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ORIGINAL ARTICLE

Evaluation of LDH, AFP, β-hCG and Tumour Markers CEA and CA-125 in Sera of Iraqi Patients With Ovarian Cancer

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Abstract

Background/Aim: Ovarian cancer is still a big health concern, with few early detection options. The present research aimed to explore the test's usefulness of blood levels of cancer antigen 125 (CA-125), carcinoembryonic antigen (CEA), alpha-fetoprotein (AFP), lactate dehydrogenase (LDH) and beta-human chorionic gonadotropin (β-hCG) in detecting and managing ovarian cancer.

Methods: Samples were collected from 30 ovarian cancer patients and 30 healthy controls. The levels of CA-125, CEA, AFP; LDH and β-hCG were evaluated by ELISA.

Results: Results indicated that ovarian cancer patients had considerably greater concentrations of CA-125, AFP, CEA and β-hCG than controls. LDH levels were not substantially different between the two groups. The ROC curve study indicated outstanding diagnostic performance for CA-125, AFP, CEA and β-hCG, with AUC values of 1.000. LDH had reasonable clinical precision, with an AUC of 0.721.

Conclusion: The correlation analysis revealed strong positive relationships between all biomarkers in the patient group. These data imply that CA-125, AFP, CEA and β-hCG may be useful biomarkers for diagnosing and treating ovarian cancer in Iraqi women. Additional studies with bigger sample numbers are needed to corroborate these findings.

Key words: Ovarian neoplasms; Biomarkers, tumour; Carcinoembryonic antigen (CEA); Lactate dehydrogenase (LDH).

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Introduction

Ovarian cancer is still among the most frequent gynaecologic malignancies and is the fifth most common cause of cancer mortality in women. The majority of ovarian cancer patients have epidermal ovarian neoplasms that develop from coelomic epithelium or mesothelium tissues.[1] In nations with poor infrastructure, ovarian cancer is the seventh most common malignancy among women, with 239,000 new cases reported globally in 2012.[2]

Notwithstanding concentrated efforts to uncover and discover original effective populace-constructed showing tests, no biological markers have yet been established. However, numerous putative ovarian cancer diagnostics biomarkers are being studied, including, cancer antigen 125 (CA-125), carcinoembryonic antigen (CEA), alpha-fetoprotein (AFP), lactate dehydrogenase (LDH) and beta-human chorionic gonadotropin (β-hCG). For many years, researchers have been

studying the function of extracellular proteolysis in cancer growth, with a particular emphasis on secreted proteases.[3, 4]

LDH is a compound identified by several organs, including the heart, liver, kidneys, muscles, brain and red blood cells. LDH is required for the metabolism of glucose to energy within cells. The concentration of LDH may be increased in ovarian cancer patients.[5] Elevated LDH levels may suggest tissue damage and accelerated cell turnover, this can arise in several conditions, including cancer. However, LDH levels are not particular to ovarian cancer; they can be high in a variety of other illnesses as well.[6] Ovarian cancer patients have significantly more abdominal fluid and serum LDH levels compared to individuals with typical ovarian cancers or other gynaecological cancers.[7]

The foetal liver, yolk sac and digestive system primarily generate AFP. Adult AFP levels are normally modest, but they might rise under specific situations.[8] Tumour marker AFP is not a major marker for ovarian cancer, although it can be raised in specific forms of germ cell tumours that can develop in the ovaries. The most important forms of ovarian tumours are dysgerminomas and other non-w, which are used to assess treatment responses and screen for recurrences in individuals with germ cell tumours.[9] The association between AFP and ovarian cancer includes both risk factors and clinical manifestations. Elevated AFP levels can suggest a variety of ovarian tumours, both benign and malignant and may also serve as a diagnostic marker.[10]

During pregnancy, the placenta produces a hormone β-hCG. However, ovarian tumours can create β-hCG, resulting in high levels of the hormone. This is especially true for ovarian germ cell tumours, a kind of ovarian cancer that arises from egg-producing cells. These tumours can release hormones such as β-hCG, which can be discovered by blood testing.[11, 12] The hormone β-hCG is also believed to be secreted from certain malignancies in both men and women, which include malignant tumours in the genital tract of males and ovarian cancer in females, where their behaviour may be a marker for distinguishing between certain ovarian tumours.[13] In many respects, recognising the free component in the blood of a person with cancer is like identifying an indication of a dismal prognosis.[14]

