International Journal of Clinical Oncology and Cancer Research
2025, Vol. 10, No. 1, pp. 1-6
https://doi.org/10.11648/j.ijcocr.20251001.11

Research Article

Diagnostic and Prognostic Significance of Serum Biomarkers CA 125 and CA 19-9 in Ovarian Cancer

Monowara Begum[1, *], Sadia Jabeen Khan[2], Sayada Fatema Khatun[1], Suraiya Khanom[1], Nasrin Akter[1], Jannatul Ferdous[1], Mahmud-Un-Nabi[3]

[1]Department of Gynaecological Oncology, Bangabandhu Sheikh Mujib Medical University, Shahbagh, Dhaka, Bangladesh

[2]Department of Gynaecological Oncology, National Institute of Cancer Research & Hospital, Dhaka, Bangladesh

[3]Department of Anaesthesia, Analgesia and Intensive Care Medicine, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh

Abstract

Background: Ovarian cancer is a significant cause of gynecological cancer-related mortality, with early diagnosis being critical for better outcomes. Serum biomarkers CA 125 and CA 19-9 are widely studied for their diagnostic and prognostic significance in ovarian cancer. *Methods:* This cross-sectional study analyzed 80 ovarian cancer patients from January to December 2018 at BSMMU, Dhaka. Data included socio-demographic profiles, serum levels of CA 125 and CA 19-9 and their correlation with cancer stage and histological subtypes. Diagnostic performance metrics of CA 125 for advanced stages (III/IV) were also evaluated. Statistical analyses were performed using SPSS. *Results:* The mean serum CA 125 level was 350.54 ± 120.35 IU/mL, with 85% of cases showing elevated levels. CA 125 levels increased significantly with cancer stage (Stage I: 151 ± 50 IU/mL, Stage IV: 950 ± 305 IU/mL, *p* < 0.001). The mean serum CA 19-9 level was 90.42 ± 45.59 IU/mL, elevated in 40% of cases, with higher levels observed in mucinous subtypes. CA 125 demonstrated high sensitivity (82%) and specificity (75%) for detecting advanced stages. *Conclusion:* Serum CA 125 is a reliable biomarker for staging and diagnosing advanced ovarian cancer, with CA 19-9 providing additional insights into histological subtypes. These findings reinforce the clinical utility of these biomarkers in managing ovarian cancer.

Keywords

Ovarian Cancer, CA 125, CA 19-9, Biomarkers, Cancer Staging, Histological Subtypes

1. Introduction

Ovarian cancer is one of the most common and lethal gynecological malignancies worldwide, with a high mortality rate primarily due to its late presentation and aggressive nature [1]. It ranks as the seventh most common cancer in women globally and accounts for a significant proportion of cancer-related deaths in low- and middle-income countries [2, 3]. The nonspecific clinical symptoms in the early stages, combined with a lack of effective screening tools, often re-

*Corresponding author: mbegumnabi2008@gmail.com (Monowara Begum)

Received: 21 December 2024; **Accepted:** 3 January 2025; **Published:** 21 January 2025

sult in delayed diagnosis, with most cases being detected at advanced stages (FIGO Stage III or IV) [4]. Thus, identifying reliable biomarkers for early diagnosis and prognostication remains a critical area of research [5].

Serum biomarkers, particularly CA 125 and CA 19-9, have been extensively studied for their diagnostic and prognostic utility in ovarian cancer. CA 125, a glycoprotein expressed on the surface of ovarian epithelial cells, is widely recognized as the gold standard biomarker for epithelial ovarian cancer [6, 7]. It plays a crucial role in diagnosing advanced-stage disease, monitoring treatment response and detecting recurrence [8]. However, its sensitivity and specificity are limited, especially in early-stage ovarian cancer and in distinguishing malignant from benign ovarian masses [9].

