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# Role of Osteopontin and CA125 for early detection of Ovarian Tumor

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## ABSTRACT

**Introduction:** There is a significant rate of morbidity and mortality linked to ovarian cancer. This is because there are no reliable screening techniques and the symptoms are vague. Although it has its own limitations, carbohydrate antigen-125 (CA125) is being employed as a tumor biomarker for the detection of ovarian cancer. Therefore, more tumor indicators are required for ovarian cancer detection.

**AIM:** The study's goal was to evaluate the role of plasma osteopontin (OPN) and CA125 in subjects with ovarian cancer and compare its efficacy with CA125.

**Methods and Materials:** This is a prospective, cross-sectional assessment of a diagnostic test. Suspected instances were women whose adnexal masses were found by radiological or clinical testing. As controls, women who had other gynecological issues were included. All enrolled subjects had their OPN and CA125 levels tested.

**Results:** Among 70 women enrolled, 16 were ovarian cancer, 19 had benign ovarian masses, and 35 were controls. Median plasma CA125 levels were higher in subjects with ovarian cancer (480±418.48). Median plasma OPN levels were higher in subjects with ovarian cancer (4809.84 ±5273.33). The sensitivity and specificity of OPN were 94.30 % and 97.10%, and CA125 77.10% & 85.70 % respectively, with AUC 0.927 (0.846–1.00) and 0.858 (0.769-0.946).

**Conclusion:** OPN levels were higher in ovarian cancer than in the benign ovarian mass and had better specificity than CA125. OPN can better differentiate between benign and malignant ovarian mass as compared to CA125.

***Keywords:*** *Carbohydrate antigen-125, osteopontin, ovarian cancer, tumor marker.*

## 1. INTRODUCTION

Ovarian cancer (OC) is the leading cause of gynecological cancer-associated death; indeed, according to reports from the National Cancer Institute (NCI), about 140,000 people die each year from OC worldwide (1). This disease is named the “silent killer” related to the fact that cancer becomes widespread without the occurrence of symptoms, and even if they are present (2), these symptoms are shared with a variety of more common benign gastrointestinal, genitourinary and gynecological conditions, making them difficult to attribute to ovarian cancer (3,4). When the disease is detected in stage I (still limited to the ovaries), according to the International Federation of Obstetrics and Gynecology (FIGO) classification (5), up to 90% of patients can be cured successfully with currently available surgery and chemotherapy (6). Even when the

disease has spread to the pelvis in stage II, 70% of patients can be cured, but when the disease has spread throughout the abdominal cavity or beyond can be cured in less than 20% of cases. Unfortunately, despite the improvement in overall survival for OC patients, a fraction of patients with advanced-stage disease fails to respond to primary therapy and relapses in 70% of cases (7-9).

The best currently available method for early detection of ovarian cancer is the combination of raised carbohydrate antigen 125 (CA125) and transvaginal ultrasonography (10,11).However, CA125 has certain limitations as a biomarker for ovarian cancer. It is elevated in less than half of the early-stage ovarian tumors, and it is raised most in serous histology. CA125 can be false positive in many benign and malignant conditions (12,13). In addition, it is influenced by age, race, obesity, smoking, and history of hysterectomy(14).However, till now, no other dependable biomarker has been developed to replace CA125 or to further improve its sensitivity and specificity.

Osteopontin (OPN) is an extracellular matrix phosphoglycoprotein which is secreted by osteoblast and epithelial cells of different organs. It is also secreted by the macrophages, activated T-lymphocytes, and leukocytes (15,16). It regulates physiological processes such as bone resorption, wound healing, immune response, and vascularization. Pathological conditions such as cancer metastasis and wound healing a defect in posttranslational modification cause changes in its functions (17).OPN plays a crucial role in cancer progressions such as tumor invasion, angiogenesis, and metastasis (18). OPN is increased in various cancers such as ovarian, cervical, breast, colorectal, liver, lung, pancreas, prostate, and melanoma (19).Recent studies have shown that combining OPN with CA125 increases the sensitivity and specificity for the detection of ovarian cancer (20-23).The levels of biomarkers are influenced by the ethnicity of the population, and no such study has been done in the Indian population. Hence, this study was planned to evaluate the role of OPN and CA125 in subjects with ovarian cancer.

