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CLINICAL ASSOCIATION OF AGE, MENOPAUSAL STATUS, AND SERUM CA-125 IN WOMEN WITH SUSPECTED OVARIAN CANCER RISK. A RETROSPECTIVE STUDY

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Abstract

Background: *Ovarian cancer remains one of the most lethal gynecologic malignancies, particularly in low-resource settings where early detection is challenging. CA-125 is the most widely used biomarker in evaluating suspected ovarian cancer, yet its interpretation is influenced by demographic factors such as age and menopausal status.*

Objective: *To assess the association between serum CA-125 levels, age, and menopausal status in women clinically suspected of having ovarian cancer, and to evaluate the diagnostic performance of CA-125 in this population.*

Methods: *This retrospective study included 200 women aged 31–65 years who presented with suspected ovarian pathology at Bahawalpur Victoria Hospital. Medical records were reviewed for age, menopausal status, CA-125 levels, risk categorization, and confirmed ovarian cancer diagnosis. CA-125 was measured using CLIA, with >35 U/mL considered elevated. Statistical analyses included Chi-square tests, ANOVA, and logistic regression, with significance set at $p < 0.05$.*

Results: *Elevated CA-125 was observed in 70.5% of participants. Postmenopausal women had significantly higher CA-125 levels and were more frequently categorized as high-risk ($p < 0.001$). CA-125 showed strong associations with both high-risk category ($p < 0.001$) and confirmed ovarian cancer ($\chi^2 = 104.375$, $p < 0.001$); all cancer-positive patients had elevated CA-125. CA-125 levels increased progressively with age, with the highest values observed in the 51–60 and >60 years groups ($p < 0.001$). Logistic regression identified elevated CA-125 as the strongest predictor of suspected ovarian cancer, while menopausal status and age showed no significant independent effect.*

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Conclusion: *CA-125 remains a valuable biomarker for evaluating suspected ovarian cancer, particularly among postmenopausal and older women. However, age- and menopause-related variations in CA-125 highlight the need for context-specific interpretation. These findings provide important local reference data and support the development of refined diagnostic strategies for resource-limited settings.*

INTRODUCTION

Ovarian cancer remains one of the most lethal gynecologic malignancies worldwide and represents a significant public health challenge due to its high mortality-to-incidence ratio [1, 2]. A major contributor to poor survival outcomes is delayed diagnosis, as early-stage disease often presents with vague, nonspecific symptoms such as abdominal bloating, pelvic discomfort, early satiety, or gastrointestinal disturbances. These symptoms are frequently misattributed to benign conditions, resulting in late clinical presentation when disease has already progressed to advanced stages [3, 4]. Globally, more than two-thirds of ovarian cancer cases are diagnosed at stage III or IV, where five-year survival rates drop dramatically compared to early-stage disease [5].

The lack of an effective, widely applicable screening strategy further complicates early detection. While imaging modalities such as transvaginal ultrasound and advanced radiologic techniques may aid diagnosis, their availability and affordability are limited in low- and middle-income countries (LMICs). Consequently, there is a critical need for accessible, cost-effective biomarkers that can assist in early risk stratification and clinical decision-making, particularly in resource-limited healthcare settings [6].

Cancer Antigen 125 (CA-125) remains the most extensively studied and commonly utilized serum biomarker in the evaluation of suspected ovarian malignancy. CA-125 is a high-molecular-weight mucin-type glycoprotein encoded by the MUC16 gene and was first identified in epithelial ovarian cancer tissues in the early 1980s [7, 8]. Since its discovery, CA-125 has been widely incorporated into clinical practice for supporting diagnosis, monitoring therapeutic response, assessing prognosis, and detecting disease recurrence in patients with confirmed ovarian cancer [9].

Traditionally, a serum CA-125 concentration of ≤35 U/mL has been adopted as the upper limit of normal for both premenopausal and postmenopausal women. However, the application of this single universal cutoff is controversial. Numerous studies have demonstrated that CA-125 has limited sensitivity in early-stage ovarian cancer, with elevated levels observed in only 23–50% of patients with stage I disease [10, 11]. This significantly restricts its utility as a standalone screening or early diagnostic tool.

In addition to suboptimal sensitivity, CA-125 lacks disease specificity. Elevated serum levels are frequently observed in a wide range of benign gynecological conditions, including endometriosis, uterine fibroids, benign ovarian cysts, and pelvic inflammatory disease [12]. Physiological states such as menstruation and pregnancy, as well as non-gynecological conditions involving peritoneal or systemic inflammation (e.g., liver disease, tuberculosis, and heart failure), can also result in increased CA-125 concentrations [13, 14]. These confounding factors contribute to false-positive results, potentially leading to unnecessary anxiety, invasive diagnostic procedures, and increased healthcare costs.

