Journal of Carcinogenesis
Covering Genesis to Therapeutics

Journal of Carcinogenesis, ISSN: 1477-3163
2025; Vol 24: Issue 2s, https://carcinogenesis.com/

Serum Albumin Predicts Chemotherapy Response In Advanced Epithelial Ovarian Cancer: A Cohort Study

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ABSTRACT

Background and aim: Most ovarian cancer cases are diagnosed at an advanced stage, where predicting chemotherapy response is critical but currently depends on operative assessments and complex biomarkers. This study evaluated whether pre-chemotherapy easily accessible blood-based biomarkers such as D-dimer, albumin, and systemic inflammatory indices (NLR, PLR, MLR) could provide a practical way to estimate chemotherapy response.

Methods: This cohort study, conducted at Dr. Wahidin Sudirohusodo Hospital, Indonesia, included 46 women with advanced epithelial ovarian cancer. Pre-chemotherapy levels of D-dimer, albumin, and inflammatory markers (NLR, PLR, MLR) were measured. Chemotherapy response was assessed using RECIST criteria, and predictive value was analysed.

Results: Among the 46 patients, higher pre-chemotherapy serum albumin levels were significantly associated with a better treatment response ($p = 0.001$). Logistic regression showed that each unit increase in albumin was associated with over ninefold higher odds of response (OR = 9.11; 95% CI: 2.35–35.25). The predictive model based on albumin demonstrated good diagnostic performance, with sensitivity of 73.3%, specificity of 75%, positive predictive value of 84.6%, and negative predictive value of 60%. In contrast, pre-chemotherapy levels of D-dimer and inflammatory markers (NLR, PLR, MLR) were not significantly associated with chemotherapy response in this cohort

Conclusions: Serum albumin measured before chemotherapy found to be a significant predictor of treatment response, providing a simple and reliable tool to help guide treatment planning in women with advanced epithelial ovarian cancer.

Keywords: *Advanced epithelial ovarian cancer; chemotherapy response; serum albumin; D-dimer; neutrophil-to-lymphocyte ratio; prognostic biomarkers; systemic inflammatory markers*

How to Cite: Rakha Sulthan Salim, Nugraha Utama Pelupessy, Imam Ahmadi Farid, Andi Alfian Zainuddin, Syahrul Rauf, David Lotisna, (2025) Serum Albumin Predicts Chemotherapy Response In Advanced Epithelial Ovarian Cancer: A Cohort Study, *Journal of Carcinogenesis*, *Vol.24, No.2s*, 158-163

1. INTRODUCTION

Ovarian cancer remains a significant global health burden and is recognized as one of the most lethal gynecologic malignancies, contributing substantially to morbidity and mortality among women. According to the Global Cancer Observatory (GLOBOCAN), more than 300,000 new cases of ovarian cancer were reported worldwide in 2020, with an estimated 185,000 deaths, ranking it as the eighth most common cancer among women and the most fatal of all gynecological cancers (1,2). The lifetime risk of developing ovarian cancer is approximately 1 in 75, and the overall lifetime risk of dying from the disease is 1 in 100, reflecting its poor prognosis and the challenges in early detection (3,4). Unlike cervical and breast cancers, which have established screening programs, ovarian cancer lacks reliable population-based screening methods. Consequently, more than 70% of cases are diagnosed at advanced stages (FIGO stage III–IV), when curative treatment options are limited, and survival outcomes are significantly compromised (3,4).

Histologically, epithelial ovarian cancer (EOC) accounts for nearly 90% of all ovarian malignancies and represents a heterogeneous group of tumors classified into several subtypes, including serous, endometrioid, mucinous, and clear cell carcinomas. Among these, high-grade serous carcinoma is the most prevalent and aggressive, often associated with widespread peritoneal dissemination at the time of diagnosis and a high propensity for recurrence despite initial treatment response. The dualistic model of ovarian carcinogenesis further stratifies EOC into type I tumors (low-grade serous, endometrioid, mucinous, and clear cell) that are generally indolent and genetically stable, and type II tumors (high-grade serous and undifferentiated carcinomas) that are biologically aggressive and genetically unstable (5).

