dysfunction, autoimmune disorders, active infection, or other inflammatory states that could not be fully accounted for. Third, the optimal AGR threshold of 1.00 was derived from this cohort and requires external validation before broader clinical application. Fourth, important molecular prognostic variables, including BRCA mutation status and homologous recombination deficiency, were unavailable for a proportion of patients. Finally, although AGR was independently associated with survival, its relatively limited discriminatory ability suggests that it should be interpreted within a comprehensive prognostic framework rather than used as an isolated biomarker.

Despite these limitations, this study provides additional real-world evidence supporting the prognostic value of pretreatment AGR in patients with advanced epithelial ovarian cancer receiving neoadjuvant chemotherapy. The relatively large cohort, survival-based determination of the AGR cut-off, and multivariable adjustment for established prognostic factors strengthen the reliability of the findings. Future prospective multicenter studies incorporating molecular biomarkers, standardized nutritional assessments, and external validation cohorts are warranted to clarify the role of AGR in risk stratification and individualized treatment planning

In conclusion, pretreatment albumin-to-globulin ratio (AGR) is an inexpensive, readily available biomarker that provides independent prognostic information in patients with advanced epithelial ovarian cancer undergoing neoadjuvant chemotherapy. Patients with an AGR <1.00 experienced significantly shorter progression-free and overall survival than those with an AGR ≥1.00. Although the discriminatory performance of AGR was modest, it reflects the combined effects of systemic inflammation and nutritional status and may serve as a practical adjunct to established clinicopathological factors for baseline risk stratification. Prospective multicenter studies are required to validate these findings and determine the role of AGR in future prognostic models and clinical decision-making.

Abbreviations

AGR: Albumin Globulin Ratio, AUC: Area Under the Curve, CBC: Complete Blood Count, CI: Confidence Interval, FIGO: International Federation of Gynecology and Obstetrics, HR: Hazard Ratio, IDS: Interval Debulking Surgery, NACT: Neoadjuvant Chemotherapy, OS: Overall Survival, PFS: Progression-Free Survival, ROC: Receiver Operating Characteristic, SD: Standard Deviation

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Ethics Committee of Dr. B. Borooah Cancer Institute. Owing to the retrospective design of the study, the requirement for informed consent was waived by the Ethics Committee. All procedures were performed in accordance with the ethical standards of the institutional and national research committees and the Declaration of Helsinki.

Ethics approval number

BBCI-TMC/Misc-01/MEC/398/2024.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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No specific funding was received for this study.

Authors' contributions

PSR and KM conceptualized the study. KM contributed to data collection. KM performed the statistical analysis. PSR and KM drafted the manuscript. PSR and DB supervised the manuscript finalization process. All authors

contributed to manuscript revision, read, and approved the final version.

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