Importantly, demographic and biological factors—particularly age and menopausal status—have a significant influence on baseline CA-125 levels. Premenopausal women tend to exhibit greater variability in CA-125 concentrations due to hormonal fluctuations and menstrual cycle-related changes, whereas postmenopausal women generally demonstrate lower baseline levels [15, 16]. Several investigators have suggested that menopausal status-specific reference ranges may improve the interpretive accuracy of CA-125 testing, yet such adjustments are not uniformly applied in routine clinical practice [17].

Moreover, CA-125 levels are more frequently elevated in advanced-stage ovarian cancer, often

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reflecting tumor burden, peritoneal spread, or ascites. While this characteristic supports its role in disease monitoring, it further undermines its value for early detection, where biomarker elevation may be absent or minimal [18]. Systematic reviews and meta-analyses have reported wide variability in diagnostic performance, with sensitivity and specificity differing markedly depending on study population, disease prevalence, and inclusion criteria [19].

Recent research has explored the integration of CA-125 with other biomarkers, such as Human Epididymis Protein 4 (HE4), and multivariate algorithms to enhance diagnostic accuracy. Although promising, these approaches are often costly and technologically demanding, limiting their applicability in LMICs where healthcare resources are constrained [20]. Consequently, CA-125 remains the most practical and widely available biomarker in many clinical settings, despite its known limitations.

In South Asia, and particularly in Pakistan, there is a notable scarcity of population-specific data evaluating CA-125 distributions in relation to age and menopausal status among women presenting with suspected ovarian malignancy. Ethnic diversity, environmental exposures, reproductive patterns, and the prevalence of benign gynecological diseases may influence baseline CA-125 levels and alter its diagnostic performance compared to Western populations. Reliance on externally derived cutoff values without local validation may therefore lead to misclassification, delayed diagnosis, or unnecessary interventions.

Therefore, the present retrospective study conducted at Bahawalpur Victoria Hospital aims to investigate the clinical association between serum CA-125 levels, age, and menopausal status in women with suspected ovarian cancer over a 1.5-year period. Specifically, this study seeks to (i) describe the distribution of CA-125 levels across different age groups and menopausal categories, (ii) evaluate the diagnostic utility of CA-125 within the local population, and (iii) identify context-specific interpretive considerations that may enhance risk stratification and clinical decision-making in resource-limited healthcare settings.

Materials and Methods

Study Design and Setting

This retrospective, hospital-based study was conducted at Bahawalpur Victoria Hospital over a period of one year, from December 2024 to November 2025 .Medical records of female patients evaluated for suspected ovarian cancer were reviewed to assess the association between age, menopausal status, and serum CA-125 levels.

Study Population and Sample Size

A total of 200 female patients were included in the study. Cases were selected through consecutive non-probability sampling from hospital records.

Inclusion & Exclusion Criteria:

The study included female patients aged 31 to 65 years who presented with clinical suspicion of ovarian pathology and had complete medical records available. Specifically, patients were required to have documented information on age, menopausal status, serum CA-125 levels, and clinical risk categorization. Patients with incomplete medical records, a history of previously treated ovarian cancer, current pregnancy, or any known non-ovarian malignancies were excluded from the study.

Laboratory Testing

Serum CA-125 levels were measured using the Chemiluminescent Immunoassay (CLIA) technique in the hospital's central diagnostic laboratory. Blood samples were collected under aseptic conditions and analyzed according to the manufacturer's standard protocols. A cut-off value of >35 U/mL was considered indicative of elevated CA-125. All measurements were performed following standard operating procedures, and tests were repeated for confirmation when necessary.

Statistical Analysis

Data were analyzed using SPSS version 26. Descriptive statistics summarized continuous and categorical variables, while t-tests, ANOVA, chi-square, and Pearson correlation assessed associations between CA-125, age, and menopausal status. A p-value < 0.05 was considered statistically significant.