The cornerstone of treatment for advanced EOC is a multimodal approach involving maximal cytoreductive surgery (debulking) aimed at achieving no gross residual disease, followed by systemic chemotherapy. Standard first-line chemotherapy typically consists of a platinum taxane doublet, most commonly carboplatin combined with paclitaxel, which has been shown to induce high response rates in initial treatment. Despite these therapeutic advances, the prognosis of advanced EOC remains poor, with five-year overall survival rates ranging between 30% and 40% depending on disease stage, residual tumor burden, and treatment response. A major clinical challenge is the high rate of recurrence and the development of resistance to platinum-based chemotherapy, which occurs in the majority of patients within 12–24 months after initial treatment, ultimately contributing to poor long-term survival outcomes (6).Although initial responses to platinum-based regimens are often favorable, the development of chemoresistance particularly platinum resistance remains a major obstacle, contributing to disease recurrence and poor survival outcomes (7). Several prognostic and predictive factors have been identified, including the International Federation of Gynecology and Obstetrics (FIGO) stage, the extent of residual disease after surgery, and molecular biomarkers such as circulating tumor DNA (ctDNA) and BRCA1/2 mutation status (3,8,9). While these molecular and genetic biomarkers have demonstrated promising roles in prognosis and therapeutic guidance, their widespread application in routine clinical practice is hampered by high costs, technological complexity, and limited accessibility in resource-constrained settings.

Consequently, there has been growing interest in identifying simple, inexpensive, and universally available biomarkers that can reliably predict treatment response and outcomes. Among these, blood-derived parameters such as D-dimer, albumin, and systemic inflammatory indices including the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio (MLR) have emerged as potential prognostic tools (10, 14). These markers reflect not only the systemic inflammatory response but also the nutritional and coagulation status of cancer patients, both of which play a critical role in tumor progression, metastasis, and response to therapy (15,16). Importantly, their measurement is inexpensive, minimally invasive, and readily available in most clinical laboratories, thereby offering significant advantages over complex molecular assays. The ultimate goal is to provide clinicians with practical, cost-effective tools that may aid in predicting chemotherapy response and optimizing individualized treatment strategies, particularly in settings where access to advanced molecular diagnostics is limited.

2. MATERIAL AND METHODS

Study Design

This cohort study was conducted at Dr. Wahidin Sudirohusodo Hospital, the study was conducted on patients who initiated chemotherapy between July 2023 until July 2024. Chemotherapy was administered in six cycles at 21-day intervals using the Carboplatin-Paclitaxel regimen. Follow-up CT scans were performed three months after completion of chemotherapy to evaluate tumor size according to the RECIST criteria and included women with FIGO stage III–IV epithelial ovarian cancer who received six cycles of platinum-based chemotherapy. Ethical approval was obtained from the Faculty of Medicine, Hasanuddin University. Pre-chemotherapy blood samples were collected to measure D-dimer, albumin, and calculate NLR, PLR, and MLR. Chemotherapy response was assessed after six cycles using RECIST criteria and classified as responsive or non-responsive. Data were analysed using SPSS. Group comparisons employed the Mann Whitney U test, and logistic regression was used to identify predictors of response.

Sample Criteria

The study population consisted of all patients diagnosed with stage III or IV ovarian carcinoma who underwent chemotherapy at Dr. Wahidin Sudirohusodo Hospital, Makassar. The research sample was obtained through a consecutive sampling technique, in which every patient who presented during the study period and fulfilled the eligibility criteria was included until the required sample size was achieved. Patients were enrolled in the order of hospital admission and were required to meet the established inclusion and exclusion criteria. The inclusion criteria specified that eligible participants must have been diagnosed with stage III or IV ovarian cancer, expressed willingness to undergo chemotherapy, and provided written informed consent to participate. Patients were excluded if they had a concurrent diagnosis of other malignancies, a history of coagulation factor disorders, renal dysfunction, platelet abnormalities, or if they had previously received chemotherapy. In addition, dropout criteria were applied to participants who failed to complete the full course of chemotherapy cycles or who died before treatment completion.

Research procedure

All subjects included in this study were women who fulfilled the predetermined inclusion criteria and voluntarily agreed to participate. Prior to enrollment, the researcher explained in detail the aims, objectives, and procedures of the study to each potential participant. Women who expressed willingness to join were then asked to provide written informed consent using a standardized consent form. After enrollment, data collection was initiated through anamnesis, physical examination, and laboratory testing. Venous blood samples of approximately 3 mL were manually collected from each subject under aseptic conditions. The collected samples were used to assess serum D-dimer, albumin, and systemic inflammatory markers. Each serum specimen was carefully labeled with a unique identification code and subsequently processed by the serology panel. To maintain sample integrity, all specimens were placed in appropriate storage tubes and immediately stored in a cool box prior to further analysis.

