Acta Pharm. Sci. Vol 64:(4), 2026
Original article
DOI: 10.23893/1307-2080.APS64036

OPEN ACCESS

The significance of vascular endothelial growth factor (VEGF) levels in the early detection of breast cancer

Haidar A. ABDULAMIR[1], Rawa M. M. TAQI[2], Hanan H. RAMADHAN[3], Mohammed J. MANNA[4*], Fatin QASSIM[5], Enas Muhsin Abbass ALKHAFAGY[6]

1 University of Hilla, College of Pharmacy, Babylon 51001, Iraq
2 Al-Nahrain University, College of Pharmacy, Department of Pharmaceutical Chemistry, Baghdad, Iraq
3 University of Basrah, College of Pharmacy, Department of Clinical Laboratory Sciences, Basrah, Iraq
4 Mustansiriyah University, College of Dentistry, Baghdad, Iraq
5 Al-Esraa University, College of Pharmacy, Baghdad, Iraq
6 Al-Mustansiriyah University, College of Medicine, Department of Chemistry and Biochemistry, Baghdad, Iraq

ABSTRACT

Malignant breast tumors are a serious health issue that needs immediate attention as more than 1.5 million women around the world are diagnosed with it every year. Recently, vascular endothelial growth factor (VEGF) has been considered as a promising tumor marker due to its role in cancer growth. The present work aims to assess the efficacy of measuring the levels of VEGF for the early diagnosis of breast cancer in a cohort of Iraqi women from Baghdad, either independently or in conjunction with established markers including CA 15-3 and CEA. A case-control study was performed with 60 female breast cancer patients and 75 healthy controls matched for age, BMI, and sex, recruited from Al-Amal National Oncology Hospital, Baghdad, Iraq, from April to November 2025. The levels of VEGF, CEA, and CA 15-3 in the blood were measured and compared between groups. Results illustrated that cancerous patients exhibited significantly higher VEGF levels than controls. Furthermore, the ROC curve

* Corresponding author: Mohammed J. MANNA
E-mail: mohammedalmanna@uomustansiriyah.edu.iq
ORCIDs:
Haidar A. ABDULAMIR: 0000-0003-3262-3061
Rawa M. M. TAQI: 0000-0002-8886-2080
Hanan H. RAMADHAN: 0000-0002-9945-2028
Mohammed J. MANNA: 0000-0001-5307-1361
Fatin QASSIM: 0009-0001-8696-0015
Enas Muhsin Abbass ALKHAFAGY: 0000-0002-1173-7417
(Received 23 Apr 2026, Accepted 18 Jun 2026)

Acta Pharmaceutica Sciencia is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.
© Medipol University Press / e-ISSN: 1307-2080

analysis revealed that the measurement of VEGF in combination with CEA and CA 15-3 provides higher specificity and sensitivity. In conclusion, VEGF may be a promising biomarker for the early diagnosis of breast cancer due to the higher sensitivity and specificity than other traditional markers.

Keywords: vascular endothelial growth factor, CEA, malignant breast tumor, CA 15-3, Iraq

INTRODUCTION

Breast cancer is a type of cancer that begins in the terminal ductal-lobular units (TDLM) or glandular lactiferous duct epithelial cells[1]. It is considered one of the most common cancers in women around the world. In 2015, it caused about 570,000 deaths, and every year, over 1.5 million women are diagnosed with it. This makes up 25% of all female cancer cases worldwide[2,3]. The tumor is referred to as non-invasive (carcinoma in situ) if it has not penetrated the basement membrane. If it has, then it is called invasive[4]. The disease is very hard to treat since it can spread to other organs, such as the lungs, bones, brain, and liver. Early detection is linked to a better prognosis and higher survival rates[5]. Currently, the blood levels of the serological markers, including cancer antigen 15-3 (CA 15-3) and Carcinoembryonic antigen (CEA), are used to diagnose breast cancer as they show how the tumor is progressing and whether it has spread to lymph nodes. They are also recommended for monitoring patients with metastatic disease during treatment. The most important limitations regarding the use of CA 15-3 and CEA in the diagnosis of breast cancer in the early stages are the low specificity and sensitivity of these markers[6]. Vascular endothelial growth factor (VEGF) has recently been identified as a promising marker for tumor diagnosis as a result of its potential role in the progression of cancer. Angiogenesis, essential for tumor proliferation, local invasion, and metastasis, is facilitated by the increased VEGF levels detected in diverse tumor tissues[7,8]. Malignant breast tumor is characterized by lymphangiogenesis, which is defined as a process in which the blood and lymphatic vessels contribute to the progressing tumor[8,9]. A lot of *in vivo* and *in vitro* studies have demonstrated that higher levels of VEGF expression are strongly linked to tumor growth and metastasis[8,10]. However, further studies are required to determine the possible role of measuring VEGF levels in the early diagnosis of breast cancer and also for monitoring its progress.

