International Journal of Medical Science and Clinical Research Studies

ISSN(print): 2767-8326, ISSN(online): 2767-8342

Volume 03 Issue 08 August 2023

Page No: 1649-1654

DOI: https://doi.org/10.47191/ijmscrs/v3-i8-39, Impact Factor: 6.597

Utilizing Indicators CD117, CK7, and C7 to Detect Breast Cancer

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ABSTRACT

Background: Breast cancer is a major global health issue, becoming one of the biggest causes deaths for women around the world, and the most costly type of cancer to treat. Breast cancer is typically diagnosed through a biopsy, an operation that causes the patient an extensive amount of pain and suffering. Recently, studies have focused on using biomarkers to predict and diagnose some types of cancer, including breast cancer. The goal of this study aims to use the blood samples of patients to identify breast cancer using the markers CD117, CK7, and C7.

Methods: the case-control study of 62 participants. 31 healthy controls and 31 patients with cancer meeting inclusion criteria, ranging in age from 30 to 74 years. An enzyme-linked immunosorbent assay (ELISA) was used to determine the levels of CD117, CK7and C7 biomarkers.

Results: the results showed Statistically significant difference P value (< 0.05) between Breast group and control group for BMI, CLDN7 serum, CLDN7 tissue, CK7 serum, CK7 Tissue, CD117 serum and CD117 tissue. Also, shown non- significant difference P value (> 0.05) for Age.

Conclusion: As a result of their various concentrations, the C7, CK7, and CD117 biomarkers all have the potential to be utilized to diagnose breast cancer, however only C7 and CK7 have decreasing concentrations in breast cancer compared to a concentration (CD117) that is rising.

KEYWORDS: Breast cancer, C7, CK7, CD117.

ARTICLE DETAILS

Published On:
18 August 2023

Available on:
https://ijmscr.org/

1. INTRODUCTION

The most common neoplasm in women of all ages is breast cancer, however in most European countries, screening for women over 50 is not offered. As a result, cancer diagnosis is based on clinical signs, which can be problematic and delayed [1]. Breast cancer represents the 2nd most common types of malignancy in women and ranks as the fifth-leading cause of death from malignancy worldwide. In our population, breast cancer ranked first among female cancers (32% of newly diagnosed cancer cases, with a mean range of 249 new cancers/year between 2011 and 2015) and second in terms of particular death (16% about the deaths caused by cancer in women), based on a most recent findings provided by the regional tumor registry [2]. In the early stages of breast cancer, when the malignant growth is small and most responsive to treatment, there are often no warning signs. For this reason, screening is essential for early detection. A painless lump is the most frequent physical symptom. Even before the first tumor in the breast is sufficiently big to be was feeling, breast cancer can migrate to the lymph nodes in the underarms and result in a lump or swell[3].

Human development and breast cancer incidence have a strong relationship. The human development index, which combines indicators of wealth, education, and life expectancy, is a more accurate way to compare countries than income alone[4]. Breast cancer rates are higher in nations with the highest levels of development. Incidence rates for females are estimated to be 48 per 100,000 worldwide, ranging from around 30 per 100,000 in sub-Saharan Africa to over 70 per 100,000 in the western parts of Europe and the North American continent[5]. Despite the fact that the comparative incidence of cancer of the breast is largest in the most developed regions of worldwide, over half of all cases are diagnosed in countries with middle or low incomes, placing a heavy strain on the health system. This is due to the greater number of people in regions that are less developed[3]. Other risk factors for breast cancer, such as a family history of the disease, age, and certain genetic mutations, can also contribute to the higher incidence of breast cancer in females compared to males [6]. However, it is important to note that breast cancer can still occur in males and that both males and females should be aware of the signs

and symptoms of breast cancer and undergo regular screenings.

Breast cancer is frequently diagnosed with an uncomfortable procedure known as a histopathological biopsy. This study's major goal was to evaluate the diagnostic accuracy of tumor biomarkers (CD117, CK7, and C7) in comparison to histopathological breast cancer biopsies.