CEA is a protein naturally created in foetal gastrointestinal tissue, although its synthesis diminishes considerably after birth. CEA is rarely utilised as a primary marker in the diagnosis or surveillance of ovarian cancer. Instead, the most widely utilised tumour marker for ovarian cancer is CA-125.[15, 16] Is a protein discovered in greater concentrations in ovarian cancer cells than in normal cells. However, in certain situations, CEA levels may be increased in people with ovarian cancer, although this is not limited to ovarian cancer and can also occur in a range of other illnesses.[17] CA-125 is a main test in ovarian cancer that is largely utilised for diagnosis and surveillance. Its levels are associated with the existence of ovarian lesions, with greater amounts frequently suggesting malignancy. However, CA-125 is not limited to ovarian cancer; increased levels can occur in benign diseases, confounding its diagnostic value. Studies demonstrate that individuals with ovarian cancer had considerably higher CA-125 concentrations (mean 64.9 U/mL) than those without (mean 28.6 U/mL).[18, 19]

This study aimed to improve understanding of the value of LDH, AFP, β-hCG, CEA and CA-125 in detecting and managing ovarian cancer, particularly in Iraq.

Methods

The study participants were divided into two categories: patients and controls. The patient collection consisted of 30 ovarian cancer patients (30 females, ages 40-50). A doctor from the Oncology Teaching Hospital in Medical City, Baghdad, Iraq, evaluated patients who had been diagnosed with breast cancer. The control cohort consisted of 30 healthy people of similar age and gender to the sick category. Between July and October 2024, all trial subjects provided informed written permission before participating and patients completed a questionnaire. No patients smoked, drank, or were pregnant. Patients with diseases other than endometrial cancer were excluded, including diabetes, hypertension, hyperthyroidism and psoriasis.

From each study participant (patient and control) 5 mL of blood from the vein was taken. The samples were collected in a gel tubes. Following collection, the gel tubes were centrifuged for ten

minutes at 3000 rpm. The resulting serum was kept at -20 °C until analysis.

Serum levels of LDH were assessed by VIDAS (*Maizy,* France), AFP was assessed using VIDAS kits and apparatus based on enzyme linked immunosorbent assay (ELISA) technology *(Monobind Inc*, Lake Forest, USA), β-hCG was assessed using VIDAS kits and ELISA provided by *Altas Medical* in Cambridge, UK. CA-125 and CEA were assessed using VIDAS kits and apparatus based on enzyme-linked fluorescence assay (ELFA) technology provided by *Biomérieux* in Marcy-l'Étoile, France.

Statistical analysis

The IBM SPSS Statistics application (IBM Corporation, New York, United States) version 25.0 was used for the analysis. The data were analysed with descriptive statistics and presented as means ± standard deviation. The average variances of the patient and control groups were compared with an independent sample t-test. Statistical significance was determined as $p < 0.05$ with a 95 % confidence interval and extremely significant as $p \leq 0.01$ with a 99 % confidence range.

Results

Figure 1 shows substantial changes in CA-125, AFP, CEA and β-hCG levels between the control and patient groups, but no significant difference in LDH levels. The average CA-125 level in the control group was 12.18 ± 5.40. In comparison, patients had a much higher mean CA-125 level of 90.42 ± 24.14. The p-value of 0.001 suggests that CA-125 levels differed significantly between the groups.

The mean LDH level in the control group was 170.29 ± 19.87. Patients group had a somewhat higher mean LDH level 189.58 ± 25.56. However, the p-value of.144 shows no substantial difference in LDH levels between the control and patient groups.

The mean AFP level in the control collection was 5.24 ± 2.29. Patients had a significantly higher

