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Association of Serum CA-125 Levels with Ovarian Tumors, Endometriosis, and Pelvic Inflammatory Disease

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ABSTRACT

Background: Cancer antigen-125 (CA-125) is a widely recognized biomarker used in the assessment of ovarian malignancies. However, elevated CA-125 levels are also observed in several benign gynecological conditions, including endometriosis and pelvic inflammatory disease (PID), which may reduce its diagnostic specificity. **Objective:** To evaluate serum CA-125 levels in women with ovarian tumors, endometriosis, and PID and determine its diagnostic significance in differentiating malignant from benign pelvic conditions. **Methods & Materials:** This cross-sectional analytical study was conducted from January to December 2024 at the Department of Obstetrics and Gynecology, Gazi Medical College Hospital, Khulna, Bangladesh. A total of 160 women aged 18–70 years were enrolled and divided into four groups: ovarian tumors (n=60), endometriosis (n=40), PID (n=30), and healthy controls (n=30). Diagnoses were established through clinical examination, imaging studies, and histopathology where applicable. Serum CA-125 levels were measured using chemiluminescent immunoassay, with values >35 U/mL considered elevated. **Results:** Mean serum CA-125 levels were significantly higher in malignant ovarian tumors (412.5 ± 210.8 U/mL) compared to benign ovarian tumors (46.3 ± 18.7 U/mL), endometriosis (78.9 ± 35.4 U/mL), PID (62.7 ± 28.9 U/mL), and controls (18.6 ± 6.2 U/mL). Elevated CA-125 levels were present in all malignant cases, while moderate elevations were also observed in endometriosis and PID. Postmenopausal women showed comparatively higher CA-125 levels than premenopausal women. **Conclusion:** CA-125 is a useful biomarker for identifying ovarian malignancy, particularly at markedly elevated levels. Nevertheless, benign gynecological disorders may also increase CA-125, limiting its specificity. Therefore, CA-125 should be interpreted alongside clinical findings and imaging for accurate diagnosis.

Keywords: *CA-125, ovarian tumors, endometriosis, pelvic inflammatory disease, tumor markers.*

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INTRODUCTION

Ovarian cancer remains one of the most lethal gynecological malignancies worldwide due to its insidious onset and late-stage presentation. Early diagnosis significantly improves survival rates yet effective screening strategies remain limited. Among available biomarkers, cancer antigen-125 (CA-125) is the most extensively studied and clinically utilized tumor marker for ovarian epithelial cancers [1]. CA-125 is a high-molecular-weight glycoprotein expressed by tissues derived from the coelomic epithelium, including the ovaries, fallopian tubes, peritoneum, pleura and pericardium [2]. Elevated serum CA-125 levels are found in approximately 80% of women with advanced ovarian cancer but in only 50% of early-stage disease limiting its sensitivity for screening purposes [3]. Despite its utility in monitoring treatment response and detecting disease recurrence, CA-125 lacks disease specificity. Elevated levels have been documented in various benign gynecological conditions such as endometriosis uterine fibroids and pelvic inflammatory disease (PID) [4,5]. Non-gynecological conditions including liver disease, tuberculosis, and heart failure may also raise CA-125 levels [6]. Endometriosis is a chronic inflammatory condition characterized by ectopic implantation of endometrial tissue, commonly affecting women of reproductive age. CA-125 is often elevated in moderate to severe disease and correlates with disease burden [7]. Similarly, PID, an ascending infection of the upper genital tract, causes peritoneal irritation and inflammation leading to increased CA-125 synthesis [8]. The diagnostic challenge arises when patients with benign inflammatory conditions present with adnexal masses and elevated CA-125, mimicking ovarian malignancy. In resource-limited settings reliance on CA-125 without adequate imaging or histopathology may result in misdiagnosis and overtreatment. Therefore, understanding the pattern and degree of CA-125 elevation across malignant and benign gynecological diseases is essential. This study aims to compare serum CA-125 levels among ovarian tumors, endometriosis, and PID, and to evaluate its diagnostic relevance in distinguishing malignant from benign pelvic pathology.

