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Original Research Article

Association of Ca-125 Levels and Clinico-Pathological Presentation of Females with Endometriosis

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Abstract:

Introduction: Endometriosis is an estrogen-based disorder, resulting in severe pelvic pain, dysmenorrhea, dyspareunia, along with infertility. The level of CA-125 in serum has been cited as a biomarker for the evaluation of the severity of disease and different clinico-pathological relationships among women suffering from endometriosis.

Method: This cross-sectional observational study was conducted in the Department of Obstetrics and Gynaecology at GCS Medical College over 1 year, from June 2024 to August 2025, involving 50 clinically diagnosed endometriosis patients undergoing laparoscopy or laparotomy. Preoperative serum CA-125 levels were measured, with 35 U/mL as the upper limit. Clinical, radiological, and intraoperative findings, disease stage, adhesion severity, and pain scores were correlated with CA-125 levels using appropriate statistical tests, with $p < 0.05$ considered significant.

Result: Serum CA-125 levels did not differ significantly by age (≤40 years: 57.10 ± 14.05 vs >40 years: 53.84 ± 11.98; $p = 0.72$) or marital status (single: 36.92 ± 11.88 vs married: 42.15 ± 5.12; $p = 0.81$). In contrast, CA-125 increased significantly with advancing endometriosis stage ($p < 0.001$) and higher adhesion scores ($p = 0.03$). Lesion size was significantly associated with CA-125 levels ($p = 0.03$), whereas clinical complaints ($p = 0.23$) and VAS pain scores ($p = 0.68$) were not.

Conclusion: The study has concluded that the CA-125 level in serum is a significant marker for the severity of disease and the pathological challenge for endometriosis. This does not correlate with different demographic parameters or the intensity of pain.

Keywords: Endometriosis; CA-125; Pelvic pain; Disease staging; Adhesion severity.

Introduction

Endometriosis is a chronic estrogen-dependent gynaecologic condition that is characterized by the appearance of endometrial-like tissue outside the uterine cavity. It is an estimated 10 percent prevalence in all of the reproductive age women in the world and is the primary cause of pelvic and dysmenorrhea pain, dyspareunia and infertility. Clinical manifestations are heterogeneous: whereas some women with prolonged pelvic disease report mild symptoms, other women with smaller lesions report severe pains or infertility, which makes it difficult to diagnose and treat early. Due to the fact that definitive diagnosis still depends on laparoscopy and histological confirmation, clinical interest in non-invasive biomarkers that may be used in the diagnosis, stage, or monitoring is great [1]. Cancer antigen 125 is a high-molecular-weight glycoprotein that was initially created as a tumour marker in ovarian cancer of epithelial type. In benign gynaecologic diseases, such as endometriosis, CA-125 has been repeatedly researched, and it seems that peritoneal inflammation and ectopic endometrial tissue are the mediators of high serum levels. A series of observational studies have demonstrated an increased mean CA-125 level in women with endometriosis than in controls, and in those women with peritoneal disease, adhesions, or ovarian endometriomas, but not in women with minimal pelvic/peritoneal irritation, indicating the existence of a biologic relationship between the presence of pelvic/peritoneal irritation and the release of CA-125 [2]. CA-125 does not have perfect diagnostic performance in the face of endometriosis in spite of

continuous associations. Systematic reviews and meta-analyses demonstrate that CA-125 has modest sensitivity but great specificity at standard cut-offs: e.g., pooled data with a threshold of about 30 U/mL has specificities of over 90 per cent but with sensitivities of about 50 per cent and much better at detecting moderate-severe disease than minimal-mild disease. The trend renders CA-125 more beneficial as a rule-in test to verify clinical suspicion of remarkable endometriosis than as a screening or exclusion test. The test performance is influenced by cut-off selection, the menstrual cycle in the patient, and comorbid conditions, which makes it impossible to use a universal cut-off [3].