## 2. MATERIALS AND METHODS

This prospective cross-sectional diagnostic test evaluation study was conducted at NIMS Medical College Jaipur (RJ) India and Rajshree medical Research Institute, Bareilly (UP), in the department of biochemistry in collaboration with the department of obstetrics and gynaecology. The study was approved by the institutional ethics committee. The study was done from January 2024 to February 2025. Written informed consent was obtained from all the enrolled subjects. Subjects were enrolled consecutively with consideration of inclusion and exclusion criteria. During the study period, a total 35 subjects and 35 controls were enrolled. Subjects with newly suspected or diagnosed adnexal mass had any of the following: complex adnexal mass, adnexal mass which is not decreasing in size on conservative management of adnexal mass which had ultrasound features suggestive of malignancy. Subjects who were already on treatment for cancer ovary or tube and whose ultrasound features were not suggestive of adnexal malignancy were excluded from the study.

Detailed history and examination were performed in all enrolled subjects. 5 ml of blood sample was obtained for measurement of plasma OPN, serum CA125, and other routine investigations. Pelvic ultrasonography was performed in all subjects. Computed tomography or magnetic resonance imaging of pelvis and abdomen was done as per clinical indication. Further management such as fine-needle aspiration cytology (FNAC) or surgery was done as per the clinical protocol of the department. Samples of OPN and CA125 were taken preoperatively. Treating team was blinded to values of OPN till the report of FNAC or histopathology was received. Thus, case treatment was not influenced by OPN levels or because of the study. After the cases were operated, they were followed up with examination, ultrasound, and CA125 levels.

**Processing of sample**

Estimation of carbohydrate antigen-125 and Osteopontin levels A plain vial blood sample of 5 ml for CA125 and 2-ml EDTA blood sample for OPN were immediately sent to the department of biochemistry. Samples were stored at −20°C. Stored serum for CA125 and blood for OPN levels were used for estimating their levels later. However, no more than one freeze and thaw cycle was permitted. CA125 was measured by chemiluminescence immunoassay kits on ADVIA Centaur Siemens. OPN was measured using enzyme-linked immunoassay methods. Human OPN ELISA (RayBiotech, Norcross, Georgia) was used as per the manufacturer's protocol for the estimation of OPN.

**Result:**

**Table 1: Descriptive statistic of OPN & CA125 value for healthy, MALIGNANT & BENIGN population**

| | | NO. of study participants | Mean value | Minimum | Maximum | P-Value (ANOVA ) |
|---|---|---|---|---|---|---|
| **OPN** | **Healthy** | 35 | 200.60 ± 216.95 | 103.02 | 1436.10 | **0.001**** |
| | **MALIGNANT** | 16 | 4809.84 ± 5273.33 | 611.50 | 22460.00 | |

| | | | | | | |
|---|---|---|---|---|---|---|
| | **BENIGN** | 19 | 750.03 ±1043.28 | 49.07 | 4960.50 | |
| **CA125** | **Healthy** | 35 | 15.61 ±11.58 | 4.80 | 41.30 | **0.001**** |
| | **MALIGNANT** | 16 | 480.33 ± 418.48 | 6.30 | 1198.00 | |
| | **BENIGN** | 19 | 39.85 ± 31.18 | 5.40 | 131.00 | |

Table 1 shows the levels of Osteopontin **(OPN) and CA125** in three groups: **healthy individuals, patients with malignant tumors, and patients with benign tumors**. The results indicates that there highly significant differences among these groups for both biomarkers ($p<0.05$).

Mean OPN levels were 200.61 for Healthy individuals, 750.04 for patients with benign tumors. And 4809.85 for patients with malignant tumors, with a high standard deviation i.e.5273.34. Similarly, mean CA125 levels were 15.61 for Healthy individuals, 39.86 for patients with benign tumors and 480.34 for patients with malignant tumors, showing a marked increase in malignancy.

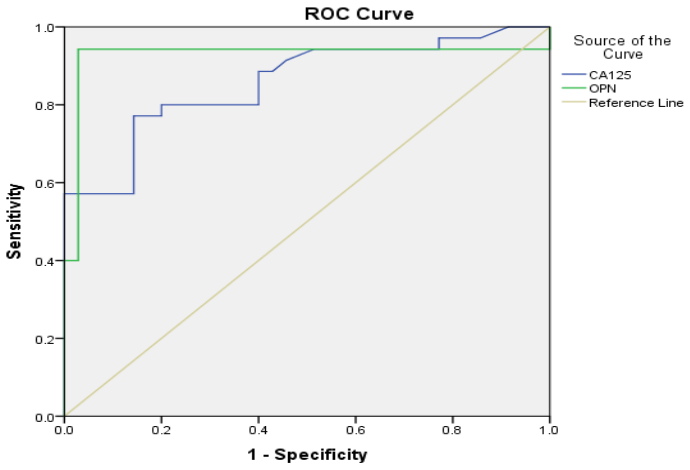
**Table 2: Multiple Comparison of Mean Differences in OPN and CA125 Levels among Healthy, Malignant, and Benign Groups**