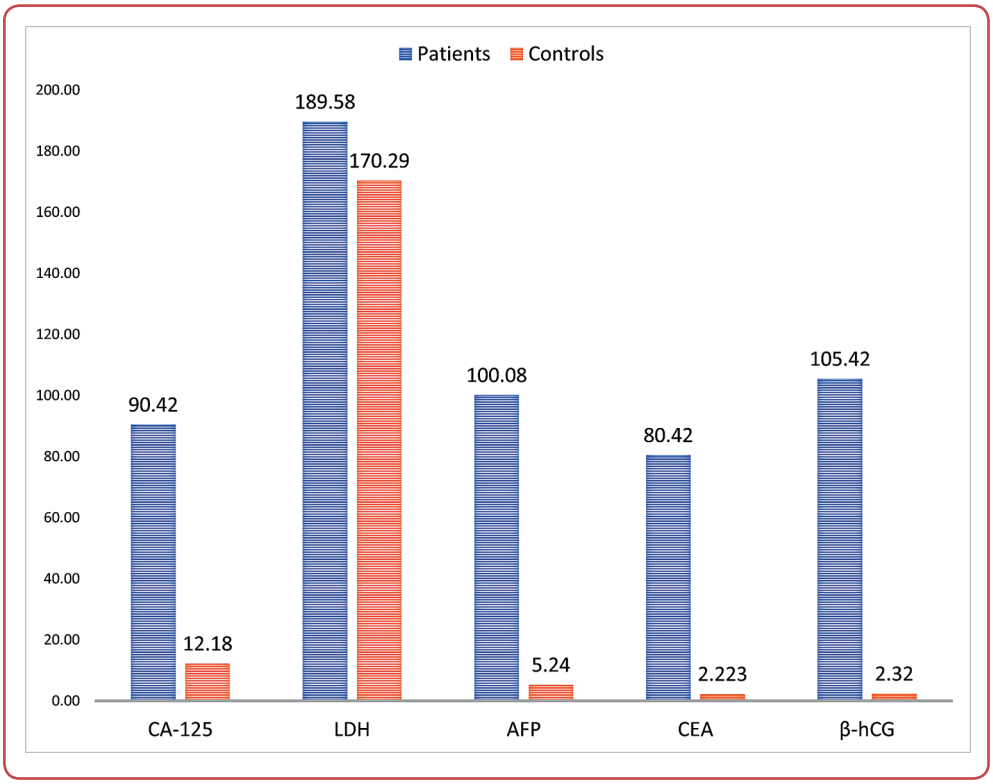

Figure 1: Serum levels of cancer antigen 125 (CA-125), carcinoembryonic antigen (CEA), alpha-fetoprotein (AFP), lactate dehydrogenase (LDH) and beta-human chorionic gonadotropin (β-hCG) in the control and patient group

mean AFP level of 100.08 ± 24.31. A p-value of 0.001 indicates that the distinction was statistically significant.

The average CEA level in the control group was 2.22 ± 0.99. Patients had a considerably higher mean CEA level 80.42 ± 24.14. The p-value of 0.001 indicates a significant difference in CEA levels between the control and patient groups. The average β-hCG level in the control group was 2.32 ± 0.99. Patients had a significantly higher mean β-hCG level 105.42 ± 19.91. The p-value of 0.001 suggests that β-hCG levels differed substantially between groups.

Table 1: The area under the curve (AUC) for cancer antigen 125 (CA-125), carcinoembryonic antigen (CEA), alpha-fetoprotein (AFP), lactate dehydrogenase (LDH) and beta-human chorionic gonadotropin (β-hCG)

Test result variable(s)	Area	SE	p-value	95 % CI	
				Lower bound	Upper bound
CA-125	1.000	0.000	0.000	1.000	1.000
LDH	0.721	0.066	0.003	0.593	0.850
AFP	1.000	0.000	0.000	1.000	1.000
β-hCG	1.000	0.000	0.000	1.000	1.000
CEA	1.000	0.000	0.000	1.000	1.000

CI: confidence interval; SE: standard error;

Table 1 shows the area under the curve (AUC), which is an instant measure of the receiver operating characteristic (ROC) curve that indicates the diagnostic test's overall presentation. An AUC of 1 represents a seamless model, whereas an AUC of 0.5 indicates that the model achieved no recovery other than by mistake. CA-125 has an AUC of 1.000, suggesting that the classification model was excellent and error-free. The AUC for LDH is 0.721, with a standard deviation of 0.066 (Figure 2).

