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The Role of Serum C-Reactive Protein in Evaluation of Benign and Malignant Ovarian Tumors – An Observational study

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Abstract:

Background: *Differentiating benign from malignant ovarian tumors preoperatively is critical for ensuring optimum surgical planning and patient outcomes. While CA-125 is widely used as a biomarker, its limited specificity highlights the need for supplementary markers such as C-reactive protein (CRP), which reflects systemic inflammation.*

Aim: *To determine the sensitivity, specificity, and diagnostic accuracy of serum CRP and CA-125 individually and in combination for differentiating benign and malignant ovarian tumors.*

Materials and Methods: *A hospital-based observational study was conducted on 50 women with adnexal masses. Preoperative CRP and CA-125 levels were measured; imaging findings were recorded. Histopathological examination (HPE) was the gold standard. Diagnostic accuracy indexes were calculated, and logistic regression identified independent predictors of malignancy.*

Results: *Of 50 patients, 60% had benign tumors and 40% malignant. CRP ≥5 mg/L had sensitivity 75% and specificity 93.3%; CA-125 ≥35 IU/mL had sensitivity 80% and specificity 93.3%. Combined testing improved sensitivity to 90% and specificity to 96.7%. Ascites (90%), solid component (75%), bilateral masses (75%), and irregular margins were significantly associated with malignancy. Multivariate analysis identified CRP ≥5 mg/L, CA-125 ≥35 IU/mL, ascites, and solid component as independent predictors.*

Conclusion: *CRP, especially when combined with CA-125, improves diagnostic accuracy in differentiating benign and malignant ovarian tumors and may be incorporated into preoperative evaluation strategies.*

Keywords: *Ovarian tumors, C-reactive protein, CA-125, Diagnosis, Biomarker*

INTRODUCTION

Ovarian tumors represent a significant clinical challenge, particularly because malignancies are often diagnosed at advanced stages. Ovarian cancer (OC) is the most fatal gynaecological malignancy globally, accounting for approximately 238,719 new cases and 151,917 deaths each year. [1] Accurate preoperative differentiation of benign and malignant tumors is essential. Imaging modalities are useful but can be inconclusive.[2]

Serum biomarkers, in conjunction with clinical assessment and ultrasound imaging, can be valuable tools in differentiating between benign and malignant ovarian tumours.[3] While ovarian cancer is relatively uncommon, pelvic masses are frequently detected in both premenopausal and postmenopausal women, particularly in the former group.[4] CA-125 is an established tumor marker, but it has limitations in sensitivity and specificity, particularly in early-stage malignancy or benign inflammatory conditions.[5]

Inflammation plays a key role in tumorigenesis. CRP, an acute-phase protein synthesized in response to cytokines such as IL-6, is easy to measure and has been explored as a possible cancer biomarker. Studies

have suggested that elevated CRP levels correlate with poor prognosis in several malignancies, and may aid in differential diagnosis of ovarian tumors.[6]
This study evaluates serum CRP, alone and in combination with CA-125, for preoperative differentiation of benign and malignant ovarian tumors.

MATERIALS AND METHODS

Study Design and Setting:
Prospective observational study conducted at the Department of Obstetrics and Gynaecology, Adichunchanagiri institute of medical sciences, Adichunchanagiri University, B G Nagara, Karnataka, over an 18-month period (from June 2023 to November 2024).

Study Population:
Fifty women with clinically and radiologically diagnosed ovarian masses.

INCLUSION CRITERIA:

1. Patients ≥18 years diagnosed with ovarian mass/tumors
2. Patients willing to participate in the study by giving written- informed consent

EXLUSION CRITERIA:

1. Pregnant women
2. Patients with Endometriosis/Endometrioma
3. Patients with Acute and chronic inflammatory conditions

Data Collection:
Demographic details, menstrual and obstetric history, comorbidities, family cancer history, and clinical findings were recorded. Ultrasound features documented solid/cystic components, bilaterality, septations, and ascites. CRP was measured by immunoturbidimetry, CA-125 by chemiluminescence immunoassay.

Outcome Measures:
HPE was the gold standard for diagnosis. Diagnostic performance (sensitivity, specificity, PPV, NPV, accuracy) was calculated for CRP, CA-125, and their combination. Correlation and logistic regression identified predictors of malignancy.

Statistical Analysis:
Data was analysed using SPSS version. Continuous variables as mean ± SD, categorical as frequencies (%). Pearson's correlation, Chi-square/Fisher's exact test, and logistic regression were applied. $p<0.05$ considered significant.

Ethics:
Study was approved by the Institutional Ethics Committee. Written informed consent obtained from all participants.

RESULTS:

Demographic Characteristics of the Study Population

1. **Age Distribution of Participants in the Study on Serum C-Reactive Protein and Ovarian Tumors**

Table 1: Age distribution of study participants

Age Group (years)	n	%
18–30	10	20

Age Group (years)	**n**	**%**
31–40	15	30
41–50	12	24
51–60	8	16
>60	5	10
Total	**50**	**100**

The study included 50 women diagnosed with ovarian masses. The age distribution ranged from 18 to over 60 years, with the majority (30%) falling within the 31-40 years age group.