METHODS & MATERIALS

Study Design and Setting

A cross-sectional analytical study was conducted over a period of one year, from January 2024 to December 2024, at the Department of Obstetrics and Gynecology of Gazi Medical College Hospital, Khulna, Bangladesh. Ethical approval was obtained from the Institutional Review Board, and informed consent was taken from all participants before enrollment.

Study Population

Women aged 18–70 years presenting with pelvic pain, abnormal uterine bleeding, or an adnexal/pelvic mass were considered for inclusion. A total of 160 participants were enrolled and categorized into four groups based on clinical, imaging, and histopathological evaluation:

- **Group I:** Ovarian tumors (benign and malignant)
- **Group II:** Endometriosis
- **Group III:** Pelvic inflammatory disease (PID)
- **Group IV:** Healthy controls

Inclusion Criteria

- Women with a confirmed diagnosis of ovarian tumor

(benign or malignant) based on histopathology
- Women with laparoscopically or clinically confirmed endometriosis
- Women with PID diagnosed clinically and supported by imaging or laboratory findings
- Healthy women attending routine gynecological check-ups as controls

Exclusion Criteria
- Pregnancy
- History of non-gynecological malignancies
- Chronic liver disease, autoimmune disorders, or heart failure
- Incomplete clinical records or unwillingness to provide consent

Data Collection
Demographic data (age, menopausal status) and clinical features (pelvic pain, mass, menstrual irregularities) were recorded using a structured proforma. Imaging data from ultrasound and/or MRI were used to assess tumor characteristics, endometriotic lesions, and inflammatory involvement. Histopathological confirmation was obtained for all ovarian tumors following surgery or biopsy.

Serum CA-125 Measurement
Venous blood samples were collected prior to any surgical or medical intervention. Serum CA-125 levels were measured using a chemiluminescent immunoassay. Values above 35 U/mL were considered elevated according to established guidelines. All assays were performed in the hospital laboratory under standard quality control measures.

Statistical Analysis
Data were analyzed using SPSS software (version 25.0). Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. Comparisons among the four groups were performed using ANOVA for continuous variables and Chi-square test for categorical variables. Post-hoc analysis with Tukey's test was applied to identify significant differences between individual groups. A p-value <0.05 was considered statistically significant.

RESULTS

The baseline demographic and clinical characteristics of the study participants are presented in *Table I*. A total of 160 women were enrolled in the study and categorized into four groups: ovarian tumors (n=60), endometriosis (n=40), pelvic inflammatory disease (PID, n=30), and healthy controls (n=30). Patients with ovarian tumors were comparatively older, with a mean age of 48.6 years, whereas the mean ages in the endometriosis, PID, and healthy control groups were 32.8, 29.5, and 31.2 years, respectively. Most women with endometriosis and PID were premenopausal, while more than half of the ovarian tumor patients were postmenopausal. Pelvic pain was highly prevalent among patients with endometriosis and PID, occurring in 90% and 100% of cases, respectively, whereas only 38% of ovarian tumor patients reported pelvic pain. Adnexal masses were present in all ovarian tumor patients but were uncommon in the endometriosis and PID groups and absent among healthy controls (*Table I*).

Table I
Baseline Demographic and Clinical Characteristics.

Variable	Ovarian Tumors (n=60)	Endometriosis (n=40)	PID (n=30)	Controls (n=30)
Mean age (years)	48.6 ± 10.4	32.8 ± 6.9	29.5 ± 7.2	31.2 ± 5.8
Premenopausal (%)	42	95	100	100
Postmenopausal (%)	58	5	0	0
Pelvic pain (%)	38	90	100	0
Adnexal mass (%)	100	25	10	0

The histopathological distribution of ovarian tumors is shown in *Table II*. Among the 60 ovarian tumor cases, benign lesions constituted 53.3% of tumors, while malignant tumors accounted for 46.7%. Serous carcinoma was identified as the most common malignant subtype, followed by mucinous carcinoma. Less frequent malignant histological types included endometrioid carcinoma and clear cell carcinoma. These findings indicate that epithelial ovarian malignancies predominated among malignant ovarian tumors in this study population.