Data and statistical analysis

Statistical analysis was carried out using SPSS 24 software for the Windows® operating system. To assess the relationship between D-Dimer, Albumin, and Systemic Inflammatory Markers in ovarian cancer patients undergoing chemotherapy, the Mann-Whitney test was used. The data normality test was carried out with the Saphiro-Wilk test. A logistic regression test will be used to assess the relationship. A p value of <0.05 indicates a significant relationship.

3. RESULTS

A total of 46 patients with FIGO stage III–IV epithelial ovarian cancer were analysed. Based on RECIST criteria, 30 patients (65.2%) were classified as responders and 16 patients (34.8%) as non-responders to platinum-based chemotherapy. The median age was 52 years, and most patients were at stage III. Both groups were similar in characteristics including age, disease stage, and parity.

Table 1. Comparison of pre-chemotherapy Biomarkers Between Chemotherapy Responders and Non-responders in Advanced Epithelial Ovarian Cancer

Laboratory tests	Responders (n = 30) Median (range)	Non-responders (n = 16) Median (range)	p-value*
D-dimer (µg/mL)	1.61 (0.19–12.4)	2.63 (0.40–14.9)	0.390
Albumin (g/dL)	4.30 (2.4–5.1)	3.30 (2.3–4.3)	**< 0.001**
Neutrophil–lymphocyte ratio (NLR)	4.4 (0.43–23.1)	3.0 (0.50–28.7)	0.937
Monocyte–lymphocyte ratio (MLR)	0.59 (0.12–1.30)	0.63 (0.15–1.53)	0.721
Platelet–lymphocyte ratio (PLR)	50.60 (10.13–52.66)	52.66 (10.13–132.85)	1.000

Data compared using Mann–Whitney U test. Significant p-values are shown in bold.

In this result, higher pre-chemotherapy serum albumin levels were significantly associated with a positive chemotherapy response, with responders having a median albumin level of 4.3 g/dL (range: 2.4–5.1) compared to 3.3 g/dL (range: 2.3–4.3) in non-responders ($p < 0.001$). Logistic regression showed that each unit increase in albumin increased the odds of response approximately ninefold (OR = 9.11; 95% CI: 2.35–35.25; $p = 0.001$) (**Table 1.**).

Figure 1. Receiver operating characteristic (ROC) curve of serum albumin (cut-off 4.0 g/dL) for predicting chemotherapy response in advanced ovarian cancer.

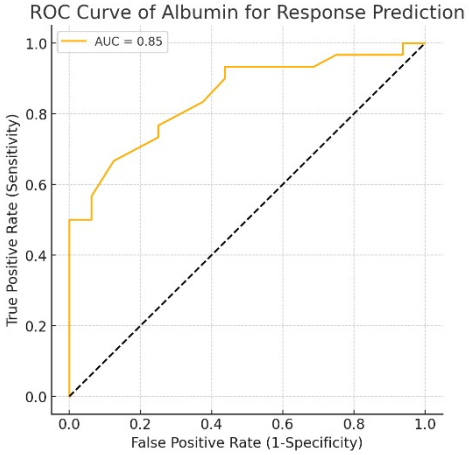

Table 2. Predictive performance of Albumin for Chemotherapy Response

Variable	Cut-off (g/dL)	AUC	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Albumin	4.0	0.85	73.3	75.0	84.6	60.0

AUC: area under the receiver operating characteristic curve; PPV: positive predictive value; NPV: negative predictive value

The predictive model using albumin demonstrated good performance, with a cut-off of 4.0 g/dL yielding an area under the ROC curve (AUC) of 0.85. At this threshold, sensitivity was 73.3%, specificity 75%, positive predictive value (PPV) 84.6%, and negative predictive value (NPV) 60%. In contrast, D-dimer, neutrophil–lymphocyte ratio (NLR), platelet–lymphocyte ratio (PLR), and monocyte–lymphocyte ratio (MLR) showed no significant differences between responders and non-responders ($p > 0.05$).