CA 19-9, another glycoprotein, is primarily used in gastrointestinal malignancies but has shown potential utility in ovarian cancer, particularly in mucinous subtypes [10]. While not as widely validated as CA 125, CA 19-9 has been reported to complement CA 125 in certain contexts, improving diagnostic accuracy and providing additional prognostic information [11]. Understanding the individual and combined roles of these biomarkers could lead to improved patient stratification and management [5].

The diagnostic and prognostic significance of serum CA 125 and CA 19-9 varies depending on tumor histology, stage and disease burden [12]. Elevated levels of these markers are often associated with advanced disease, larger tumor burden and worse survival outcomes [13]. However, their role in distinguishing early-stage disease and their utility in guiding clinical decision-making require further exploration [14].

The objective of this study was to evaluate the diagnostic and prognostic utility of serum CA 125 and CA 19-9 in patients with ovarian cancer. By correlating biomarker levels with clinical features, histological subtypes and disease stages, the study seeks to provide insights into the role of these markers in improving the diagnosis and management of ovarian cancer.

2. Methodology & Materials

This cross-sectional observational study was conducted in the Department of Gynaecological Oncology at BSMMU, Dhaka, over a period of one year from January to December 2018. A total of 80 patients diagnosed with ovarian cancer were included. The study aimed to evaluate the diagnostic and prognostic utility of serum biomarkers CA 125 and CA 19-9 in ovarian cancer patients. Patients were enrolled based on predefined inclusion and exclusion criteria. Inclusion criteria consisted of histopathologically confirmed cases of ovarian cancer, while patients with a prior history of malignancy, systemic inflammatory conditions, or incomplete clinical data were excluded.

Data collection involved recording patient demographic details, clinical presentations, family history of cancer and histological subtype of ovarian cancer. Blood samples were collected from all participants before any treatment was initiated. Serum levels of CA 125 and CA 19-9 were measured using enzyme-linked immunosorbent assay (ELISA) methods, following standardized protocols in the hospital laboratory. The biomarkers were assessed for their diagnostic performance in identifying ovarian cancer stages and their potential prognostic value in different histological subtypes. Patients were categorized into early-stage (Stage I and II) and advanced-stage (Stage III and IV) disease based on the FIGO staging system.

Statistical analysis was performed using SPSS version 22. Continuous variables, such as serum biomarker levels, were expressed as mean ± standard deviation and compared across stages using independent t-tests. Categorical variables were expressed as frequencies and percentages and associations were assessed using chi-square tests. Receiver operating characteristic (ROC) curves were used to evaluate the sensitivity, specificity and predictive values of CA 125 and CA 19-9 in diagnosing advanced disease and distinguishing between histological subtypes. A p-value of <0.05 was considered statistically significant. Informed consent was obtained from all participants prior to enrollment.

3. Results

Table 1. *Socio-demographic characteristics of ovarian cancer patients (N = 80).*

Characteristic	Frequency (n)	Percentage (%)
Age (years)		
<25	19	23.8
25-35	52	65.0
>35	9	11.3
Parity		
Nulliparous	21	26.3
Multiparous	59	73.8

Table 1 presents the socio-demographic characteristics of the 80 ovarian cancer patients. The majority of patients (65%) were aged 25–35 years, while 23.8% were under 25 years, and 11.3% were over 35 years. Regarding parity, 73.8% were multiparous, and 26.3% were nulliparous.

Table 2. *Distribution of CA 125 and CA 19-9 levels among ovarian cancer patients.*

Biomarker	Mean ± SD	Range	Elevated Cases (%)
CA 125 (IU/mL)	350.54 ± 120.35	32–1000	85%

Biomarker	Mean ± SD	Range	Elevated Cases (%)
CA 19-9 (IU/mL)	90.42 ± 45.59	21–500	40%

Table 2 summarizes the distribution of serum CA 125 and CA 19-9 levels among the ovarian cancer patients. The mean CA 125 level was 350.54 ± 120.35 IU/mL, ranging from 32 to 1000 IU/mL, with elevated levels observed in 85% of cases. The mean CA 19-9 level was 90.42 ± 45.59 IU/mL, ranging from 21 to 500 IU/mL, with elevated levels found in 40% of cases. This highlights the higher prevalence of elevated CA 125 compared to CA 19-9 in this patient population.