For all the above-mentioned literatures regarding the VEGF role in the breast cancer incidence and progress, the present work aims to assess the efficacy

of measuring the levels of VEGF for the early diagnosis of breast cancer in a cohort of Iraqi women from Baghdad, either independently or in conjunction with established markers including CA 15-3 and CEA.

METHODOLOGY

Study design

A case-control study was conducted in the duration between April and November 2025, where sixty women between the ages of 29 and 48 who had breast cancer were recruited from Al-Amal National Oncology Hospital, Baghdad, Iraq. These patients were compared to a control group of seventy-five age- and BMI-matched healthy women. The laboratory procedures were conducted at the College of Pharmacy, University of Hilla, Babylon. To be eligible, participants had to have a confirmed diagnosis of a breast lesion that was found at an early stage (stage I) through clinical examination or imaging, followed by histological confirmation.

Exclusion criteria

1. Individuals with a history of any malignancy (past and/or present) or any chronic or acute medical condition.

2. Patients who had received chemotherapy or hormonal treatment.

3. Women who are pregnant.

4. Older than 65 years

All control subjects and examined patients underwent:

Comprehensive clinical assessments alongside complete medical history

A baseline check of the biochemical tests for VEGF CEA, and CA 15-3.

Sample collection and processing

The samples were obtained by extracting five milliliters of blood from all subjects subjected to the present study and placed in serum separator tubes. After allowing the samples to clot for half an hour at room temperature, we spun them for ten minutes at 4000 rpm (1252xg). Before being tested, the prepared sera were divided into smaller portions and stored at -20°C. As directed by the companies that manufactured the ELISA kits, we used them to measure CEA, CA 15-3, and VEGF. The kits were obtained from Elabscience/ China) and Cell Biolabs/USA.

Statistical analysis

Data were examined utilising SPSS software version 20. Quantitative variables were expressed as mean ± standard deviation (SD) and used the t-test to compare them, with a significance level of $p \leq 0.05$. The Pearson's correlation test was used to examine how the measured parameters were related to each other. Receiver Operating Characteristic (ROC) curve analysis was used to check the biomarkers' diagnostic accuracy and reliability[11]. To compare how well the markers worked as tests, the area under the ROC curve (AUC) was calculated. An AUC close to 1.0 means the markers were very useful for diagnosis, while an AUC close to 0.5 means they were not very useful[12,13].

RESULTS and DISCUSSION

Results illustrated in Figure 1 and Table 1 clarified that there were non-significant differences in age and body mass index between patients and control groups.

Table 1. Comparison of the demographic characteristics of patients with malignant tumors and controls

	Control	Patients	p-value
N	75	60	
Age (year) (mean ± SD)	36.55 ± 4.87	36.75 ± 5.88	0.971
BMI (kg/cm^3) (mean ± SD)	26.23 ± 3.89	27.07 ± 3.62	0.389