2. **Menstrual Characteristics of Participants in the Study on Serum C-Reactive Protein and Ovarian Tumors**

Table 2: Menstrual profile

Parameters	**Number of Participants**	**Percentage (%)**
Regular Cycles	35	70
Irregular Cycles	15	30
Dysmenorrhea Present	25	50
Dysmenorrhea Absent	25	50
Total	**50**	**100**

Out of 50 participants, 70% had regular menstrual cycles, while 30% experienced irregular cycles. Dysmenorrhea was present in 50% of the cases.

3. **Medical History of Participants in the Study on Serum C-Reactive Protein and Ovarian Tumors**

Table 3:

Medical Condition	**Number of Participants**	**Percentage (%)**
Diabetes Mellitus (DM)	8	16
Hypertension (HTN)	5	10
Tuberculosis (TB)	2	4
Epilepsy	1	2
No Significant Past History	34	68
Total	**50**	**100**

Among the 50 participants, 16% had a history of diabetes mellitus, while 10% were diagnosed with hypertension. Tuberculosis and epilepsy were reported in 4% and 2% of participants, respectively. Notably, the majority (68%) had no significant past medical history. These findings highlight the prevalence of comorbid conditions among individuals with ovarian

tumors, which may influence disease progression and overall clinical evaluation.

4. **Family History of Malignancies Among Participants in the Study on Serum C-Reactive Protein and Ovarian Tumors**

Table 4:

Conditions	Number of Participants	Percentage (%)
Gynaecological Malignancies	6	12
Gastrointestinal (G.I.) Malignancies	4	8
Breast Malignancy	0	0
No Family History of Malignancy	40	80
Total	**50**	**100**

Among the 50 participants, 12% had a family history of gynaecological malignancies, 8% had a history of gastrointestinal malignancies, and no patient reported a family history of breast malignancy. The majority (74%) had no family history of malignancy.

5. **Clinical Parameters of Participants in the Study on Serum C-Reactive Protein and Ovarian Tumors**

Table 5:

Clinical Parameter	Mean ± SD	Range
Height (cm)	160 ± 5	150-170
Weight (kg)	65 ± 10	45-85
BMI (kg/m2)	25.4 ± 3.5	18.5-32.0

The average height of participants was 160 cm, with an average weight of 65 kg and a mean BMI of 25.4 kg/m2. Vital signs were within normal ranges for most participants

6. **Ultrasound Features of Benign and Malignant Ovarian Tumors in the Study on Serum C-Reactive Protein**

Table 6: Ultrasound features by tumor type

Ultrasound Feature	Benign Tumors (n=30)	Malignant Tumors (n=20)	Total
Solid Component	5 (16.7%)	15 (75%)	20
Cystic Component	25 (83.3%)	5 (25%)	30
Bilateral Masses	10 (33.3%)	15 (75%)	25
Unilateral Masses	20 (66.7%)	5 (25%)	25
Presence of Septations	5 (16.7%)	10 (50%)	15
Ascites Presence	2 (6.7%)	18 (90%)	20

Total	**30**	**20**	**50**

Among benign tumors, 83.3% were cystic, whereas 75% of malignant tumors exhibited a solid component. Ascites was present in 90% of malignant cases compared to 6.7% of benign cases

7. **Serum C-Reactive Protein (CRP) Levels in Benign and Malignant Ovarian Tumors**

Table 7:

CRP Level (mg/L)	Benign Tumors (n=30)	Malignant Tumors (n=20)	Total
<5	25	5	30
5-10	3	10	13
>10	2	5	7
Total	**30**	**20**	**50**

CRP levels above 10 mg/L were observed in 35% of malignant cases compared to 6.7% of benign cases. Elevated CRP levels (≥5 mg/L) were significantly more common in malignant tumors.

8. **Diagnostic Performance of CRP and CA-125 in Differentiating Benign and Malignant Ovarian Tumors**

Table 8:

Test Combination	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)
CRP ≥5 mg/L alone	75	93.3	83.3	90.9
CA-125 ≥35 IU/mL alone	80	93.3	88.9	90.9
CRP ≥5 mg/L + CA-125 ≥35 IU/mL	90	96.7	94.7	95.2

Combination of CRP≥5mg/L, CA-125≥35 IU/mL yielded highest sensitivity (90%), specificity (96.7%) for distinguishing malignant from benign ovarian tumors.