In addition to diagnosis, researchers have been able to discuss the relationship between CA-125 and clinico-pathological characteristics, disease stage, lesion size, adhesion burden, and presenting symptoms, including pelvic pain and infertility. Some surgical cohorts present large correlations of preoperative CA-125 with objective surgical results, which may indicate prognostic and operative-planning utility, but correlations with the severity of symptoms are not consistently found in the literature. Certain reports have indicated high levels of CA-125 in women with deep infiltrating endometriosis or large adhesions. Other people are not associated or only marginally with subjective measures of pain, indicating that the relationship between the burden of the lesion and the symptomatology is complex and dissociative [4].

Recent studies that assess CA-125 network meta-analyses have indicated that the combination of CA-125 with other markers are better than CA-125 alone at diagnosing endometriosis, especially earlier or atypical presentations, with other markers or integrate clinical scores may enhance diagnostic yield. However, the study design heterogeneity, small sample sizes and variability in translation into sound clinical algorithms in assay thresholds remain an obstacle [5].

Considering such gaps, the research articles that rigorously determine the relation between serum CA-125 and well-characterized clinic-pathological variables in preoperative cohorts are of clinical relevance. Understanding the extent to which CA-125 is predictive of stage of disease, lesion distribution, adhesion severity, or certain clusters of symptoms can be used to inform the use of CA-125 in triage, preoperative planning and postoperative surveillance. This research paper, thus, evaluates preoperative serum CA-125 relative to finer surgical and histopathological results and relative to the presenting clinical phenotype, in order to optimize the role of the biomarker and to determine situations where it significantly changes the decision-making process.

Materials and Methods

Research Design: This is a cross-sectional observational study design for the evaluation of the association of the levels of Ca-125. The study was conducted in the Department of Obstetrics and Gynaecology of GCS Medical College, Hospital and Research Centre. The study was conducted for a period of 1 year, from June 2024 to August 2025. The study included clinically diagnosed women undergoing endometriosis, had signs and symptoms like pelvic pain, dysmenorrhea, or dyspareunia for underwent laparoscopy and laparotomy. A total of 50 samples were selected for the study. Both written and verbal consent were taken for the study. Preoperative blood samples were collected for the analysis of the CA-125 levels in the serum. 35 U/mL was considered the upper limit for the CA-125 concentration in the serum. Different clinical examination and observations was correlated with the CA-125 levels in serum for the evaluation of their relationship with different clinical parameters related to endometrosis.

Inclusion Criteria

- Patient presenting with clinical features suggestive of endometriosis, such as chronic pelvic pain and/or dysmenorrhea
- Patients of age between 21 to 54 years of age were selected for the group.
- Patients with Endometriosis confirmed intraoperatively by laparoscopy.
- Different radiological findings of 45 to 54 years of age were selected for the study.
- Endometriosis confirmed laparoscopically and staged according to the revised American Society for Reproductive Medicine (rASRM)
- Serum CA-125 level assessed preoperatively, prior to initiation of any surgical or hormonal treatment.
- Complete availability of clinical, operative, staging, and laboratory data for analysis.

Exclusion Criteria

- Any pre-history of medical or surgical treatment was excluded for the study.
- Any prior history of pelvic surgery and pelvic inflammatory disease were not considered.
- Any prior diagnosed incidence of malignancy were not considered.
- Chronic pelvic pain for musculoskeletal, infectious, neurologic, gastrointestinal or psychiatric causes were not considered.
- Any women in the period of lactation or pregnancy were not considered.