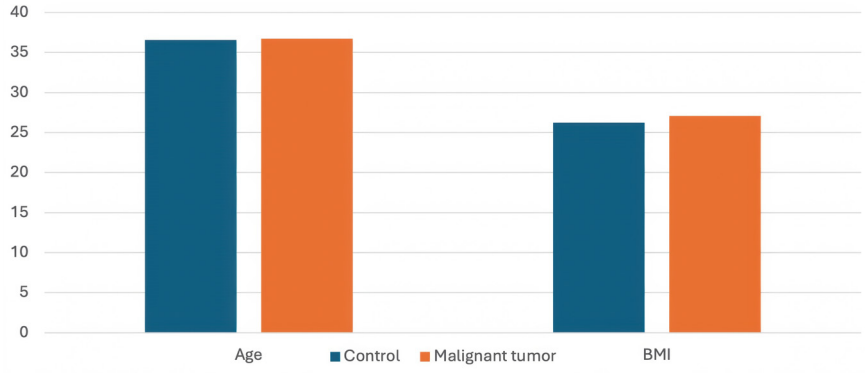

Figure 1. Age and BMI levels in all studied groups

Table 2 shows that the level of CA 15-3 was significantly higher (p=0.009) in patients with malignant tumors than in control subjects. However, there were no significant differences (p>0.05) in the levels of CEA between malignant patients and healthy controls. A distinct pattern emerged, indicating highly significant elevations in VEGF levels among malignant breast tumor patients compared to controls (p<0.001).

Table 2. Levels of VEGF, CEA and CA 15-3, in all studied groups

	Groups	Mean ± SD	p[b]
VEGF (pg/ml)	Controls (n=75)	179.72 ± 58.81	<0.001
	Patients (n=60)	271.83 ± 97.38	
CEA (ng/ml)	Controls (n= 75)	1.44 ± 0.51	0.059
	Patients (n=60)	1.62 ± 0.4	
CA 15-3 (U/ml)	Controls (n=75)	23.98 ± 7.29	0.009
	Patients (n=60)	27.76 ± 7.93	

Table 3 shows that in healthy people; CA 15-3 and CEA demonstrated a strong positive correlation (*r*=0.297; p=0.007) whereas a strong negative correlation between the serum levels of VEGF and the age of the subjects (*r*=-0.295; p=0.008). All other correlations were not significant.

Table 3. The correlations of all examined biochemical markers' levels in control subjects

		Age	S. VEGF	CA 15-3	CEA
BMI	Pearson correlation coefficient	-0.175	0.006	0.060	-0.059
	p-value	0.172	0.962	0.611	0.614
Age	Pearson correlation coefficient		-0.295**	0.098	0.106
	p-value		0.008	0.402	0.367
S. VEGF	Pearson correlation coefficient			0.061	0.104
	p-value			0.605	0.375
CA 15-3	Pearson correlation coefficient				0.297**
	p-value				0.007

**Significant at levels p<0.01

The correlations among all studied biomarkers in patients with malignant breast tumors that were presented in Table 4 indicated that CA 15-3 was correlated positively and significantly with both VEGF (r=0.302; p=0.026), and CEA (r=0.297; p=0.019). Additionally, a significant positive correlation was observed between VEGF and the patients' BMI. Conversely, VEGF levels exhibited a negative and significant correlation with the age of the patients involved in the current study.

Table 4. The correlations of all examined biochemical markers' levels in malignant patient

		Age	S. VEGF	CA 15-3	CEA
BMI	Pearson correlation coefficient	-0.097	0.301*	0.072	-0.142
	p-value	0.403	0.025	0.583	0.283
Age	Pearson correlation coefficient		-0.291*	-0.252	-0.047
	p-value		0.024	0.055	0.723
S. VEGF	Pearson correlation coefficient			0.302*	0.228
	p-value			0.026	0.080
CA 15-3	Pearson correlation coefficient				0.297*
	p-value				0.019

**Significant at levels p<0.01

To evaluate the reliability and significance of serum levels of parameters examined in the current study, ROC curve analysis for CEA, CA 15-3, and VEGF was conducted among the studied groups to determine the feasibility of utilizing these markers individually or in combination for the non-invasive diagnosis of malignant breast tumors.

Table 5 and Figure 2 showed the ROC curve results of the biochemical markers studied in patients with malignant tumors compared to controls. This was done to show how well these tests work for diagnosing breast cancer. The results showed that VEGF is a fair test for breast cancer diagnosis, with an AUC of 0.785, a sensitivity of 83.3%, and a specificity of 57.3%. When combined with CEA and CA 15-3, the results were slightly better, with an AUC of about 0.8, a sensitivity of 76.7%, and a specificity of 69.3%.