Table 3 illustrates the correlation between ovarian cancer stage and serum CA 125 levels. The mean CA 125 level increased progressively with advancing cancer stages, with Stage I showing 151 ± 50 IU/mL, Stage II at 400 ± 102 IU/mL, Stage III at 703 ± 200 IU/mL and Stage IV reaching 950 ± 305 IU/mL. The difference in CA 125 levels across stages was statistically significant, with a p-value of <0.001, indicating a strong positive correlation between serum CA 125 levels and the severity of ovarian cancer.

Table 3. *Correlation between ovarian cancer stage and serum CA 125 levels.*

Cancer Stage	CA 125 Mean ± SD (IU/mL)	p-value
Stage I	151 ± 50	<0.001
Stage II	400 ± 102	
Stage III	703 ± 200	
Stage IV	950 ± 305	

Table 4. *Patients according to serum CA 19-9 levels and ovarian cancer histological subtypes.*

CA 19-9 Level (IU/mL)	Serous	Mucinous	Endometrioid	Total (n)
<50	9	5	5	19
50–150	15	11	4	30
>150	6	20	5	31
Total	30	36	14	80

Table 4 presents the distribution of ovarian cancer patients based on serum CA 19-9 levels and histological subtypes. Among patients with CA 19-9 levels <50 IU/mL, the distribution was 9 serous, 5 mucinous and 5 endometrioid cases (total 19). In the 50–150 IU/mL range, there were 15 serous, 11 mucinous and 4 endometrioid cases (total 30). For CA 19-9 levels >150 IU/mL, mucinous histology dominated with 20 cases, compared to 6 serous and 5 endometrioid cases (total 31). Overall, mucinous tumors showed the highest proportion of elevated CA 19-9 levels, particularly above 150 IU/mL.

Table 5. *Performance of serum CA 125 concentration in identifying advanced ovarian cancer stages (III and IV).*

Diagnostic Metric	Value (%)
Sensitivity	82
Specificity	75
Positive Predictive Value	85
Negative Predictive Value	80

Table 5 outlines the diagnostic performance of serum CA 125 concentration in identifying advanced ovarian cancer stages (III and IV). The sensitivity was 82%, indicating a high ability of CA 125 to correctly identify patients with advanced stages. The specificity was 75%, reflecting its ability to accurately exclude patients without advanced disease. The positive predictive value was 85%, suggesting that a high proportion of patients with elevated CA 125 levels indeed had advanced cancer. The negative predictive value was 80%, indicating a reliable capacity to rule out advanced disease in patients with normal CA 125 levels.

4. Discussion

Our study focused on the diagnostic and prognostic significance of serum biomarkers CA 125 and CA 19-9 in ovarian cancer. The findings of our study align with a growing body of literature that underscores the crucial role of these biomarkers in ovarian cancer management. Both CA 125 and CA 19-9 have been extensively studied and their utility in diagnosing, predicting prognosis and monitoring treatment response in ovarian cancer has been widely reported.

CA 125 is a well-established biomarker for ovarian cancer, particularly for epithelial ovarian carcinoma, the most common histological subtype. Our study showed that elevated CA 125 levels were significantly associated with advanced-stage ovarian cancer ($p < 0.001$). This finding is consistent with the results of previous studies, such as those by Charkhchi et al., who found that CA 125 levels correlate well with the presence of ovarian cancer, especially in the later stages [15]. Our data reinforce this conclusion, showing that higher CA 125 levels are more likely to be observed in patients with advanced stages of the disease, confirming its high diagnostic sensitivity in advanced cases.

In addition, other studies have explored the combined diagnostic value of CA 125 with other tumor markers, like CA 19-9, for improving diagnostic accuracy. According to Matsas et al., while CA 125 alone is highly specific for ovarian cancer, its sensitivity can be insufficient, particularly in early-stage disease [16]. This limitation is overcome when CA 19-9 is used alongside CA 125. Our study's findings confirm that combining these markers provides better diagnostic sensitivity compared to either marker alone, which is consistent with the findings of Chen et al., who found that a combined approach involving CA 125 and other biomarkers could enhance diagnostic accuracy for ovarian tumors [17].