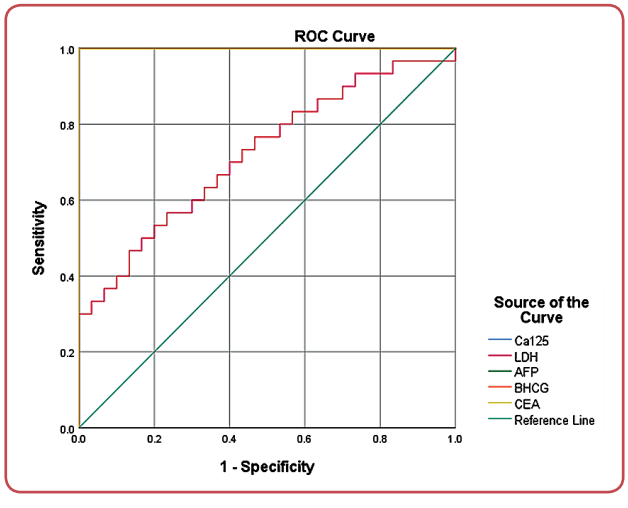

Figure 2: Receiver operating characteristic (ROC) curve for cancer antigen 125 (CA-125), carcinoembryonic antigen (CEA), alpha-fetoprotein (AFP), lactate dehydrogenase (LDH) and beta-human chorionic gonadotropin (β-hCG)

The asymptotic significance was 0.003, indicating that the AUC differs considerably from 0.5. The 95 % confidence interval for LDH's AUC was 0.593–0.850. AFP, β-hCG and CEA had AUC values of 1.000, suggesting flawless classification models for these variables.

According to the given footnote, the calculations were based on the nonparametric assumption. Furthermore, the null hypothesis states that the real area under the curve is 0.5. The findings for LDH reveal that the AUC was considerably different from 0.5, showing that the LDH model adds value beyond random chance. Finally, The AUC values indicate that the models for CA-125, AFP, β-hCG and CEA were ideal classifiers, but the model for LDH performed decently but not flawlessly. The statistical significance and confidence intervals give further information about the model's dependability and accuracy in categorising the data on which it is based.

Table 2: Person correlations (r) for cancer antigen 125 (CA-125), alpha-fetoprotein (AFP), lactate dehydrogenase (LDH) and beta-human chorionic gonadotropin (β-hCG)

Parameter	CA-125	LDH	AFP	CEA	β-hCG
CA-125	1.000	0.880**	0.941**	0.917**	0.905**
LDH	0.880**	1.000	0.896**	0.917**	0.882**
AFP	0.941**	0.896**	1.000	0.931**	0.937**
CEA	0.917**	0.917**	0.931**	1.000	0.951**
β-hCG	0.905**	0.882**	0.937**	0.951**	1.000

***: $p < 0.01$;*

Table 2 shows correlations indicating that there were significant linear links between the biomarkers CA-125, LDH, AFP, CEA and β-hCG in the patient group under research, which might give useful information about potential associations between these biomarkers in the context of the patient's health problems. CA-125 expressions had a good correlation with LDH ($r = 0.880$, $p < 0.01$). This shows that if CA-125 levels increase, so do LDH levels and *vice versa*. CA-125 and AFP showed a strong correlation ($r = 0.941$, $p < 0.01$). CA-125 and CEA showed a significant correlation ($r = 0.917$, $p < 0.01$), as well as CA-125 and β-hCG ($r = 0.905$, $p < 0.01$).

Discussion

This study intended to investigate the influence of changes in tumour marker profiles on the detection and administration of ovarian cancer in Iraq and additionally recommend areas for future studies. Gynaecological oncology has significant challenges due to the absence of reliable and non-invasive treatments.[20, 21] In this investigation, individuals with ovarian cancer showed significantly greater blood concentrations of LDH, AFP, β-hCG, CA-125 and CEA compared to healthy controls. This hypothesis receives more support from CA-125 and CEA has great sensitivity, distinguishing between those with ovarian cancer and healthy women.

The most often utilised serum biomarker in ovarian cancer testing is CA-125.[22] A prior investigation showed an accuracy of more than 73.1 % and a precision of 79 % for the serum concentration, which is equivalent to other biomarkers in forecasting ovarian cancer.[23] Yet, observations demonstrate that the surge is also evident under normal circumstances.[24] Detection data for US, pulmonary, colon and ovarian cancers from the past experiment found no mortality advantage in employing a screening technique that included the CA-125 cutoff.[25] The results of this study are consistent with previous studies when comparable with the results published in additional research that analysed blood levels of CA-125, which may be used as an effective test for the identification of ovarian cancer, in the sense of accuracy and precision.[26, 27]