Table 5. The results of receiver operating characteristic (ROC) analysis for all studied markers in malignant patients against controls

Markers	AUC	Cut-Off Value	Specificity (%)	Sensitivity (%)
VEGF	0.785	178.3	57.3	83.3
CA 15-3	0.647	19.78	42.7	76.7
CEA	0.613	1.385	49.3	66.7
Combined VEGF, CA 15-3, and CEA	0.8	-	70	76.7

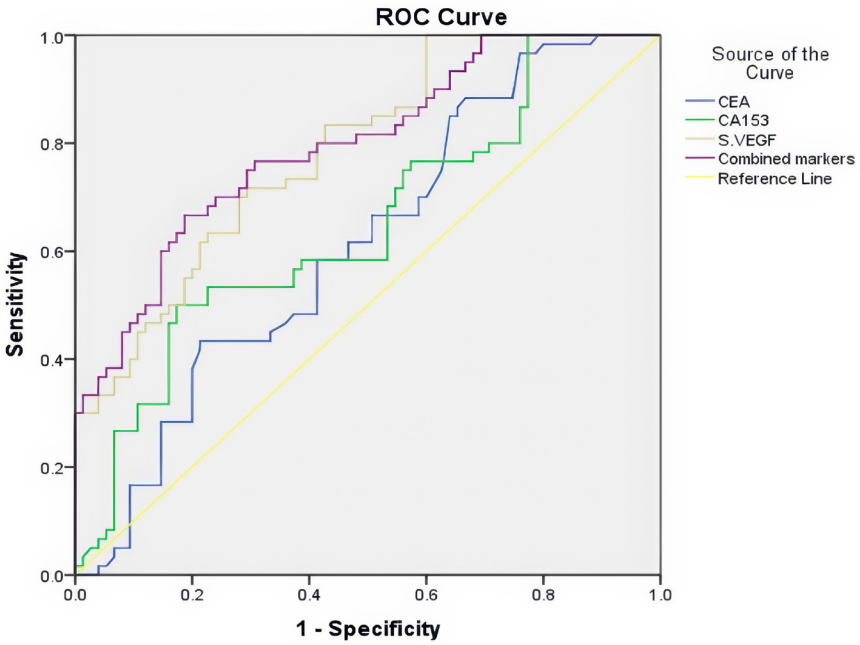

Figure 2. The ROC curves for the studied markers and their combination in malignant group against controls

The results of the present work focused on the evaluation of a novel marker that can be utilized alongside traditional markers for the early diagnosis of malignant tumors, since the traditional markers showed a low specificity and sensitivity[6]. The healthy subjects included in this study were selected to have a comparable age and BMI which did not differ significantly from that of patients enrolled in this research. The selection of such healthy patients helps in eliminating any potential influence of age and BMI on the VEGF level. This

factor was investigated extensively for its possible role in cancer progression and its potential as a marker for early cancer diagnosis.

The selection of age and BMI-matched controls was based on prior knowledge that was reported in previous study which indicated VEGF production is diminished in the elderly, both at baseline and in response to injury of tissue[14]. In addition, study conducted by Olsen et al. also found that VEGF levels were diminished in skeletal muscle cells and the media around them more in cultures from older women than in cultures from youngers. This indicates that older women possess a decreased capacity to generate new blood vessels, attributed to diminished cell division in endothelial cells and reduced concentrations of available and released VEGF protein. These results may influence the angiogenic response to training in older women[15]. In contrary, study conducted by Zaki et al. found that obese women with a BMI>30 that considered as obese exhibited markedly elevated serum VEGF levels compared to the control group[16]. This previous research that considered the age and BMI as determinants for VEGF levels necessitate the selection of controls that do not significantly differ in age and BMI from controls.

The study indicates that women with breast cancer exhibit a significant elevation in CA 15-3 levels (p=0.009) compared to controls, as demonstrated in Table 2. This finding is consistent with previous studies demonstrating a significant increase in CA 15-3 levels in women with malignant breast tumors[17,18]. Zaleski et al. (2018) found in their study a significant increase in the levels of CA 15-3 in the serum of patients with a malignant breast tumor in comparison to healthy women. Nevertheless, this increase was not noted when comparing breast cancer patients to individuals with benign conditions. This study also looked at how -3 is not very sensitive in the early stages of breast cancer. Nevertheless, it was determined that CA 15-3 is advantageous in the advanced stages of the disease for evaluating therapeutic response and identifying recurrent disease at an early stage[17].