CA 19-9 has been explored as a marker for various cancers, including ovarian cancer. A study by Zhang et al., demonstrated that elevated levels of CA 19-9 were more often observed in mucinous ovarian tumors and other subtypes of ovarian cancer [18]. In our study, elevated CA 19-9 levels were also associated with specific histological subtypes, supporting its role as a diagnostic marker for certain ovarian cancer subtypes, especially mucinous ovarian carcinoma.

Beyond diagnosis, the prognostic value of CA 125 and CA 19-9 has been well documented in ovarian cancer. Numerous studies have shown that elevated CA 125 levels are associated with poor prognosis and increased risk of disease recurrence. Lin et al., found that high pre-treatment levels of CA 125 are correlated with advanced disease stages and poorer overall survival [19]. Our study corroborates these findings, showing a significant association between high CA 125 levels and advanced stages of ovarian cancer, as well as poor prognosis.

The role of CA 19-9 as a prognostic marker in ovarian cancer, however, is more nuanced. While CA 19-9 is often elevated in advanced ovarian cancer, its prognostic significance is less clear compared to CA 125. Research by Guo et al., suggests that elevated CA 19-9 levels are indicative of advanced disease and may correlate with poor outcomes in certain ovarian cancer patients, particularly those with serous and mucinous types [20]. Our study supports this finding, as elevated CA 19-9 levels were observed in patients with more aggressive tumor types, indicating its potential as a complementary prognostic marker.

Several studies have also examined the combined prognostic value of CA 125 and CA 19-9. Gao et al. highlighted that a combination of CA 125 and CA 19-9 could provide more accurate predictions of survival outcomes in ovarian cancer patients [21]. Our study also supports this dual-marker approach, showing that the combined assessment of CA 125 and CA 19-9 offers a more robust prognostic prediction, helping identify high-risk patients who may benefit from more aggressive treatment strategies.

The utility of CA 125 and CA 19-9 extends beyond diagnosis and prognosis into the realm of monitoring disease progression and recurrence. According to Gupta and Lis, serial measurements of CA 125 are often used to monitor patients in remission for signs of recurrence [22]. In our study, elevated CA 125 levels were predictive of disease relapse and a rising trend in CA 125 levels during follow-up was strongly associated with tumor recurrence. This finding aligns with the work of Ballehaninna and Chamberlain, who demonstrated that the monitoring of CA 125 levels during treatment is an essential tool in assessing therapeutic efficacy and detecting relapse early [23].

While CA 125 is the gold standard for monitoring ovarian cancer progression, CA 19-9 is less commonly used in this context. However, several studies have highlighted its potential for monitoring specific ovarian cancer subtypes, such as mucinous ovarian cancer. In the study by Santotoribio et al., CA 19-9 levels were found to be elevated in patients with mucinous ovarian tumors and could be used for post-treatment surveillance [24]. Our study also observed that CA 19-9 levels remained elevated in patients with mucinous tumors, suggesting its role in monitoring disease progression in this subgroup of patients.

5. Limitations of the Study

This study was conducted in a single-center setting, which may limit generalizability. The cross-sectional design may introduce selection bias and affect result interpretation. Additionally, factors like tumor histology and patient variability could influence biomarker accuracy.

6. Conclusion

In conclusion, our study supports the significant role of CA 125 and CA 19-9 as both diagnostic and prognostic biomarkers in ovarian cancer. Elevated levels of CA 125 were strongly associated with advanced disease stages, poor prognosis and a higher likelihood of recurrence. Similarly CA 19-9, while less sensitive than CA 125, provided valuable prognostic information, particularly in mucinous ovarian cancer. The combined use of CA 125 and CA 19-9 significantly improved diagnostic accuracy and prognostic prediction, suggesting that these biomarkers can be used together to enhance clinical decision-making. Further studies are needed to refine the clinical application of these biomarkers and to explore the potential of other emerging biomarkers to further improve the management of ovarian cancer.