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Results

Table 1. Demographic and Clinical Characteristics of Study Participants

Variable	Category	n	%
Menopausal Status	Pre	115	57.5
	Post	85	42.5
Age Groups	31–40	59	29.5
	41–50	61	30.5
	51–60	54	27
	>60	26	13
Suspected Ovarian Cancer	Yes	111	55.5
	No	89	44.5
Risk Category	High	114	57
	Low	86	43
CA-125	Elevated	141	70.5
	Normal	59	29.5

The table 1 summarizes the demographic and clinical characteristics of the study participants (n = 200). Among them, 57.5% were premenopausal and 42.5% were postmenopausal. The age distribution showed that 29.5% of participants were aged 31–40 years, 30.5% were 41–50 years, 27% were 51–60 years, and 13% were older than 60 years. More than half of the participants (55.5%) were suspected of having ovarian cancer. Based on the risk assessment, 57% were categorized as high-risk, while 43% were low-risk. Serum CA-125 levels were elevated in 70.5% of participants, whereas 29.5% had normal CA-125 values.

Table 2. Association of Menopausal Status with Risk Category and CA-125 Levels (χ^2 Analysis)

Analysis	Category	Menopausal status		Total	Chi-Square (χ^2)	p-value
		Post	Pre			
Risk Category	High Risk	73	41	114	50.312	0.000
	Low Risk	12	74	86		
	Total	85	115	200		
CA-125 Level	Normal	2	57	59	52.382	0.000
	Elevated	83	58	141		
	Total	85	115	200		

Table 2 presents the association between menopausal status and both ovarian cancer risk category and CA-125 levels using Chi-square (χ^2) analysis. A significant association was observed between menopausal status and risk category ($\chi^2 = 50.312$, $p < 0.001$), with a higher proportion of postmenopausal women (73/85) classified as high-risk compared to premenopausal women (41/115). Similarly, menopausal status was strongly associated with CA-125 levels ($\chi^2 = 52.382$, $p < 0.001$), as elevated CA-125 levels were more frequent among postmenopausal women (83/85) than premenopausal women (58/115).

Table 3. Association of CA-125 Levels with Risk Category and Suspected Ovarian Cancer

Variables	Category	CA-125 Level		Total	χ^2 Value	p-value
		Normal	Elevated			
Risk Category	High	0	114	114	110.935	0.000
	Low	59	27	86		

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	Total	59	141	200		
Suspected Ovarian Cancer	No	59	30	89	104.375	0.000
	Yes	0	111	111		
	Total	59	141	200		

Table 3 shows the association of CA-125 levels with both ovarian cancer risk category and confirmed ovarian cancer status using Chi-square (χ^2) analysis. A highly significant association was observed between CA-125 levels and risk category (χ^2 = 110.935, $p < 0.001$), with all participants in the high-risk category exhibiting elevated CA-125 levels, whereas most low-risk participants had normal CA-125 levels. Similarly, CA-125 levels were strongly associated with confirmed ovarian cancer (χ^2 = 104.375, $p < 0.001$); all participants diagnosed with ovarian cancer had elevated CA-125, while participants without ovarian cancer predominantly had normal CA-125 levels.

Table 4. Comparison of CA-125 Levels across Age Groups

Age Group (years)	N	Mean ± SD	Post-hoc (Tukey HSD)
31–40	59	1.37 ± 0.49	Significantly lower than 41–50, 51–60, >60
41–50	61	1.67 ± 0.47	Significantly higher than 31–40; lower than 51–60, >60
51–60	54	2.00 ± 0.00	Significantly higher than 31–50; not different from >60
>60	26	1.92 ± 0.27	Significantly higher than 31–50; not different from 51–60

Table 4 presents CA-125 levels across age groups .A one-way ANOVA revealed a significant difference in CA-125 levels among age groups ($F(3, 196) = 28.10$, $p < 0.001$). Post-hoc Tukey HSD analysis showed that the youngest group (31–40 years) had significantly lower CA-125 levels compared to all other age groups. The 41–50 years group had intermediate values, significantly higher than 31–40 years but lower than 51–60 and >60 years groups. The 51–60 and >60 years groups had the highest CA-125 levels and did not differ significantly from each other. Levene's test indicated that the assumption of homogeneity of variances was violated (Levene Statistic = 143.469, DF = 3, 196, $p < 0.001$)."

Table 5. Logistic Regression Predicting Suspected Ovarian Cancer

Predictor	OR (Exp(B))	95% CI	p-value
CA-125 (Elevated)	Very high	–	–
Menopausal Status (Post vs Pre)	0.69	0.15–3.06	0.622
Age Group	2.12	0.94–4.77	0.069

Footnotes:

- OR = Odds Ratio
- CI = Confidence Interval
- CA-125 shows perfect separation → strongest predictor
- Model correctly classified 85% of participants (Hosmer-Lemeshow p = 0.658)

Table 5 presents the logistic regression analysis for predictors of suspected ovarian cancer. Elevated CA-125 was the strongest predictor of suspected ovarian cancer. Menopausal status was not significant (OR = 0.69, p = 0.622), while age group showed borderline significance (OR = 2.12, p = 0.069). The model correctly classified 85% of participants, with good fit (Hosmer-Lemeshow p = 0.658)."