Carcinoembryonic antigen (CEA) levels were found to be non-significantly elevated in patients with malignant tumors compared to controls, as shown in Table 2. This indicates that this marker is not suitable for diagnosing the early stages of breast cancer. Prior studies have indicated that the elevation in the levels of CEA were commonly found in patients with metastatic and recurrent breast cancer[19], rather than in the early stages, as evidenced by the current study and existing literature, which show that these markers do not exhibit significant increases and thus rendering them unsuitable for early diagnosis[6]. According to Yang et al., high serum CEA levels were particularly prevalent in

cases of metastatic and recurrent disease[20]. Wang et al. also showed that serum CEA has been less extensively studied than CA 15-3 as a prognostic marker[21].

The results of this study demonstrated a significant correlation between CEA and CA 15-3 levels in patients with malignant tumors, aligning with prior research that suggests these two markers typically elevate simultaneously, especially with progression in tumor stage and other clinicopathological characteristics[22]. This substantiates the functions of CEA and CA 15-3 in cancer progression and development. The increased levels of CA 15-3 found in breast cancer patients are probably because the apical surface of epithelial ducts and acinar breast cells produces it and then releases into the milk. In cancer, changes in the structure of breast tissue let CA 15-3 into the bloodstream[23,24]. The link between CEA levels and advanced stages of cancer is thought to be due to its role in many endothelial cell functions, such as adhesion, proliferation, and migration, both in living organisms and in the lab[25]. This connection might explain why these markers are not very sensitive. Their levels go up a lot and are easier to find in circulation during late-stage metastasis. CEA helps cells move around, and the changed structure of the breast makes it easier for CA 15-3 to be released. The ROC analysis that performed in the present work to determine the reliability of the tests used[26] in this study confirmed what was already known about these markers' low sensitivity and specificity[27]. It showed that CA 15-3 had moderate sensitivity but not enough specificity to be used to find early breast cancer. Earlier studies found that CEA could tell the difference between malignant tumors and controls with a sensitivity of 56.7%, CA 15-3 with a sensitivity of 44.5%, and both together with a sensitivity of 68.9%[21]. In this study, the sensitivities of CEA and CA 15-3 were higher, at 66.7% and 76.7%, respectively. The specificities were 49.3% and 42.7%.

In the present study, results obtained showed that the levels of VEGF increased significantly in cancerous patients, closely resembling the levels of CA 15-3. These findings align with prior studies indicating elevated levels of VEGF in cancer patients, attributed to its role in angiogenesis[28], regarded as a hallmark characteristic of cancer[29,30]. VEGF is a very effective stimulator for endothelial cells and is essential in both normal physiological and tumor angiogenesis. It enhances the permeability of tumor vasculature and promotes the proliferation, migration, differentiation, and angiogenesis of endothelial cells with pro-inflammatory properties[31].

The results obtained in the current study are consistent with research which indicates a significant elevation of VEGF levels in patients with malignant tumors compared to controls, potentially serving as an effective biomarker

for the early diagnosis of breast cancer alongside traditional tumor markers such as CA 15-3[32]. Much research has focused on examining VEGF levels and expression in cancer, with the goal of finding effective treatments that inhibit VEGF expression and may help prevent or slow cancer progression[33-35].

VEGF levels were influenced by age and body mass index, as evidenced by a significant direct correlation with BMI and a significant inverse correlation with age in breast cancer patients. These findings are consistent with earlier research showing that baseline, post-exercise, and post-ischemia levels of VEGF mRNA and protein are lower in older individuals than in younger controls[36]. Additionally, previous study demonstrated that VEGF released from myocytes is lower in elderly women compared to younger counterparts[15]. Moreover, elevated VEGF levels were correlated with a high visceral fat index in obese women[16]. These findings suggest that women with elevated BMI may exhibit increased levels of VEGF, potentially influencing the risk of cancer progression and metastasis. Furthermore, obesity may be regarded as a risk factor for breast cancer due to its association with elevated levels of VEGF. These findings necessitate further investigation to clarify the precise role of obesity in tumorigenesis.