Procedure: Endometriosis was evaluated on the basis of different clinical and sonographic findings. The severity of the disease was classified on the basis of the American Society for Reproductive Medicine**.** The intensity of the perioperative pain

was evaluated by the use of the Visual Analogue Scale (VAS) for the application of analgesics. Different questionnaires were used for all of the participants for different demographic and clinical information, such as age, body mass, marital status of marriage, history of menstruation, and status of occupation, medical or surgical history, along with features of pain. The intraoperative findings consist of the site and the progression of the endometriotic lesions, the severity of the adhesion and the stage of disease. All of the parameters were recorded by the use of standardised checklist. Different stage of endometriosis was evaluated on the basis of the revised American Fertility Society (r-AFS) classification system of stages I–IV. The severity of the adhesion was graded by the use of the modified American Fertility Society (mAFS) scoring method**.**

Statistical Analysis: Data analysis was done by the use of SPSS version 24. Continuous variables were presented by mean ± SD or median (IQR), and the categorical variables were expressed as frequencies and percentages. Student's unpaired t-test or Mann–Whitney U test was done for the comparison among groups. The categorical analysis was done by the use of Chi-square or Fisher's exact test**.** The correlation was evaluated by the use of Pearson's or Spearman's correlation coefficients. The p-value < 0.05 was maintained for statistical significance.

Result

Table 1 demonstrates that serum CA-125 levels did not vary significantly across age groups or marital status among women diagnosed with endometriosis. Women aged ≤40 years showed a mean CA-125 level of 57.10 ± 14.05 compared with 53.84 ± 11.98 in those aged >40 years, with a p-value of 0.72, indicating the absence of a statistically significant age-related difference. Similarly, although married women exhibited a numerically higher mean CA-125 level than single women (42.15 ± 5.12 versus 36.92 ± 11.88), the association was not statistically significant ($p = 0.81$). These findings suggest that demographic factors such as age and marital status do not have a measurable influence on serum CA-125 levels in this cohort.

Table 1: The association of the level of CA-125 level in serum according to age or the marital status among women of endometriosis

Characteristic	Serum CA-125 level (Mean ± SD)	p-value
Age (years)		
≤ 40	**57.10 ± 14.05**	**0.72**
> 40	**53.84 ± 11.98**	
Marital status		
Single	**36.92 ± 11.88**	**0.81**
Married	**42.15 ± 5.12**	

Table 2 shows a clear and statistically significant association between serum CA-125 levels, stage of endometriosis, and severity of adhesions. Mean CA-125 levels increased progressively from stage 1 (31.12 ± 6.03) to stage 3 (58.46 ± 7.05), with an overall highly significant association between disease stage and CA-125 concentration ($p < 0.001$), indicating that advancing disease stage is accompanied by higher biomarker levels. Although stage 4 showed a slight numerical decline compared with stage 3, levels remained substantially elevated relative to early-stage disease. In parallel, adhesion severity demonstrated a significant relationship with CA-125 levels, as women with higher adhesion scores (5–6) had markedly increased mean values (55.91 ± 7.34) compared with those with minimal adhesions (1–2: 30.85 ± 6.21), with a statistically significant p-value of 0.03. These results support the role of CA-125 as a marker reflecting both disease extent and adhesion severity.

Table 2: The association of the level of CA-125 level along with the endometriosis stage with high severe form of adhesion

Characteristic	Serum CA-125 level (Mean ± SD)	p-value
Stage of disease		
Stage 1	31.12 ± 6.03	
Stage 2	51.78 ± 7.12	<0.001
Stage 3	58.46 ± 7.05	
Stage 4	47.63 ± 8.02	
Adhesion score		
1–2	30.85 ± 6.21	
3–4	52.64 ± 7.08	0.03
5–6	55.91 ± 7.34	

Table 3 examines the association of serum CA-125 levels with clinical presentation, lesion size, and pain severity. Although higher mean CA-125 values were observed in women presenting with combined symptoms such as infertility with pain (63.15 ± 19.88) and AUB with pain (59.84 ± 9.21), the overall association between type of clinical complaint and CA-125 level was not statistically significant (p = 0.23), indicating considerable variability within symptom categories. In contrast, pain severity assessed by VAS score did not demonstrate a significant correlation with CA-125 levels (p = 0.68), despite numerically higher values in the severe pain category. Collectively, these findings indicate that CA-125 is more closely linked to structural disease characteristics, such as stage, adhesions, and lesion size, than to subjective symptom severity or pain intensity.

