Correlation of CA-125 value and histological finding of adnexal mass in a Cancer Hospital

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Abstract

Background: To predict the nature of the adnexal mass, CA-125 is commonly used as a tumor marker. The diagnostic and prognostic value depends on the serum value of CA-125 and the histological variant. This study aims to determine the correlation between serum CA-125 levels and histopathological findings in adnexal masses.

Methods: This retrospective study was conducted at a tertiary care cancer hospital. Medical records of patients who underwent surgery for adnexal masses were reviewed. Preoperative serum CA-125 values were categorized into five ranges: <35, 35–135, 136–235, 236–335, and ≥336 U/ml. Histopathological diagnoses were recorded, and the correlation between CA-125 levels and histological types was assessed using Pearson's correlation coefficient (r).

Results: For CA-125 levels <35 U/mL, a very weak positive correlation was noted (r = 0.12), while a moderate negative correlation was found in the 35–135 U/mL group (r = -0.45), indicating malignancy may be present even at lower CA-125 levels. A strong positive correlation (r = 0.60) was observed for CA-125 levels between 136–235 U/mL, mostly associated with serous and mucinous carcinomas. The 236–335 U/mL range showed negligible correlation (r = 0.05), possibly due to histological heterogeneity or small sample size. A very strong positive correlation (r = 0.75) was observed for CA-125 levels ≥336 U/mL, especially with high-grade serous carcinoma.

Conclusion: Serum CA-125 levels are variably correlated with histological findings in adnexal masses. Higher CA-125 levels are more predictive of specific malignant subtypes, particularly serous carcinoma, but should be interpreted alongside clinical and radiological findings.

Keywords: Adnexal mass, CA-125, Correlation, Histopathology, Ovarian tumor

Introduction

Adnexal masses are one of the common clinical presentations faced in everyday practice. Both benign conditions and early-stage ovarian cancer can manifest as adnexal masses observed in imaging tests conducted for various unrelated reasons.[1]

Ovarian cancer is the seventh most frequently diagnosed cancer and is the eighth leading cause of cancer-related fatalities. The annual incidence of ovarian cancer is 1.6%, based on GLOBOCAN 2020 data.[2]The most prevalent type of ovarian cancer is epithelial ovarian cancer, which makes up 90% of all cases, while the remaining 10% consist of other malignancies, including non-epithelial tumors, germ cell tumors, and sex cord-stromal tumors.[3]

CA-125, initially identified in 1981, is a protein produced by the mucin 16 (MUC16) gene. It can be detected in ovarian cancer tissues using OC 125 monoclonal antibodies. The normal upper limit of CA-125 is considered to be 35.0 U/mL for both premenopausal and postmenopausal individuals.[4]

Biomarkers indicate the properties of various cell types and are therefore useful as indicators of cancer, often referred to as oncomarkers. According to FDA guidelines, relying on a single biomarker may not

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reliably represent the tumor burden, as these markers can also be produced by non-cancerous cells.[4]

Methods

This was a hospital-based retrospective analytical study took place in Bhaktapur Cancer Hospital, at the Gynecologic Oncology Department. The data were collected from hospital records from 2017 to 2023 from patients who fulfilled the inclusion criteria.

As this study was a retrospective, record-based analysis conducted at a tertiary care cancer center. Data were collected from hospital records spanning the period from 2017 to 2023. The study population included patients diagnosed with adnexal masses who underwent exploratory laparotomy during the study period. Eligible cases were identified based on predefined inclusion criteria, and samples were selected using a simple random sampling technique from the medical records database of the cancer center.

Relevant clinical and demographic information was extracted from patient record files, including age, clinical presentation, imaging findings, and operative details. Histopathological reports were reviewed to confirm the diagnosis and classify the adnexal masses as benign or malignant. Additionally, preoperative serum CA-125 levels were collected from laboratory records documented in the patient files.

All collected data were systematically entered into a Microsoft Excel spreadsheet to ensure accuracy and consistency. Data cleaning and verification were performed prior to analysis to minimize errors. Statistical analysis was carried out using Statistical Package for the Social Sciences (SPSS) version 23. Descriptive statistics, including frequency and percentage, were used to summarize categorical variables. The Pearson correlation coefficient was applied to assess the relationship between CA-125 levels and histopathological outcomes.

Ethical approval for the study was obtained from the Institutional Review Committee of National Academy of Health Sciences, Kathmandu, with reference number 348/2082/83. Confidentiality of patient information was strictly maintained throughout the study by anonymizing all personal identifiers. As this was a retrospective study, no direct patient contact was involved.

The duration of the study was two months following ethical approval, during which data collection, entry, and analysis were completed. The inclusion criteria includes women diagnosed with adnexal masses who underwent surgical exploration and had complete medical records, including histopathological reports and CA-125 values. Patients with incomplete records or missing key variables were excluded from the study.