Studies demonstrated a direct correlation between VEGF and CA 15-3 levels in cancer patients, with both markers increasing simultaneously. This finding supports the potential use of these two markers in combination as a novel diagnostic panel for the early detection of breast cancer[32,37]. ROC analysis in this study indicated that when comparing patients with malignant tumor s to controls, VEGF levels yielded moderate results that may serve a diagnostic function, exhibiting a fair AUC, good sensitivity (83%), and poor specificity (57.3%). The high sensitivity of VEGF may be due to the fact that its levels are much higher in breast cancer patients than in controls. This is because VEGF is thought to be an important factor in the progression and pathogenesis of cancer. The low specificity, on the other hand, may be because VEGF comes from many different sources and is not specific to breast cancer[38,39].

Moreover, the combination of all markers analyzed in the present study enhanced test performance, resulting in an increase in the AUC to approximately 0.8. This is regarded as a proficient diagnostic panel for the early detection of breast cancer, exhibiting a sensitivity of 76.7% and specificity of 70%. This may demonstrate the beneficial impact of determining VEGF levels on other routinely evaluated markers.

It was concluded that the levels of serum VEGF proved to be a more significant biomarkers in the diagnosis of malignant tumors, exhibiting greater specificity

and sensitivity in comparison with the traditional tumor markers that are used for breast cancer such as CA 15-3 and CEA. The combination of VEGF, CEA, and CA 15-3 demonstrated potential as a diagnostic panel, offering a significant non-invasive marker for the early detection of breast cancer in the future.

STATEMENT OF ETHICS

The Declaration of Helsinki's ethical guidelines were followed in this study. Before collecting samples, all participants gave their informed consent verbally and in writing. The scientific committee of the College of Pharmacy, Al-Nahrain University in Baghdad, Iraq, provide the study protocol, participant information, and consent form approval (Document No: 229, Date: 24.02.2026).

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

AUTHOR CONTRIBUTIONS

The authors contributed equally to the article.

FUNDING SOURCES

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

ACKNOWLEDGMENTS

We would like to express their sincere gratitude to the administration and staff of Al-Amal National Oncology Hospital in Baghdad, Iraq, for their invaluable cooperation and support. We also extend our special thanks to the medical records department and the oncology team for facilitating access to the clinical data and cases essential for this research. This work would not have been possible without their assistance and dedication to patient care and academic advancement.

REFERENCES

1. Alrubaye YSJ, Mohammed MB, Abdulamir HA. Exosome and breast cancer. Res J Pharm Technol, 2022;15(3):1393–1397. Doi: 10.52711/0974-360X.2022.00232

2. Hamzah SA, Abd BA, Mohammed MQ. Leptin and ferritin as indicators of breast cancer severity in overweight postmenopausal women. Med J Babylon, 2023;20(2):393–398. Doi: 10.4103/MJBL.MJBL_362_23

3. Mahdi FH, Mashkour MS, Siadat SOR, Ali HA, Hawi AA. Assessment of serum levels of Na, K, Mg, Fe^{+2}, and Se as potential risk markers in women with breast cancer. Hilla Univ Coll J Med Sci, 2025;3(4):61–66. Doi: 10.62445/2958-4515.1081

4. Al-Wasiti E. Male breast tumors and oxidative DNA damage. J Cell Cancer, 2016;8:1–11.

5. Khudair SF, Alshammari HN, Alkhafaji HAA-R. Association of peripheral blood parameters with TNM stage of breast cancer. Hilla Univ Coll J Med Sci, 2024;2(2):15–19. Doi: 10.62445/2958-4515.1019

6. He Z-Y, Li X, Chen Q-S, Sun J-Y, Li F-Y, Wu S-G, et al. Elevated serum carcinoembryonic antigen and CA15-3 levels and the risk of site-specific metastases in metastatic breast cancer. Transl Cancer Res, 2016;5(5):529–537. Doi: 10.21037/tcr.2016.08.39

7. Nakamura M, Abe Y, Tokunaga T. The pathological significance of vascular endothelial growth factor A isoform expression in human malignancies. Pathol Int, 2002;52(5-6):331–339. Doi: 10.1046/j.1440-1827.2002.01367.x

8. Al Balawi IA, Mir R, Abu-Duhier FM. Potential impact of vascular endothelial growth factor gene variation (-2578C>A) on breast cancer susceptibility in Saudi Arabia: a case-control study. Asian Pac J Cancer Prev, 2018;19(4):1135–1143. Doi: 10.22034/APJCP.2018.19.4.1135

9. Schoppmann SF, Horvat R, Birner P. Lymphatic vessels and lymphangiogenesis in female cancer: mechanisms, clinical impact, and possible implications for anti-lymphangiogenic therapies. Oncol Rep, 2002;9(3):455–460.