| (I) | (J) | OPN | | CA125 | |
|---|---|---|---|---|---|
| | | Mean Difference (I-J) | Sig. | Mean Difference (I-J) | Sig. |
| Healthy | **MALIGNANT** | -4609.24002 | 0.001 | -464.72321* | 0.001** |
| | **BENIGN** | -549.42998 | 0.732 | -24.24361 | 0.904 |
| MALIGNANT | **BENIGN** | 4059.81003 | 0.001 | 440.47961* | 0.001** |

Table 2 shows which groups have statistically significant differences in OPN and CA125 levels. The results indicate that malignant cases differ significantly from both healthy and benign groups for both biomarkers ($p=0.000$) Specifically, OPN levels in malignant cases are 4609.24 units higher than in healthy individuals and 4059.81 units higher than in benign cases, both with significant differences. Similarly, CA125 levels in malignant cases are 464.72 units higher than in healthy individuals and 440.48 units higher than in benign cases, also with significant differences. However, the difference between healthy and benign groups is not statistically significant for either marker ($p > 0.05$), suggesting that both OPN and CA125 effectively differentiate malignant cases but not benign from healthy individuals.

**Table 3 and graph 1: Sensitivity, specificity and AUC for Diagnostic accuracy of OPN and CA-125**

| Variables | Sensitivity | Specificity | Cut off Value | AUC | 95% CI | S.E. |
|---|---|---|---|---|---|---|
| **OPN** | 94.30% | 97.10% | 284.05 | 0.927 | 0.846-1.00 | 0.042 |
| **CA125** | 77.10% | 85.70% | 24.3 | 0.858 | 0.769-0.946 | 0.045 |



The sensitivity and specificity of OPN were 94.30 % and 97.10%, and CA125 77.10% & 85.70 % respectively, with AUC 0.927 (0.846–1.00) and 0.858 (0.769-0.946). CA125 is a more sensitive biomarker for detecting ovarian cancer as compared to OPN. However, the specificity of OPN is much better and thus can differentiate better between benign and malignant ovarian masses. Sensitivity of CA125 further improved if we combined CA125 and OPN. OPN alone is the most specific marker as compared to CA125.

## 3. DISCUSSION

Ovarian cancer is one of the most common reproductive cancers and has the highest mortality rate among gynaecologic cancers. Most of ovarian cancer diagnoses occur in the late stages of the disease and five-year survival rates fall below 20%. To overcome the significant mortality associated with ovarian cancer, research on the clinical significance of new sensitive and specific biomarkers/ panels of biomarkers are still very important.

In this paper, the authors reported that plasma OPN could augment CA125 detection, providing higher sensitivity and specificity in predicting ovarian tumor. With a sensitivity level of 62.5% alone (specificity 90%) OPN may have a lower potential than CA125 to accurately detect the presence of ovarian cancer. High sensitivity was achieved, reaching 74.9% (specificity 90%) when OPN was combined with CA125 in a biomarker screening panel.

The obtained results show better characteristics of OPN as a tumor marker from the one that was given from Nakae *et al.*(24). Regarding the present samples, there was no significant difference of plasma OPN concentration in different histological types of tumors, suggesting that all histological EOC types have increased plasma level of OPN. This is in agreement with the findings of Tiniakos *et al.*(25). However, the authors proved that plasma OPN was significantly elevated during advanced stages of the disease, but there was also border significance between benign patients and early stage of disease. All these results suggest the potential use of plasma OPN and CA125 serum values for ovarian cancer diagnostic.

Complementary to CA125 in predicting ovarian cancer. A total of 70 were enrolled, of which 16 subjects were of malignant ovarian tumor and 19 were of benign ovarian tumor. The sensitivity of CA125, OPN, and either CA125 or OPN was 84.4%, 81.3%, and 93.8%, respectively. The specificity of CA125, OPN, and either CA125 or OPN was 54.7%, 66.3%, and 87.4%, respectively. They reported combining OPN and CA125 can better predict about the tumor in ovary. We have found higher specificity of OPN and slightly better sensitivity of CA125. Cutoff taken for CA125 was almost like our study (35 U/ml). The OPN cutoff taken by Nakae *et al*. was 498 ng/ml which was 95th percentile of healthy women. However, the highest value of OPN in Group 3 of our study was 36.3 ng/ml.(26).