2. MATERIALS AND METHODS

This study included 62 individuals (31 women with cancer) and (31 healthy) as a control sample, at a range of age 30-90 years. Patients' files were reviewed for sufficient data with respect of age, gender mass body, smoking, family history. The data and samples were collected from oncology and hematology center in Basra from 1/8/2022 to 1/3/2023. Oncologists confirmed the diagnoses for each patient in this study, which were then supported by clinical and laboratory diagnoses Department of Medical Laboratory Technology at the Southern Technical University in Basra conducted the experimental analyzes of the study.

3. RESULTS AND DISCUSSION

The results shown that the distribution the status of smoker that the high percent was smoker in Breast group19(61.29%), when compared the study group with each other showed no significant difference P- value= 0.069. Also, this table shown that the high percent in Breast groups were at tumor stage two (70.97%) (Table 1).

Table 1. Distribution and compared smoker status and tumor stage variable s between study groups.

Variables		Breast group		Control group		P- Value
		N	%	N	%	
Smoker status	YES	12	38.71	18	58.06	0.069
	NO	19	61.29	13	41.94	
	Total	31	100	31	100	
Tumor stage	G1	3	9.68			0.009
	G2	22	70.97			
	G3	6	19.35			
	Total	31	100	31	100	
n: number of cases SD: standard deviation significant at p < 0.05						

The results are consistent with those of several published studies, where it was stated in the report of the World Health Organization that tobacco smoking is one of the major challenges to public health in all parts of the world and is the second leading risk factor for early death and disability worldwide in men and women were a daily smoker and 6.4 million deaths were attributable to smoking globally[7]. Radhi et al (2022) reported that the highest percentage of patient's subgroup are those with Stage II (68%)[4]

Also, From Table (2), we note that there are no diagnostic differences P value (0.072) in the samples of breast cancer patients in terms of age compared to the control samples, and this is consistent with Ho et al., 2020; Marrazzo et al., 2020 and Piechocki et al., 2022 [8]–[10]

If there are no diagnostic differences (with a P-value greater than 0.05) in the samples of breast cancer patients compared to the control samples in terms of age, it suggests that the age distribution of the breast cancer patients is not significantly different from that of the control group. In other words, the age of individuals in both groups is similar. There could be several reasons why this might be the case:

1. Age is not a significant factor in determining breast cancer diagnosis: It is possible that age does not play a crucial role in the development or diagnosis of breast cancer. Other factors, such as genetic mutations, hormonal factors, or lifestyle choices, may be more influential in the development of the disease.
2. Sample characteristics: The samples used for the analysis may not accurately represent the general population or may be too small to detect any significant differences. If the samples are not representative of the larger population or the sample size is too small, it can limit the ability to identify significant associations.
3.Random chance: It is also possible that the lack of diagnostic differences in terms of age is simply due to random chance. Even if there is no true association between age and breast cancer, there is still a possibility of observing a statistically insignificant difference purely by random variation. It is important to consider these possibilities and interpret the results within the context of the specific study design, sample size, and characteristics of the population under investigation.

Table 2. Statistical analysis for Age, BMI, CLDN7, CK7 and CD117 in Breast group compared to the control group.

Parameter	Breast group (N=31)		Control group (N=31)		*P value*
	Mean	SD	Mean	SD	
Age (year)	51.6	14.4	50.3	13.1	0.720
BMI (Kg/m^2)	30.1	5.12	26.6	6.05	0.017
CLDN7 serum	23.3	11.2	117	28.1	<0.001
CLDN7 tissue	13.9	9.41	130	27.2	<0.001
CK7 serum	16.7	6.93	4.40	1.19	<0.001
CK7 Tissue	15.1	5.72	4.70	1.19	<0.001
CD117 serum	7.56	2.15	43.7	19.4	<0.001
CD117 tissue	6.67	2.68	47.4	19.9	<0.001
N: number of cases. SD: standard deviation. significant at $p < 0.05$					