Table 3: The association of the serum level of CA-125 with different clinical complication, size of lesion and severity of pain

Characteristic	Serum CA-125 level (Mean ± SD)	p-value
Complaint		
Pelvic pain	48.92 ± 5.74	
Infertility	46.38 ± 2.41	0.23
Infertility + Pain	63.15 ± 19.88	
AUB	33.76 ± 7.94	
AUB + Pain	59.84 ± 9.21	

Table 4 examines the association of serum CA-125 levels with lesion size. Lesion size, however, showed a statistically significant association with CA-125 levels (p = 0.03), suggesting that increasing lesion burden is reflected in altered biomarker concentrations.

Table 4: The association of the serum level of CA-125 with different size of lesion

Characteristic	Serum CA-125 level (Mean ± SD)	p-value
Lesion size		
≤ 4.5	50.68 ± 8.02	0.03
5–11	48.97 ± 5.89	

Table 5 examines the association of serum CA-125 levels with severity of pain. Pain severity assessed by VAS score did not demonstrate a significant correlation with CA-125 levels (p = 0.68), despite numerically higher values in the severe pain category. Collectively, these findings indicate that CA-125 is more closely linked to structural disease characteristics, such as stage, adhesions, and lesion size, than to subjective symptom severity or pain intensity.

Table 5: The association of the serum level of CA-125 with different severity of pain

Characteristic	Serum CA-125 level (Mean ± SD)	p-value
VAS score		
2	51.96 ± 13.84	
2–5	44.72 ± 5.12	0.68
6–9	56.31 ± 8.92	

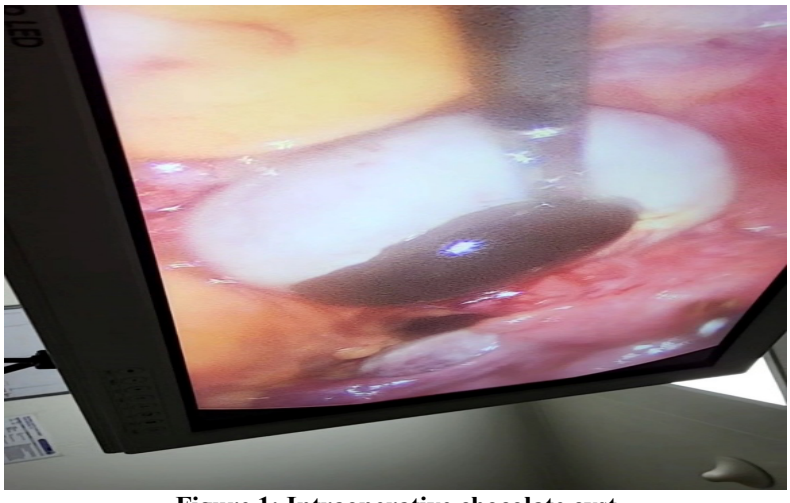

Figure 1: Intraoperative chocolate cyst

Figure 2: Intraoperative Adherent Uterus and ovaries

Discussion

The study was aimed at assessing the association between preoperative serum CA-125 levels and clinico-pathological presentation of women who demonstrated endometriosis at surgery. In general, our results contribute to a significant amount of research evidence that CA-125 correlates with objective measures of the extent of disease but does not have high sensitivity as an independent diagnostic tool, especially with minimal or mild disease [6].

The same dual trend has been observed in many prior large systematic reviews and primary cohorts: CA-125 levels are higher in advanced disease, those in ovarian endometriomas and widespread peritoneal involvement, as well as lower in normal range in superficial/minimal disease. An extensive meta-analysis revealed that CA-125 has a moderate sensitivity but a rather high specificity, implying that CA-125 is a better rule-in than a screening test. This makes CA-125 clinically useful in the instance of moderate/high pretest probability but not reliable to rule out disease [7].