Moszynski *et al*. studied the role of OPN in differentiating benign and malignant ovarian tumors. They found that the OPN levels were raised in all histologic types of ovarian cancer as compared to CA125. Furthermore, OPN was less elevated in endometriosis cyst as compared to CA125. As in our data, we do not have any subjects with endometriotic cysts so this conclusion cannot be replicated. They found almost similar diagnostic accuracy of CA125, OPN, and ultrasonographic markers. Researchers proposed that the OPN can better differentiate endometriosis cysts and has better utility in the detection of ovarian cancer at places where access to ultrasonography is difficult. Further, they had shown the ability of OPN to diagnose ovarian cancer is similar to combined ultrasonography and CA125 levels. However, they have emphasized that as ultrasonography is operator-dependent, so it should be done by an experienced sinologist (27).

Ovarian cancer is known as the “silent killer”, with very weak, nonspecific symptoms. For this reason, using a non-invasive approach, such as tumor markers for detection of the disease, is still very attractive. A number of proteins present in either blood or urine have been identified as specific markers for epithelial ovarian cancer (28). However, no single protein has provided adequate sensitivity and specificity for distinguishing malignant from benign pelvic masses. Some recent studies described panels of biomarkers that beside OPN had four (29), five (30), or more biomarkers (31) with high sensitivity and specificity for ovarian cancer detection.

Our studies also found comparable results with a little lower specificity. This is the first kind of study done in the Indian population is the strength of our study. However, due to the small number of ovarian cancer subjects in our study, the effect of stage and histology of cancer on levels of OPN could not be well established. We recommended further large multi-centric studies on larger sample sizes are required to be conducted for evaluating and establishing the role of osteopontin as a diagnostic tumor biomarker in ovarian cancer along with long-term follow-up in ovarian cancer before OPN levels can be used in routine clinical practice.

## 4. CONCLUSION

OPN has higher specificity compared to CA125 in detecting ovarian cancer. OPN can better differentiate between benign and malignant ovarian cancer as compared to CA125.

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## REFERENCES


[1] Torre LA, Trabert B, DeSantis CE, et al. Ovarian cancer statistics, 2018. CA Cancer J Clin 2018;68:284-96.

[2] Goff BA, Mandel L, Muntz HG, et al. Ovarian carcinoma diagnosis. Cancer 2000;89:2068-75.

[3] Guadagno E, Pignatiello S, Borrelli G, et al. Ovarian borderline tumors, a subtype of neoplasm with controversial behavior. Role of Ki67 as a prognostic factor. Pathol Res Pract 2019;215:152633.

[4] Giampaolino P, Della Corte L, Foreste V, et al. Unraveling a difficult diagnosis: the tricks for early recognition of ovarian cancer. Minerva Med 2019;110:279-91.

[5] Prat J; FIGO Committee on Gynecologic Oncology. Staging classification for cancer of the ovary, fallopian tube, and peritoneum. Int J Gynaecol Obstet 2014;124:1-5.

[6] Gueli Alletti S, Capozzi VA, Rosati A, et al. Laparoscopy vs. laparotomy for advanced ovarian cancer: a systematic review of the literature. Minerva Med 2019;110:341-57.

[7] Gallotta V, Conte C, Giudice MT, et al. Secondary Laparoscopic Cytoreduction in Recurrent Ovarian Cancer: A Large, Single-Institution Experience. J Minim Invasive Gynecol 2018;25:644-650.

[8] Cianci S, Ronsini C, Vizzielli G, et al. Cytoreductive surgery followed by HIPEC repetition for secondary ovarian cancer recurrence. Updates Surg 2019;71:389-394.

[9] Chiofalo B, Bruni S, Certelli C, et al. Primary Debulking Surgery vs. Interval Debulking Surgery for Advanced Ovarian Cancer: Review of the Literature and Meta- Analysis; Minerva Med 2019;110:330-40.

[10] Menon U. Ovarian cancer screening. CMAJ 2004;171:323-4.

[11] Urban N, McIntosh MW, Andersen M, Karlan BY. Ovarian cancer screening. Hematol Oncol Clin North Am 2003;17:989-1005.

[12] . Clarke-Pearson DL. Clinical practice. Screening for ovarian cancer. N Engl J Med 2009;361:170-7.

[13] Jacobs I, Bast RC Jr. The CA 125 tumour-associated antigen: A review of the literature. Hum Reprod 1989;4:1-12.