From Table (2), the results showed that the BMI increased (Statistically significant difference P value (< 0.05))) increases the risk of developing breast cancer, these results are consistent with Atoum & Alparrey, 2022; Chan et al., 2019. Obesity is a complex process that arise from complex relationships between genes, socioeconomic, cultural influences, lifestyle and environmental factors. It is a condition of having excess body fat and defined as having a body mass index (BMI) dividing the weight of an individual by the square of their height of ≥30, whereas BMIs from 18.5 to 24.9 are normal while BMIs ≥25 to <30 are considered overweight , elevated BMI and weight gain have been associated with increased postmenopausal breast cancer risk among ER-positive and PR-positive breast cancer [11] Studies showed that for every 5-unit increase in BMI above 25 kg/m2, mortality increases by 29%, vascular mortality by 41%, and diabetes-related mortality by 210% [12].

Table (2) showed statistically significant differences (P value (< 0.05)) between the concentration of CLDN7 in samples of breast cancer patients and control samples. The low concentration expressed in breast cancer patients is much lower than the concentration of CLDN7 in control samples and agrees with Hollis et al., 2022; Yun, 2022; Zunaira Fatima et al., 2022 [13]–[15].

Claudin-7, is a protein that plays a role in the formation and maintenance of tight junctions between cells. Tight junctions are critical for maintaining the integrity of tissues, including epithelial tissues such as breast tissue. Research has shown that low expression of CLDN7 is associated with breast cancer progression and metastasis. When CLDN7 expression is reduced, the tight junctions between cells become more permeable, which can allow cancer cells to invade surrounding tissues and spread to other parts of the body [14]. in a recent study, claudin 7 Low expression also significantly affects tight junction strength and metastasis of breast cancer cells. Hence, low claudin7 affect tumor progression also reduce cell adhesion [15]. In addition, low CLDN7 expression has been linked to increased resistance to chemotherapy in breast cancer. This may be because the loss of tight junctions makes it easier for cancer cells to pump out chemotherapy drugs before they can do their job. Therefore, low CLDN7 expression in breast cancer is considered a negative prognostic factor, as it is associated with more aggressive disease and poorer outcomes [16] Figure (1) shows statistically significant differences (P value (<0.05)) between the concentration of CLDN7 in samples of breast cancer patients and control samples.

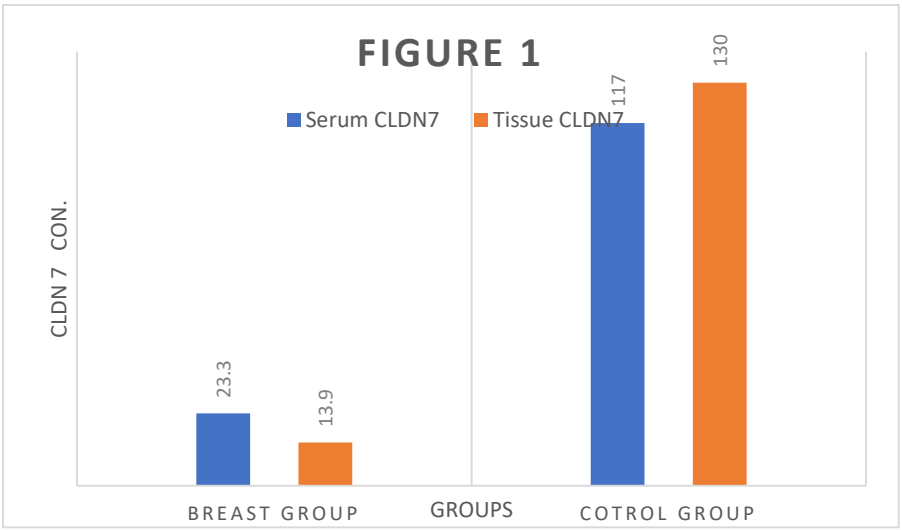

Figure 1. Statistically significant differences between CLDN7 in samples of breast cancer patients and control samples.

Table (2) shown a statistically significant difference, P value (<0.05) between the breast group and the control group for CK7, as the rise in CK7 concentrations in breast cancer patients is much higher than its concentration in control samples, and this is consistent with Nobili et al., 2021; Roy et al., 2020; Yang et al., 2023 [17]–[19].