Our finding is in agreement with surgical cohorts which identified correlations between preoperative CA-125 and operative parameters. Some of the studies showed strong positive relationship existences between CA-125 and adhesion score, the existence of ovarian endometrioma and the number or the degree of deep infiltrating lesions. Indicatively, previous studies by Garzetti et al. reported a correlation that exists between serum CA-125 and peritoneal irritation/adhesions, which is indicative of a biologic equation in which the presence of peritoneal inflammation promotes the secretion of MUC16 into serum. These results have been replicated by more recent surgical series and systematic studies, which have strengthened the link between CA-125 and anatomic burden as compared to symptom severity alone [8].

However, the correlation between CA-125 and symptoms of the patients, especially the severity of pain, is less coherent. Other studies indicate more CA-125 on subsets with deep invading endometriosis, whereas others report that little or no relationship exists between CA-125 and subjective pain scores. Such discordance can probably be attributed to the already established clinicopathological dissociation in endometriosis: lesion burden and location can only justify a subset of the symptom complex, but central sensitization, comorbid dysfunction of the pelvic floor, and psychosocial factors also have a role to play. In this way, normal CA-125 is not correlated with a lack of clinically significant disease, and high CA-125 is not always coupled with the severity of pain [9].

The heterogeneity in the methods used in studies is useful in describing differences in reported diagnostic performance. Significant sources of heterogeneity are the difference between CA-125 assay platforms and cut-offs, when a sample was taken in relation to the menstrual cycle, inclusion criteria and the possibility that cohorts had more advanced disease due to them being surgical series. Meta-analyses have shown that these aspects have a strong effect on pooled sensitivity and specificity, thus, standardized sampling and reporting would enhance comparability between studies and clinical utility [10].

Recently, efforts have been put toward enhancing the accuracy of the diagnosis through combination of CA-125 with other biomarkers or clinical indicators. The panels proposed by the network meta-analyses and cohort studies include CA-125 + CA19-9 + IL-6, or CA-125 with hematologic indices, which are better than CA-125, especially in

the earlier disease. Despite the promise of these combinations, the current evidence is moderate, and would need external validation in future multicentre cohorts before it can be widespread in clinical practice. This lesson is highlighted in our study: CA-125 is a valuable, yet incomplete, data that can only be well understood in a clinical and imaging framework [11].

Our strengths are (1) operative and pathological diagnosis of all participants, (2) routine documentation of the operative data, and (3) utilization of preoperative samples with assay information provided, which minimizes bias and allows comparing the results with the previous groups of surgeries. Limitations are due to the single-centre design, which may have caused variability in cycles phase to sampling unless observed uniformly timed and because of observational design, the study cannot be causally inferred.

Lastly, even though CA-125 is associated with anatomical burden, it is a surrogate of biologic process, not a direct measure of symptom production and this should moderate clinical interpretation. Finally, our results stand even despite the greater literature: CA-125 is related to more progressive and ovarian endometriosis, and to peritoneal inflammation/adhesions, and it is not sensitive enough to serve as a diagnostic test itself, particularly minimal disease. Its most recent application is inclusion in a combined preoperative assessment to guide triage and surgical planning. The research should focus on prospective validation of multimarket panels, standardized sampling procedures, and investigation of markers that represent the pain processes to fill the gap between anatomy and symptoms.

Conclusion

The study has concluded that the level of CA-125 in the serum has shown a significant association with different clinico-pathological severity for endometriosis. The variation present in the level of CA-125 for different age group of age has been observed, and it was not statistically significant. Whereas the level of CA-125 in serum had been increased with the progression of endometriosis stage and high severity of adhesion.

High levels of CA-125 have been observed among patients with clinical signs and symptoms like infertility associated with pain and abnormal bleeding with pain in the uterus. Also, statistical significance has been seen in the case of the size of the lesion for the level of CA-125 in serum. No association was observed for the level of CA-125 and pain, and the severity of pain was evaluated by the Visual Analogue Scale. Thus, CA-125 reflects the burden or challenge of disease with severity compared to different demographic parameters for pain among women suffering from endometriosis.

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