Results

Out of the total 62 cases in our study, there were 46 (74.19%) malignant and 16 (25.81%) cases that were benign based on histological findings. The mean age of participants in this study was 50.82 years.

Table 1: Frequency and percentage of malignancy

CA-125 value in range	Frequency of malignancy	Percentage of malignancy
Less than 35	13	28.89%
35-135	4	8.89%
136-235	5	11.11%
236-335	2	2.22%
336 and above	22	48.89%

In this table, the higher the value of the tumor marker CA125, there was more chance of malignancy. Nearly 22(48.89%) percentage of malignant cases had CA125 level above 336 and above, indicating a strong association between elevated CA-125 levels and malignancy.

Table 2: Histopathological variants of adnexal mass

Histopathological variant	Frequency	Percentage
Serous carcinoma	21	45.65%
Mucinous carcinoma	13	28.26%
Brenner	6	13.00%
Sex cord stromal	5	10.86%
Germ cell	1	2.17%

In this table**,** serous carcinoma is the most common histopathological variant of adnexal mass, accounting for 45.65% of cases, followed by mucinous carcinoma (28.26%). Brenner tumors (13.00%) and sex cord stromal tumors (10.86%) are less frequent, while germ cell tumors are the least common, comprising only 2.17% of cases.

Table 3: Coefficient of Correlation (r- value) with CA-125 Value

CA-125 value	Histological type	Coefficient of correlation (r)
Less than 35	0.12	Very weak positive correlation
35-135	-0.45	Moderate negative correlation
136-235	0.60	Strong positive correlation
236-335	0.05	Negligible correlation
336 and above	0.75	Very strong positive correlation

This table illustrates the correlation between serum CA-125 levels and specific histopathological types of adnexal masses, represented by the correlation coefficient (r). For CA-125 levels below 35, the r value is 0.12, indicating a very weak positive correlation and suggesting minimal association between low CA-125 levels and particular tumor types and CA-125 levels of 336 or higher show a very strong positive correlation (r = 0.75), clearly indicating a strong association with specific malignant histologies especially serous carcinoma, which is known to significantly elevate CA-125 levels.

Discussion

This retrospective hospital-based study was to find the prevalence of adnexal mass malignancy and establish a correlation between the CA-125 and histological findings of the adnexal mass in the tertiary care cancer center of Nepal.

According to this study, the serum level CA-125 value positively correlates with the percentage of malignancy in adnexal mass patients. Similar findings seen in the UKCTOCS-trial showed the sensitivity and specificity of multimodal screening for detection of invasive epithelial-ovarian cancer were 85.8% (95% CI, 79.3–90.9%) and 99.8% (95% CI, 99.8–99.8%), respectively. Multimodal screening used a sequential strategy with annual serum CA-125 and repeat CA-125 and transvaginal ultrasound as second-line tests.[5] None of the randomised trials have demonstrated a mortality benefit. Therefore, ovarian cancer screening is not currently recommended in women at average population risk. More frequent surveillance for ovarian cancer every three to four months in women at high risk has shown good performance characteristics and significant down staging, but there is no available information on a survival benefit. Population testing offers an emerging novel strategy to identify women at high risk who can benefit from ovarian cancer prevention. Novel multicancer early detection biomarker, longitudinal multiple marker strategies, and new biomarkers are being investigated and evaluated for ovarian cancer screening. Risk and risk-reducing salpingo-oophorectomy (RRSO).

The study done by V Kumar et al. in the year 2019, concluded that the ROMA score is useful in predicting the malignancy in adnexal mass. It used the CA-125 as a tumor marker and it combines with HE4. So this scoring and individual parameters help in diagnosing and monitoring the adnexal mass malignancy.[1]

In our study, most of the patient were asymptomatic, and incidental findings of adnexal masses were common occurrences in this study. Similar findings were seen in a study done in 2024, which indicates that while many ovarian cancers may be asymptomatic, a considerable proportion present with symptoms at the time of diagnosis.To detect in the ovarian cancers, there should be a high degree of suspicion from examination, imaging, and oncomarkers. However, the guideline does not recommend particular screening for the general population.[6]

In this study, the most common histological variant was the serous type, and a similar finding was seen in a study done in 2020 by N. Thapa et.al taken total of 69 patients, and most of them had, serous ovarian cancer, and mucinous carcinoma, which accounted for 63.8% (n=44) and 31.9% (n=22), respectively. The remaining patients had clear cell carcinoma (2.9%, n=2) and endometrioid carcinoma (1.4%, n= 1). In this analysis, they found a significant linear correlation between log (serum CA125 level) and the PCI (95% CI 0.017–0.07, P=0.002, R2=0.152). Despite this linear relationship, it turned out that a large proportion of EOC patients presented an opposite relationship between log.[7]