10. Ferrara, N. VEGF and the quest for tumour angiogenesis factors. Nat Rev Cancer, 2002;2:795–803. Doi: 10.1038/nrc909

11. Abdulhussein HA, Alwasiti EA, Khiro NK. The role of VEGF levels in the differentiation between malignant and benign breast tumor. J Res Pharm, 2024;28(3):603–611. Doi: 10.12991/jrespharm.1686003

12. Mohammad HR, Manna MJ, Alsa'adi MML, AlSaeed MA, M. Abdulamir HA. The use of 5-fluorouracil vs. triamcinolone intralesional injection for treatment of oral lichen planus. Bahrain Med Bull, 2025;47(4):2662–2666.

13. Manna MJ, Baqir LS, Abdulamir HA. Verapamil versus tamoxifen in treatment of experimentally induced infertility. J Res Pharm, 2024;28(5):1485–1491. Doi: 10.29228/jrp.826

14. Moriya J, Minamino T. Angiogenesis, cancer, and vascular ageing. Front Cardiovasc Med, 2017;4:65. Doi: 10.3389/fcvm.2017.00065

15. Olsen LN, Hoier B, Hansen CV, Leinum M, Carter HH, Jorgensen TS, et al. Angiogenic potential is reduced in skeletal muscle of aged women. J Physiol, 2020;598(22):5149–5164. Doi: 10.1113/JP280189

16. Zaki ME, Basha W, Yousef RN, Awad M. Serum vascular endothelial growth factor in Egyptian obese women with insulin resistance. Open Access Maced J Med Sci, 2019;7(8):1330–1334. Doi: 10.3889/oamjms.2019.156

17. Zaleski M, Kobilay M, Schroeder L, Debald M, Semaan A, Hettwer K, et al. Improved sensitivity for detection of breast cancer by combination of miR-34a and tumor markers CA 15-3 or CEA. Oncotarget, 2018;9(32):22523–22536. Doi: 10.18632/oncotarget.25077

18. Singh I, Singh J, Kaur R, Banipal RPS. A comparative study of CA 15.3 levels in pretreated breast cancer patients and controls. Int J Contemp Med Res, 2018;5(3):C1–C4.

19. Anoop TM, Joseph PR, Soman S, Chacko S, Mathew M. Significance of serum carcinoembryonic antigen in metastatic breast cancer patients: a prospective study. World J Clin Oncol, 2022;13(6):529–539 Doi: 10.5306/wjco.v13.i6.529

20. Yang Y, Zhang H, Zhang M, Meng Q, Cai L, Zhang Q. Elevation of serum CEA and CA 15-3 levels during antitumor therapy predicts poor therapeutic response in advanced breast cancer patients. Oncol Lett, 2017;14(6):7549–7556. Doi: 10.3892/ol.2017.7164

21. Wang W, Xu X, Tian B, Wang Y, Du L, Sun T, et al. The diagnostic value of serum tumor markers CEA, CA 19-9, CA 125, CA 15-3, and TPS in metastatic breast cancer. Clin Chim Acta, 2017;470:51–55. Doi: 10.1016/j.cca.2017.04.023

22. Uygur MM, Gümüş M. The utility of serum tumor markers CEA and CA 15-3 for breast cancer prognosis and their association with clinicopathological parameters. Cancer Treat Res Commun, 2021;28:100402. Doi: 10.1016/j.ctarc.2021.100402

23. Fakhari A, Gharepapagh E, Dabiri S, Gilani N. Correlation of cancer antigen 15-3 (CA 15-3) serum level and bony metastases in breast cancer patients. Med J Islam Repub Iran, 2019;33:142. Doi: 10.34171/mjiri.33.142

24. Fejzić H, Mujagić S, Azabagić S, Burina M. Tumor marker CA 15-3 in breast cancer patients. Acta Med Acad, 2015;44(1):39–46. Doi: 10.5644/ama2006-124.125