4. DISCUSSION

In this study, serum albumin was identified as the only significant biomarker, with elevated levels correlating with improved chemotherapy response. The role of albumin as a prognostic and predictive biomarker in oncology cytotoxic therapy is increasingly recognized.(17) Albumin as the highest circulating protein, contributes to oncotic pressure, has anti-inflammatory properties, also facilitates the transport of molecules that affects chemotherapeutic agents.(16, 18, 19) Study already described that albumin has shown promises as carrier of anti-cancer agents by prolong the circulation and accumulation within tumor.(19) As cytotoxic drugs like paclitaxel has high plasma protein binding (89-98%) and bound mainly by albumin for transport. Its ability integrates with the efficacy of chemotherapy.(6) Albumin also promotes better tolerance from cytotoxic treatment.(20)

Albumin is a readily accessible and widely utilized clinical parameter for evaluating patients' nutritional status, which has been strongly linked to disease outcomes (18). Previous studies have consistently demonstrated that higher serum albumin levels are associated with improved prognosis in ovarian cancer. For instance, Dai et al. reported that albumin serves as a predictor of overall survival, underscoring its prognostic and predictive significance (13). Similarly, Ayhan et al. highlighted that preoperative albumin level is an independent prognostic factor for overall survival in patients with epithelial ovarian cancer (21). While the prognostic value of various biomarkers, including albumin, has been well-documented in relation to long-term outcomes such as survival and recurrence across ovarian and other gynecologic malignancies (13, 18, 21–26), relatively few investigations have specifically addressed its predictive role in determining chemotherapy responsiveness. Building upon these earlier observations, our study emphasizes the potential utility of albumin not only as a prognostic biomarker but also as a predictor of chemotherapy response in advanced-stage epithelial ovarian cancer.

This study proposes and demonstrates that a serum albumin with 4.0 g/dL as a cut-off, which is higher than the commonly accepted threshold for normal serum albumin level (3.5 g/dL),(15) effectively predicts chemotherapy response. At this threshold, the model achieved an AUC of 0.848, indicating excellent discriminative ability, with good sensitivity (73.3%) and specificity (75%), a high positive predictive value (84.6%), and a moderate negative predictive value (60%). This finding supports the concept that higher albumin levels reflect superior nutritional and inflammatory status, which may lead to better treatment tolerance and efficacy (13, 16, 27).

To our knowledge, there is no established cut-off for pre-chemotherapy serum albumin to predict chemotherapy response. Our results suggest that a threshold around 4.0 g/dL could be clinically useful and deserves further investigation. Identifying patients with low albumin, who are at higher risk of poor chemotherapy response, may help clinicians to personalize the treatment, perform nutritional and inflammatory status improvement, potentially leading to better treatment outcomes.

While markers of inflammation, namely NLR, PLR, MLR, and D-dimer are associated with prognosis in previous study (3, 25, 28), inflammatory markers were not significantly correlated with chemotherapy response in this cohort. A different result when comparing previous studies that shows inflammatory markers as prognostic value for survival(28-32), and also with chemoterapy resistance(3) in ovarian cancer. In this study, albumin appeared to be a more sensitive predictor of chemotherapy response than inflammatory markers.

The number of negative predictive value in this study indicates that patients with low albumin level might still benefit from chemotherapy, highlighting the chances of combining albumin with other clinical and molecular markers to improve prediction in future research. While these findings offer valuable insights, the single-center design and small sample size may limit their generalizability. Larger and multicenter prospective studies are valuable to confirm the role of albumin as a predictive biomarker for chemotherapy response.

5. CONCLUSIONS

This study demonstrates that pre-chemotherapy serum albumin is a simple and accessible predictor to chemotherapy response in advanced stage epithelial ovarian cancer. Patients with higher albumin levels were more likely to respond to treatment, whereas D-dimer and inflammatory markers (NLR, PLR, MLR) were not predictive in this study. Given its low cost and ease of measurement, serum albumin could serve as a useful marker to guide clinical treatment decisions.

Ethic approval: All research designs were reviewed and approved by the Health Research Ethics Committee of Dr Wahidin Sudi- rohusodo Hospital, Faculty of Medicine, Hasanuddin University (94/UN4.6.4.5.31/PP36/2023) on February 14, 2023.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a con- flict of interest in connection with the submitted article.

Authors Contribution: RSS, NUP: Conceptualization, data collection, data analysis, and manuscript writing; IAF: Supervision, data interpretation, and manuscript revision; SR, DL: Supervision and manuscript revision; AAZ: Statistical analysis and manuscript revision.

Declaration on the use of AI: Artificial intelligence tools were used solely for generating illustrative figures, and the authors take full responsibility for the accuracy and integrity of the final images.

Consent for publication: All subjects have provided consent for publication.

Acknowledgments: The authors thank the Faculty of Medicine, Hasanuddin University, and Dr. Wahidin Sudirohusodo Hospital, Makassar, for their support and facilities provided for this research.

Funding: This research received no external funding.

Data Availability Statement: All the data are available from the corresponding author upon a reasonable request.

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