Another study done in 2024 to evaluate CA-125 as a tumor marker showed histological analysis revealed benign cystadenoma as the most prevalent subtype (31.8%), followed by serous carcinoma (27.3%) and borderline tumors (22.7%).[2]

A study done in 2025 in Egypt, out of 76 patients, fifty patients had their data analyzed. Out of the included patients, 56% had benign ovarian lesions, 12% had borderline ovarian tumors, and 24% had malignant ovarian tumors.[8]But in our study, there were a total of 74% malignant cases and 16% benign cases. The differences of finding could be due to the case being collected from a cancer hospital, and preoperative suspicion was high for the malignant variant.

In our study, the diagnostic value of CA-125 is significant, as there were a positive correlation between higher levels of CA-125 and malignant varieties of adnexal mass. Similar findings noted in a study done in 2023 by Huang et al. showed that the diagnostic sensitivity of CA-125 significantly improves the diagnostic accuracy of ovarian-adnexal malignant lesions, providing new clinical references for the evaluation and management of ovarian-adnexal malignancies and contributing to better patient prognosis. The combination of O-RADS, CEUS, and CA-125 further enhanced the diagnostic performance, achieving a sensitivity 82.35%, a specificity of 98.08%, and an accuracy of 94.20%.[9] Related risk factors and temporal incidence trends of ovarian cancer in population subgroups. Data from Global Cancer Observatory and the Cancer Incidence in Five Continents Plus were used for the ovarian cancer incidence. Age-standardized rates (ASR) were calculated.

In this study a single tumor marker was taken for the study, but the combined parameter gives better sensitivity as compared to a single marker. CA-125, when combined with HE4, shows improved diagnostic value, particularly in early-stage detection. A prospective multicenter trial by Moore et al. demonstrated the accuracy of the RMI and ROMA scores for diagnosing ovarian cancer. ROMA, utilizing HE4 and CA-125, demonstrated higher sensitivity (94.3% at 75% specificity) than RMI (84.6%) in distinguishing between benign and EOC status.[4]

The National Specialized Commission on Gynecologic Oncology of the Brazilian Federation of Gynecology and Obstetrics Associations (FEBRASGO) concluded that the tumor markers can be used alone as markers and is more precise when used in combination with other markers and clinical examination. Serum markers value indicates the likelihood of malignancy and the need for management and consultation. CA-125 is a serum protein marker elevated in nearly about 80% of adnexal malignancies.[10]

A study done at a tertiary care hospital in 2020, showed that a single tumor marker like CA-125 does not correlate strongly with malignancy, so multiple parameters should be considered to predict the malignancy, in this study, the higher the value of tumor marker stronger the correlation with the nature of the adnexal mass. For the final diagnosis, histological examination is always necessary.[12]

In our study, the mean age of participants was 50.82 years, and 74% of cases were malignant. A similar finding seen in a study done in 2022 in India shows that the mean age of the participants was 52.1 years and there were 100 participants in the study. Among them, 70 (70%) had histologic confirmation of malignancy.[13]

In one study done in 2023 by taking 82 menopausal women to calculate the risk of malignancy index (RMI) for ovarian malignancy by using CA-125 as a tumor marker, it showed 75.8% sensitivity, 91.8% specificity, 86.2% positive predictive value, and 84.9% negative predictive value by considering a cut-off value of RMI 200. CA-125 can be used as a predictive marker for adnexal mass malignancy. In this study, CA-125 showed a strong correlation to malignancy as the value increases.[14]

In the cohort study done in 2025, in a large number of patients with adnexal cancer, showed that the value of CA-125 varies according to ethnicity, and population specific range were existed in a large cohort study. The value of CA-125 was 23% less likely to increase in Indian and Black patients at the diagnosis, so the diagnostic value should be established according to population-specific range to remove diagnostic dilemmas regarding the value of the tumor marker.[11]

The study done by S. Moukas et al. in 2025, concluded that the variant of CA-125 glycoprotein to detect ovarian epithelial cancer is more precise as compared to the conventional CA-125 value as a marker, although the testing is more complex.[15]

Conclusion

In Nepal, Adnexal carcinoma is relatively common compared to other malignancies. The incidence of adnexal cancer has become more common even at younger ages recently, has been primarily diagnosed in perimenopausal and postmenopausal females. The CA-125 level is a tumor marker for adnexal tumors and correlates with the histological type of adnexal masses. A higher value of tumor marker strongly correlates with adnexal masses malignancy, though in our study, this relation was not seen, maybe due to the limited sample size.

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