25. Zi-Yang Y, Kaixun Z, Dongling L, Zhou Y, Chengbin Z, Jimei C, et al. Carcinoembryonic antigen levels are increased with pulmonary output in pulmonary hypertension due to congenital heart disease. J Int Med Res, 2020;48(11):300060520964378. Doi: 10.1177/0300060520964378

26. Hatroosh AH, Ali MAM, Ali JA. Investigation of growth differentiation factor-15, and lipid-based indices in assessing cardiovascular risk in overt and subclinical hypothyroidism. Hilla Univ Coll J Med Sci, 2025;3(3):34–40. Doi: 10.62445/2958-4515.1071

27. Kabel AM. Tumor markers of breast cancer: new prospectives. J Oncol Sci, 2017;3(1):5–11. Doi: 10.1016/j.jons.2017.01.001

28. Ghalehbandi S, Yuzugulen J, Pranjol MdZI, Pourgholami MH. The role of VEGF in cancer-induced angiogenesis and research progress of drugs targeting VEGF. Eur J Pharmacol, 2023;949:175586. Doi: 10.1016/j.ejphar.2023.175586

29. Majidpoor J, Mortezaee K. Angiogenesis as a hallmark of solid tumors – clinical perspectives. Cell Oncol, 2021;44(4):715–737. Doi: 10.1007/s13402-021-00602-3

30. Lugano R, Ramachandran M, Dimberg A. Tumor angiogenesis: causes, consequences, challenges and opportunities. Cell Mol Life Sci, 2020;77(9):1745–1770. Doi: 10.1007/s00018-019-03351-7

31. Sambyal V, Guleria K, Kapahi R, Manjari M, Sudan M, Uppal MS, et al. Association of VEGF haplotypes with breast cancer risk in North-West Indians. BMC Med Genomics, 2021;14(1):209. Doi: 10.1186/s12920-021-01060-4

32. Będkowska GE, Gacuta E, Zbucka-Krętowska M, Ławicki P, Szmitkowski M, Lemancewicz A, et al. Plasma levels and diagnostic utility of VEGF in a three-year follow-up of patients with breast cancer. J Clin Med, 2021;10(22):5452. Doi: 10.3390/jcm10225452

33. Al Kawas H, Saaid I, Jank P, Westhoff CC, Denkert C, Pross T, et al. How VEGF-A and its splice variants affect breast cancer development – clinical implications. Cell Oncol, 2022;45(2):227–239. Doi: 10.1007/s13402-022-00665-w

34. Ayoub NM, Jaradat SK, Al-Shami KM, Alkhalifa AE. Targeting angiogenesis in breast cancer: current evidence and future perspectives of novel anti-angiogenic approaches. Front Pharmacol, 2022;13:838133. Doi: 10.3389/fphar.2022.838133

35. Fujii T, Hirakata T, Kurozumi S, Tokuda S, Nakazawa Y, Obayashi S, et al. VEGF-A Is associated with the degree of TILs and PD-L1 expression in primary breast cancer. In Vivo, 2020;34(5):2641–2646. Doi: 10.21873/invivo.12082

36. Lähteenvuo J, Rosenzweig A. Effects of aging on angiogenesis. Circ Res, 2012;110(9):1252–1264. Doi: 10.1161/CIRCRESAHA.111.246116

37. Ławicki S, Będkowska GE, Szmitkowski M. VEGF, M-CSF and CA 15-3 as a new tumor marker panel in breast malignancies: a multivariate analysis with ROC curve. Growth Factors, 2013;31(3):98–105. Doi: 10.3109/08977194.2013.797900

38. Adams J, Carder PJ, Downey S, Forbes MA, MacLennan K, Allgar V, et al. Vascular endothelial growth factor (VEGF) in breast cancer: comparison of plasma, serum, and tissue VEGF and microvessel density and effects of tamoxifen. Cancer Res, 2000;60(11):2898–2905.

39. Khudhair DA, Abdullateef AH, Khudhair AH. The concept of preeclampsia in biochemistry: molecular mechanisms, oxidative stress, and emerging biomarkers. Hilla Univ Coll J Med Sci, 2025;3(3):26–33. Doi: 10.62445/2958-4515.1070