Table II
Histopathological Distribution of Ovarian Tumors (*n*=60).

Tumor Type	Number (%)
Benign ovarian tumors	32 (53.3%)
Malignant ovarian tumors	28 (46.7%)
Serous carcinoma	14 (50.0%)
Mucinous carcinoma	8 (28.6%)
Endometrioid carcinoma	4 (14.3%)
Clear cell carcinoma	2 (7.1%)

Serum CA-125 levels among the study groups are summarized in *Table III*. Patients with malignant ovarian tumors demonstrated markedly elevated CA-125 levels, with a mean value of 412.5 U/mL, which was significantly higher than the levels observed in all other groups. Benign ovarian tumors showed only mild elevation, with a mean CA-125 level of 46.3 U/mL. Moderate elevations were observed among women with endometriosis and PID, with mean values of 78.9 U/mL and 62.7 U/mL, respectively. In contrast, healthy controls maintained normal CA-125 levels, with a mean value of 18.6 U/mL.

Table III
Serum CA-125 Levels Across Study Groups.

Group	Mean CA-125 (U/mL) ± SD	Range (U/mL)
Malignant ovarian tumors	412.5 ± 210.8	120–980
Benign ovarian tumors	46.3 ± 18.7	20–85
Endometriosis	78.9 ± 35.4	40–180
PID	62.7 ± 28.9	38–140
Controls	18.6 ± 6.2	8–30

The proportion of patients with elevated CA-125 levels above the normal cutoff value of 35 U/mL is presented in *Table IV*. All patients with malignant ovarian tumors exhibited elevated CA-125 levels. Elevated values were also found in 56.3% of benign ovarian tumor cases. Similarly, 80% of patients with endometriosis and 80% of PID patients had CA-125 levels above the normal threshold. Among healthy controls, only 6.7% demonstrated elevated values. These findings indicate that although CA-125 is highly sensitive for ovarian malignancy, elevated levels may also occur in several benign gynecological inflammatory conditions.

Table IV
Proportion of Patients with Elevated CA-125 (>35 U/mL).

Group	Elevated CA-125 n (%)
Malignant ovarian tumors	28 (100%)
Benign ovarian tumors	18 (56.3%)
Endometriosis	32 (80.0%)
PID	24 (80.0%)
Controls	2 (6.7%)

The relationship between menopausal status and CA-125 levels is demonstrated in *Table V*. Postmenopausal women showed significantly higher mean CA-125 levels (356.2 U/mL) compared to premenopausal women (96.4 U/mL), reflecting the greater frequency of ovarian malignancy in the postmenopausal group. In contrast, premenopausal women with endometriosis or PID demonstrated moderate but variable elevations in CA-125 levels, which may overlap with malignant conditions. Overall, these findings suggest that markedly elevated CA-125 levels strongly indicate ovarian malignancy, whereas moderate increases are commonly associated with benign inflammatory disorders. Therefore, CA-125 should be interpreted cautiously alongside clinical evaluation and imaging findings to minimize diagnostic errors.

Table V
CA-125 Levels Stratified by Menopausal Status.