CEA is a widely used tumour marker in clinical practice, with significant diagnostic significance for gynaecology, breast, lung, liver and digestive system malignant tumours.[28, 29] As a whole, the current results are similar to the results published in previous studies that examined blood levels of CEA.[30, 31]

Elevated levels of (CEA) in ovarian cancer may suggest an advanced stage of the illness or metastases. The more cancer in the body, the more CEA the tumour cells make. As a result, elevated CEA levels can signal a greater tumour load in ovarian cancer.[32] The cancer spreads (metastasizes) from the ovaries to other organs including the liver, breathing, or peritoneum. CEA levels rise. This is because cancer cells in these new sites also generate CEA. CEA levels are also utilised as a tumour marker to diagnose and monitor ovarian cancer. However, CEA levels alone are not conclusive; they must be read in conjunction with other clinical observations and testing.[33]

People with ovarian melanoma were shown to have greater levels of LDH in their total serum.[34, 35] Similarly, Schneider et al found that individuals with ovarian malignancies had considerably greater concentrations of LDH than those with innocent ovarian tumours.[36] Study by Boran showed that blood LDH concentrations in people with ovarian malignancy were identified as significantly greater than those in people with benign ovarian tumours, but there were no significant variations in LDH concentrations across different types of ovarian cancer and phases of the illness.[7] In the current investigation, in the levels of LDH there were no notable distinctions between the control and patient groups. The findings are consistent with earlier research.[37, 38] LDH levels are not commonly employed as a diagnostic or prognostic indication in ovarian cancer patients. This is because LDH is not limited to ovarian cancer and may be high in a variety of illnesses. Other indicators, such as CA-125, are increasingly commonly used in the diagnosis and monitoring of ovarian cancer.[39]

Both AFP and β-hCG are utilised as indicators for ovarian germ cell tumours and to assess the likely causes of poorly differentiated metastatic disease. Both indicators are used to test for various cancers.[40, 41] In this particular investigation, scientists discovered that the concentrations of AFP and β-hCG changed considerably between the control and patient groups. The results are consistent with past studies. It is uncommon to observe elevated levels of AFP in ovarian cancer. AFP is a protein that is commonly linked to liver cancer (hepatocellular carcinoma) and some forms of germline cell tumours. High levels of AFP may be detected in rare cases of ovarian germ cell tumours, such as yolk sac tumours (endodermal sinus tumours). Yolk sac tumours, a form of ovarian cancer, can generate AFP.[10]

Elevated levels of blood β-hCG in ovarian cancer can be caused by a rare condition known as paraneoplastic syndrome. Paraneoplastic syndromes are a range of signs and symptoms that appear in cancer patients but are not caused by the tumour's local presence or metastasis. In the case of ovarian cancer, high β-hCG levels can indicate a paraneoplastic syndrome in which tumour cells create and release β-hCG into circulation. This

production of β-hCG can result in greater than usual amounts of the hormone in the blood, which can be identified *via* blood testing. The results of the current studies are consistent with previous studies.[37, 42]

Conclusion

CA-125, AFP, CEA and β-hCG concentrations were significantly greater in the ovarian cancer group compared to healthy controls. The ROC curve study indicated good diagnostic performance for CA-125, AFP, CEA and β-hCG, with AUC values of 1.000. Correlation analysis found strong positive connections between all biomarkers in the patient group. These data imply that CA-125, AFP, CEA and β-hCG may be useful biomarkers for diagnosing and treating ovarian cancer in Iraqi women. However, it is critical to emphasise that additional studies with a greater sample are necessary to verify these results and evaluate the prospective treatment implications of these biomarkers in the Iraqi population.

Ethics

The ethical approval was taken from the Ethical Committee in the Iraqi National Cancer Research Centre, University of Baghdad, Baghdad, Iraq. The ethical number is 1, dated 20 November 2024. All patients and participants were given an oral acceptance for blood collecting and work. All procedures performed in studies involving human participants followed the ethical standards of the research committee of "Iraqi National Cancer Research Centre, University of Baghdad, Baghdad, Iraq" and with the 1964 "Helsinki Declaration" and its later amendments or comparable ethical standards.

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Conflicts of interest

The authors declare that there is no conflict of interest.

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Data access

The data that support the findings of this study are available from the corresponding author upon reasonable individual request.

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Data curation: YJD, RS, MAM, AHJ
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Writing - review and editing: YJD, RS
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