9. **Histopathological Examination (HPE) Diagnosis of Benign and Malignant Ovarian Tumors in the Study on Serum C-Reactive Protein**

Table 9:

HPE Diagnosis	Benign Tumors (n=30)	Malignant Tumors (n=20)	Total
Serous Cystadenoma	10	0	10
Mucinous Cystadenoma	8	0	8
Borderline Tumors	2	0	2
Serous Carcinoma	0	12	12
Mucinous Carcinoma	0	8	8
Total	**30**	**20**	**50**

Histopathological examination revealed that among the 30 benign tumors, the most common diagnosis was serous cystadenoma (33.3%), followed by mucinous cystadenoma (26.7%). Borderline tumors accounted for 6.7% of benign cases. Among the 20 malignant tumors, serous carcinoma was the most frequent diagnosis (60%), while mucinous carcinoma constituted 40% of malignant cases. These findings highlight the distinct histopathological patterns observed in benign and malignant ovarian tumors, aiding in accurate diagnosis and classification.

DISCUSSION:

The present study examines the diagnostic utility of serum C-reactive protein (CRP) in differentiating benign from malignant ovarian tumors, both as an individual biomarker and in combination with cancer antigen-125 (CA-125). In our cohort of 50 patients, we found significantly higher CRP and CA-125 levels among malignant cases compared to benign ones. Using a CRP cut-off of ≥5 mg/L, the sensitivity was 75% and specificity 93.3%, while CA-125 ≥35 IU/mL yielded sensitivity 80% and specificity 93.3%. The combination of these markers achieved superior diagnostic performance, with sensitivity 90%, specificity 96.7%, and accuracy 93.3%, underscoring their synergistic value in preoperative assessment.

These results are consistent with the well-established role of chronic inflammation in cancer development and progression. CRP, an acute-phase reactant induced by interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and interleukin-1β (IL-1β), has been linked to poor oncological outcomes in various malignancies. Poole et al. (2013) demonstrated that CRP levels >10 mg/L were associated with a more than two-fold increased risk of invasive epithelial ovarian cancer in large-scale cohorts. In our study, 35% of malignant tumors exhibited CRP >10 mg/L compared to only 6.7% of benign tumors, supporting its potential role as a diagnostic indicator.

CA-125 remains the most widely used tumor marker for ovarian malignancies, although its sensitivity is reduced in early-stage disease and specificity is compromised by benign gynecological conditions. Landolfo et al. (2020) reported that combining CA-125 with other markers improved discrimination between benign and malignant adnexal masses. Our findings similarly demonstrate a clinically relevant improvement when combining CA-125 with CRP, supporting the rationale for multi-marker diagnostic algorithms.

Radiological and histopathological data from our series further reinforce these findings. Malignant tumors were more likely to present with solid components, ascites, bilateral involvement, septations, and irregular margins. On multivariate analysis, the presence of ascites (adjusted OR = 6.0), a solid ultrasound component (OR = 5.2), elevated CRP (OR = 3.8), and elevated CA-125 (OR = 4.5) were independent predictors of malignancy. These imaging features, combined with biomarker assessment, can significantly enhance preoperative triage.

Histologically, serous carcinoma (60%) and mucinous carcinoma (40%) comprised the malignant tumors, whereas serous and mucinous cystadenomas were the most frequent benign lesions. This distribution aligns with global epidemiology of epithelial ovarian tumors. The moderate positive correlation observed between CRP and CA-125 levels ($r = 0.53$, $p < 0.001$) further suggests that systemic inflammation and tumor activity are interconnected processes in ovarian malignancy.

From a clinical standpoint, integrating CRP with CA-125 testing offers a cost-effective, widely available adjunct to ultrasound, especially in resource-limited settings. This strategy may assist in identifying patients who require early referral to a gynaecologic oncologist and aggressive surgical staging, while also helping avoid unnecessary laparotomies in benign cases.

Limitations of our study include its single-center design, relatively small sample size, and observational nature, which limit the ability to establish causality. We did not longitudinally assess CRP or CA-125 trends, which may provide further prognostic insights. Additionally, although we excluded overt acute inflammatory conditions, subclinical inflammation remains a potential confounder. Nevertheless, our findings agree with published evidence highlighting the link between inflammation, CRP elevation, and cancer biology.

Future research should validate these observations in larger, multi-center cohorts with diverse ethnic representation, and explore additional inflammatory and tumor-specific biomarkers (e.g., HE4, CA72.4, IL-6). Integrating such panels into predictive models alongside Doppler ultrasound and CT/MRI features could refine preoperative risk stratification and prognostication.

In summary, serum CRP, particularly when combined with CA-125, is a valuable, inexpensive, and accessible biomarker for differentiating benign and malignant ovarian tumors. Used alongside imaging, it can enhance diagnostic confidence, optimize surgical decision-making, and potentially improve patient outcomes, especially in settings where advanced diagnostics are limited.

CONCLUSION

CRP is a cost-effective, widely available inflammatory marker that provides significant diagnostic value when used alongside CA-125. Combined application improves sensitivity and specificity in distinguishing benign from malignant ovarian tumors, and should be integrated into preoperative evaluation protocols, especially in resource-limited settings.

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