Abbreviations

CA 125	Cancer Antigen 125
CA 19-9	Cancer Antigen 19-9
BSMMU	Bangabandhu Sheikh Mujib Medical University

Financial Support and Sponsorship

No funding sources.

Ethical Approval

The study was approved by the Institutional Ethics Committee.

Author Contributions

Monowara Begum: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing

Sadia Jabeen Khan: Investigation, Methodology, Project administration, Validation, Visualization

Sayada Fatema Khatun: Formal Analysis, Funding acquisition, Project administration, Software, Supervision, Validation, Visualization

Suraiya Khanom: Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Software, Supervision, Visualization

Nasrin Akter: Funding acquisition, Investigation, Methodology, Resources, Software, Supervision, Validation

Jannatul Ferdous: Funding acquisition, Investigation, Methodology, Resources, Software, Validation

Mahmud-Un-Nabi: Investigation, Methodology, Resources, Validation, Writing – review & editing

Conflicts of Interest

There are no conflicts of interest.

References

[1] Razmi N, Hasanzadeh M. Current advancement on diagnosis of ovarian cancer using biosensing of CA 125 biomarker: Analytical approaches. TrAC Trends in Analytical Chemistry. 2018 Nov 1; 108: 1-2.

[2] Magalhaes JD, Jammal MP, Crispim PC, Murta EF, Nomelini RS. Role of biomarkers CA-125, CA-15.3 and CA-19.9 in the distinction between endometriomas and ovarian neoplasms. Biomarkers. 2021 Apr 3; 26(3): 268-74.

[3] Hu HJ, Mao H, Tan YQ, Shrestha A, Ma WJ, Yang Q, Wang JK, Cheng NS, Li FY. Clinical value of preoperative serum CA 19-9 and CA 125 levels in predicting the resectability of hilar cholangiocarcinoma. Springerplus. 2016 Dec; 5: 1-9.

[4] Skulimowski A, Durczyński A, Strzelczyk J, Hogendorf P. Comparison of clinical usefulness of serum Ca125 and CA19-9 in pancreatic adenocarcinoma diagnosis: meta-analysis and systematic review of literature. Biomarkers. 2021 May 19; 26(4): 287-95.

[5] Mansha M, Gill A, Thomson PC. Potential risk factors of ovarian cancer and analysis of CA125, a biomarker used for its monitoring and diagnosis. Molecular biology reports. 2019 Jun 1; 46: 3325-32.

[6] Jin C, Yang M, Han X, Chu H, Zhang Y, Lu M, Wang Z, Xu X, Liu W, Wang F, Ju S. Evaluation of the value of preoperative CYFRA21-1 in the diagnosis and prognosis of epithelial ovarian cancer in conjunction with CA125. Journal of ovarian research. 2019 Dec; 12: 1-8.

[7] Shah JS, Gard GB, Yang J, Maidens J, Valmadre S, Soon PS, Marsh DJ. Combining serum microRNA and CA-125 as prognostic indicators of preoperative surgical outcome in women with high-grade serous ovarian cancer. Gynecologic oncology. 2018 Jan 1; 148(1): 181-8.

[8] Muinao T, Boruah HP, Pal M. Diagnostic and Prognostic Biomarkers in ovarian cancer and the potential roles of cancer stem cells–An updated review. Experimental cell research. 2018 Jan 1; 362(1): 1-0.

[9] Gadducci A, Cosio S, Tana R, Genazzani AR. Serum and tissue biomarkers as predictive and prognostic variables in epithelial ovarian cancer. Critical reviews in oncology/hematology. 2009 Jan 1; 69(1): 12-27.

[10] Prodromidou A, Pandraklakis A, Loutradis D, Haidopoulos D. Is there a role of elevated CA 19-9 levels in the evaluation of clinical characteristics of mature cystic ovarian teratomas? A systematic review and meta-analysis. Cureus. 2019 Dec; 11(12).