Discussion

This retrospective study evaluated 200 women presenting with suspected ovarian cancer at Bahawalpur Victoria Hospital, focusing on the

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relationship between serum CA-125 levels, age, and menopausal status. The findings reinforce the clinical utility of CA-125 as a biomarker for ovarian cancer risk stratification and highlight the influence of demographic factors on its interpretation [21, 22].

Our results demonstrated a strong association between menopausal status and both ovarian cancer risk category and CA-125 levels. Postmenopausal women were more likely to be classified as high-risk and had elevated CA-125 levels compared to premenopausal women. These findings are consistent with previous literature suggesting that serum CA-125 levels tend to rise with age and are particularly higher in postmenopausal women with malignant ovarian pathology [23, 24]. The elevated CA-125 levels in postmenopausal women may reflect the increased baseline risk of ovarian malignancy in this population, supporting its use as a key diagnostic and risk stratification tool in clinical practice [25, 26].

The association between CA-125 levels and ovarian cancer risk was highly significant. All participants classified as high-risk exhibited elevated CA-125 levels, whereas the majority of low-risk participants had normal CA-125 values. Similarly, all patients with confirmed ovarian cancer had elevated CA-125, highlighting the biomarker's high sensitivity in this cohort [27, 28]. These findings underscore the importance of CA-125 measurement in the initial evaluation of women with suspected ovarian malignancy, consistent with established clinical guidelines [29, 30].

Age was also a significant factor influencing CA-125 levels. One-way ANOVA revealed that younger women (31–40 years) had significantly lower CA-125 levels compared to older age groups, with the highest values observed in the 51–60 and >60 years cohorts. This age-dependent increase aligns with prior studies showing that CA-125 levels can rise with advancing age, independent of menopausal status, reflecting both physiological changes and increased likelihood of malignancy [31, 32]. Clinicians should consider age when interpreting CA-125 results to avoid misclassification or overestimation of cancer risk in younger women [33].

Logistic regression analysis identified elevated CA-125 as the strongest predictor of suspected ovarian cancer, showing perfect separation in the model. While age group showed borderline significance and menopausal status was not statistically significant, the overall predictive accuracy of the model was high (85%), demonstrating the central role of CA-125 in risk stratification [34, 35]. This finding aligns with previous research emphasizing CA-125 as a primary biomarker for ovarian cancer detection, although it should be interpreted alongside other clinical and demographic variables for optimal accuracy.

Despite the strong associations observed, certain limitations should be considered. The retrospective design and single-center setting may limit generalizability. Additionally, reliance on hospital records and consecutive non-probability sampling may introduce selection bias. Future studies with larger, multicenter cohorts and prospective designs are warranted to validate these findings and further explore the interaction between CA-125, age, and menopausal status [21, 22].

Conclusion

This study demonstrates that serum CA-125 is a robust biomarker for ovarian cancer risk assessment, with its levels strongly influenced by menopausal status and age. Postmenopausal women and older age groups are more likely to exhibit elevated CA-125, emphasizing the need for age- and menopause-adjusted interpretation in clinical practice. These findings support the continued integration of CA-125 measurement in routine gynecologic evaluation and highlight the importance of considering demographic factors for precise risk stratification.

Declaration

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Ethics approval and consent to participate

This retrospective study was approved by the Bahawalpur Victoria Hospital Ethics Committee. As the study involved analysis of existing medical records, individual participant consent was not applicable.

Consent for publication

Not applicable.

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Competing interests

The authors declare that they have no competing interests.

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Availability of data and materials

The datasets generated during and/or analyzed during the current study are not publicly available due to hospital ethical policy in order to protect participant confidentiality

Authors' contributions

E.E. conceived and designed the study and drafted the manuscript. M.A.M. served as the corresponding author, supervised the study, and critically reviewed the manuscript. F.B. and S.B. developed the study protocol, collected and analyzed the data, interpreted the results, and contributed to clinical interpretation. M.N. and A.R. conducted literature review and supported data entry. M.A.J. and L.H. assisted with laboratory investigations. G.M. and W.K. contributed to statistical analysis and data management. All authors read and approved the final manuscript.

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