The exact reason why CK7 expression is increased in breast cancer is not fully understood, but it is thought to be related to the transformation of normal breast cells into cancerous cells. Cytokeratins, including CK7, are intermediate filaments that are part of the cytoskeleton of epithelial cells, which line the surfaces of the body's organs and glands. In normal breast tissue, CK7 is expressed in the glandular cells that line the milk ducts, as well as in some of the lobular units [20]. In breast cancer, it is believed that alterations in the genetic and molecular pathways that control cell growth and differentiation may lead to changes in CK7 expression. For example, some studies have suggested that increased CK7 expression in breast cancer may be related to the activation of certain signaling pathways, such as the Wnt/beta-catenin pathway, which is known to be involved in cell proliferation and differentiation [21]. It is important to note that there is still much that is not fully understood about the mechanisms that lead to increased CK7 expression in breast cancer. Further research is needed to fully understand the role of CK7 and other cytokeratins in breast cancer development and progression. Figure (2) show an increase in CK7 concentrations in breast cancer patients compared to control samples.

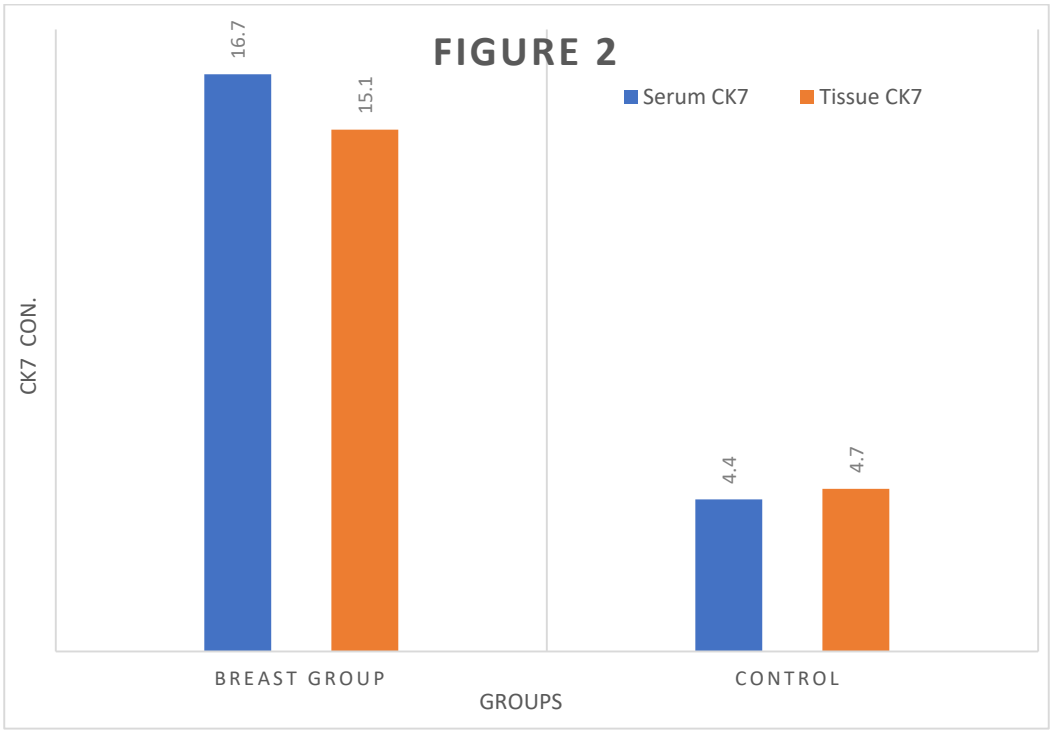

Figure 2. Shows the statistical differences in CK7 for breast cancer patients compared to control samples.