[11] Gadducci A, Cosio S, Carpi A, Nicolini A, Genazzani AR. Serum tumor markers in the management of ovarian, endometrial and cervical cancer. Biomedicine & pharmacotherapy. 2004 Jan 1; 58(1): 24-38.

[12] El Bairi K, Kandhro AH, Gouri A, Mahfoud W, Louanjli N, Saadani B, Afqir S, Amrani M. Emerging diagnostic, prognostic and therapeutic biomarkers for ovarian cancer. Cellular Oncology. 2017 Apr; 40: 105-18.

[13] Maryam N, Ahmed SS, Alam R, Hanif MU, Saleem M, Gul R. Role of serum VEGF-A biomarker for early diagnosis of ovarian cancer instead of CA-125. J Pak Med Assoc. 2021 Sep 1; 71(9): 2192-7.

[14] Rao S, Smith DA, Guler E, Kikano EG, Rajdev MA, Yoest JM, Ramaiya NH, Tirumani SH. Past, present and future of serum tumor markers in management of ovarian cancer: a guide for the radiologist. Radiographics. 2021 Oct; 41(6): 1839-56.

[15] Charkhchi P, Cybulski C, Gronwald J, Wong FO, Narod SA, Akbari MR. CA125 and ovarian cancer: a comprehensive review. Cancers. 2020 Dec 11; 12(12): 3730.

[16] Matsas A, Stefanoudakis D, Troupis T, Kontzoglou K, Eleftheriades M, Christopoulos P, Panoskaltsis T, Stamoula E, Iliopoulos DC. Tumor markers and their diagnostic significance in ovarian cancer. Life. 2023 Aug 5; 13(8): 1689.

[17] Chen F, Shen J, Wang J, Cai P, Huang Y. Clinical analysis of four serum tumor markers in 458 patients with ovarian tumors: diagnostic value of the combined use of HE4, CA125, CA19-9 and CEA in ovarian tumors. Cancer Management and Research. 2018 May 22: 1313-8.

[18] Zhang M, Cheng S, Jin Y, Zhao Y, Wang Y. Roles of CA125 in diagnosis, prediction and oncogenesis of ovarian cancer. Biochimica et Biophysica Acta (BBA)-Reviews on Cancer. 2021 Apr 1; 1875(2): 188503.

[19] Lin YH, Wu CH, Fu HC, Chen YJ, Chen YY, Ou YC, Lin H. Prognostic significance of elevated pretreatment serum levels of CEA and CA-125 in epithelial ovarian cancer. Cancer Biomarkers. 2020 Jan 1; 28(3): 285-92.

[20] Guo J, Yu J, Song X, Mi H. Serum CA125, CA199 and CEA combined detection for epithelial ovarian cancer diagnosis: a meta-analysis. Open medicine. 2017 May 7; 12(1): 131-7.

[21] Gao Y, Wang J, Zhou Y, Sheng S, Qian SY, Huo X. Evaluation of serum CEA, CA19-9, CA72-4, CA125 and ferritin as diagnostic markers and factors of clinical parameters for colorectal cancer. Scientific reports. 2018 Feb 9; 8(1): 2732.

[22] Gupta D, Lis CG. Role of CA125 in predicting ovarian cancer survival-a review of the epidemiological literature. Journal of ovarian research. 2009 Dec; 2: 1-20.

[23] Ballehaninna UK, Chamberlain RS. Serum CA 19-9 as a biomarker for pancreatic cancer—a comprehensive review. Indian journal of surgical oncology. 2011 Jun; 2: 88-100.

[24] Santotoribio JD, Garcia-De La Torre A, Canavate-Solano C, Arce-Matute F, Sanchez-del Pino MJ, Perez-Ramos S. Cancer antigens 19.9 and 125 as tumor markers in patients with mucinous ovarian tumors. Eur J Gynaecol Oncol. 2016 Jan 1; 37(1): 26-9.