[14] Johnson CC, Kessel B, Riley TL, Ragard LR, Williams CR, Xu JL, *et al.* The epidemiology of CA-125 in women without evidence of ovarian cancer in the prostate, lung, colorectal and ovarian cancer (PLCO) screening trial. Gynecol Oncol 2008;110:383

[15] Rittling SR, Chambers AF. Role of osteopontin in tumour progression. Br J Cancer 2004;90:1877-81.

[16] Patarca R, Freeman GJ, Singh RP, Wei FY, Durfee T, Blattner F, *et al.* Structural and functional studies of the early T lymphocyte activation 1 (Eta-1) gene. Definition of a novel T cell-dependent response associated with genetic resistance to bacterial infection. J Exp Med 1989;170:145-61.

[17] Denhardt DT, Noda M, O'Regan AW, Pavlin D, Berman JS. Osteopontin as a means to cope with environmental insults: Regulation of inflammation, tissue remodeling, and cell survival. J Clin Invest 2001;107:1055-61

[18] Wai PY, Kuo PC. Osteopontin: Regulation in tumor metastasis. Cancer Metastasis Rev 2008;27:103-18.

[19] Fedarko NS, Jain A, Karadag A, Van Eman MR, Fisher LW. Elevated serum bone sialoprotein and osteopontin in colon, breast, prostate, and lung cancer. Clin Cancer Res 2001;7:4060-6.

[20] Kim JH, Skates SJ, Uede T, Wong KK, Schorge JO, Feltmate CM, *et al.* Osteopontin as a potential diagnostic biomarker for ovarian cancer. JAMA 2002;287:1671-9.

[21] Mor G, Visintin I, Lai Y, Zhao H, Schwartz P, Rutherford T, cancer. Proc Natl Acad Sci U S A 2005;102:7677-82.

[22] Nakae M, Iwamoto I, Fujino T, Maehata Y, Togami S, Yoshinaga M, *et al.* Preoperative plasma osteopontin level as a biomarker complementary to carbohydrate antigen 125 in predicting ovarian cancer. J Obstet Gynaecol Res 2006;32:309-14.

[23] Meinhold-Heerlein I, Bauerschlag D, Zhou Y, Sapinoso LM, Ching K, Frierson H Jr., *et al.* An integrated clinical-genomics approach identifies a candidate multi-analyte blood test for serous ovarian carcinoma. Clin Cancer Res 2007;13:458-66.

[24] Nakae M., Iwamoto I., Fujino T., Maehata Y.,Togami Sh., Yoshinaga M., Douchi T.: "Preoperative plasma osteopontin level as a biomarker complementary to carbohydrate antigen CA125 in predicting ovarian cancer". *J. Obstet. Gynaecol. Res.*, 2006, *32,* 309.

[25] Tiniakos D.G., Yu H., Liapis H.: "Osteopontin expression in ovarian carcinomas and tumors of low malignant potential (LMP)". *Hum. Pathol.,* 1998, *29*, 1250.

[26] Ye B., Gagnon A., Mok S.C.: "Recent technical strategies to identify diagnostic biomarkers for ovarian cancer". *Expert. Rev. Proteomics,* 2007, *4,* 121.

[27] Moszynski R, Szubert S, Szpurek D, Michalak S, Sajdak S. Role of osteopontin in differential diagnosis of ovarian tumors. J Obstet Gynaecol Res 2013;39:1518-25.

[28] Langmar Z., Nemeth M., Vlesko G.,Kiraly M., Hornyak L., Bosze P.: "HE4-a novel promising serum marker in the diagnosis of ovarian carcinoma". *Eur. J. Gynaecol. Oncol.,* 2011, *32,* 605.

[29] Hwang J., Na S., Lee H., Lee D.: "Correlation between preoperative serum levels of five biomarkers and relationships between these biomarkers and cancer stage in epithelial ovarian cancer". *J. Gynecol. Oncol.,* 2009, *20,* 169.

[30] Kim K., Visinttin I., Alvero A. B., Mor G.: "Development and validation of a protein based signature for the detection of ovarian cancer". *Clin. Lab. Med.*, 2009, *29*, 47.

[31] Moore R.G., Brown A.K., Miller M.C., Skates S., Allard W.J., Verch T. *et al.*: "The use of multiple novel tumor biomarkers for the detection of ovarian carcinoma in patients with a pelvic mass". *Gynecol. Oncol.,* 2008, *108,* 402.