Menopausal Status	Mean CA-125 (U/mL) ± SD
Premenopausal	96.4 ± 58.7
Postmenopausal	356.2 ± 190.5

DISCUSSION

This study evaluated the association of serum CA-125 levels with ovarian tumors, endometriosis, and pelvic inflammatory disease (PID) to assess its diagnostic utility. Our findings demonstrate that CA-125 is markedly elevated in malignant ovarian tumors compared to benign ovarian lesions, endometriosis, PID and healthy controls, consistent with prior research [9,10]. Patients with malignant ovarian tumors had mean CA-125 levels exceeding 400 U/mL, which aligns with literature reporting higher levels in advanced-stage disease [9]. This confirms that CA-125 remains a valuable biomarker for identifying ovarian malignancy, particularly when interpreted alongside clinical and imaging findings. Benign ovarian tumors, in contrast, exhibited only mild to moderate elevations in CA-125, with a mean value of 46.3 U/mL. This suggests that while benign lesions can increase CA-125 the magnitude is generally lower than in malignancy. These results corroborate previous studies indicating that CA-125 elevation in benign ovarian conditions is nonspecific and often overlaps with inflammatory states [10,11]. Clinicians should therefore exercise caution when interpreting borderline CA-125 elevations in premenopausal women as this may lead to unnecessary surgical intervention. In patients with endometriosis, CA-125 was moderately elevated, with a mean of 78.9 U/mL. These findings are consistent with studies showing that CA-125 levels correlate with the severity and extent of endometriotic lesions [12]. Endometriotic implants induce peritoneal irritation and local inflammation, which stimulates mesothelial cells to secrete CA-125. This explains why many premenopausal women with endometriosis in our study had CA-125 above the normal threshold. While CA-125 may assist in monitoring disease progression or response to therapy it is insufficient as a standalone diagnostic tool for differentiating endometriosis from malignancy [12,13]. Similarly, patients with PID exhibited moderate elevations in CA-125 (mean 62.7 U/mL). Inflammatory processes in the upper genital tract, including the fallopian tubes and peritoneum, likely trigger the release of CA-125 [14]. This inflammatory elevation further emphasizes the importance of considering the underlying etiology when interpreting CA-125 results. Repeating CA-125 after resolution of infection can help distinguish transient inflammatory elevation from persistent elevation due to malignancy. The study also highlights the influence of menopausal status on CA-125 interpretation. Postmenopausal women demonstrated significantly higher CA-125 levels, reflecting the greater prevalence of ovarian malignancy in this age group [9]. In contrast, premenopausal women had lower but more variable CA-125 values, particularly in benign inflammatory conditions. This variability necessitates careful integration of CA-125 with imaging findings, clinical assessment, and risk assessment models such as the Risk of Malignancy Index (RMI) to avoid overdiagnosis [15]. Our findings underscore the clinical challenge posed by the overlap of CA-125 levels in benign and malignant conditions. While extremely elevated CA-

125 (>200 U/mL) strongly suggests malignancy, moderate elevations are common in endometriosis, PID and benign ovarian tumors. Therefore, CA-125 should be interpreted as part of a multimodal diagnostic approach rather than as an isolated marker. In resource-limited settings where imaging may be unavailable reliance solely on CA-125 could result in misdiagnosis and inappropriate management. In our study demonstrates that CA-125 is a reliable marker for ovarian malignancy but shows moderate elevation in benign gynecological conditions such as endometriosis and PID. Its diagnostic value is enhanced when combined with clinical assessment, imaging and risk scoring, particularly in premenopausal women where overlap is more frequent. Careful interpretation can aid in early detection of malignancy while minimizing unnecessary interventions for benign conditions [9–16]. Limitations of this study include its single-center design and relatively small sample size, which may limit generalizability. Additionally, follow-up CA-125 measurements were not performed, which could have provided insight into the dynamics of marker elevation in benign versus malignant conditions. Future multicenter studies with longitudinal follow-up are warranted to validate these findings and refine CA-125 cutoff values for different clinical scenarios.

CONCLUSION

Serum CA-125 is a valuable biomarker for ovarian malignancies, particularly when levels are markedly elevated. However, its elevation in benign conditions such as endometriosis and pelvic inflammatory disease limits its diagnostic specificity. CA-125 should not be used in isolation but interpreted in conjunction with clinical findings, imaging and histopathology to ensure accurate diagnosis and appropriate management.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this study.

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