Table (2) showed statistically significant differences (P value (< 0.05)) between the concentration of CD117 in samples of breast cancer patients and control samples. The low concentration expressed in breast cancer patients is lower than the concentration of CD117 in control samples and agrees with Zhang et al., 2021 [22]. CD117, also known as c-kit, is a protein that is found on the surface of some cells, including breast cells. In breast cancer, the concentration of CD117 may be decreased compared to normal breast tissue.

The exact reasons why CD117 concentration is decreased in breast cancer are not fully understood. However, there are several factors that may contribute to this phenomenon. For example, alterations in the genetic and molecular pathways that control cell growth and differentiation may lead to decreased CD117 expression. In addition, some studies have suggested that the loss of CD117 expression in breast cancer may be related to the activation of certain signaling pathways, such as the PI3K/Akt/mTOR pathway, which is known to be involved in cell proliferation and survival.

It is important to note that the clinical significance of decreased CD117 expression in breast cancer is not fully understood. Some studies have suggested that decreased CD117 expression may be associated with a poorer prognosis and resistance to certain types of chemotherapy. However, more research is needed to fully understand the role of CD117 in breast cancer and its potential as a diagnostic or prognostic marker. Figure (3-14) show an increase in CD117 concentrations and the statistical differences in breast cancer patients compared to control samples. Figure (3) shows the statistical differences in CD117 for breast cancer patients compared to control samples.

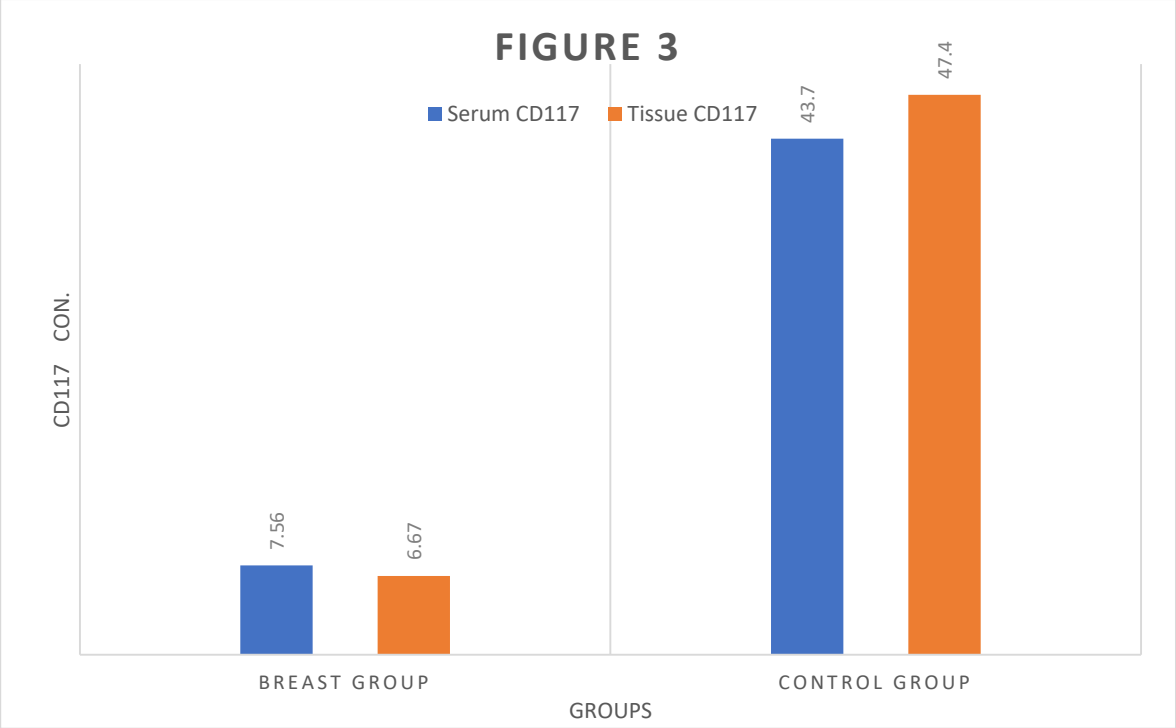

Figure 3. Statistical differences in CD117 for breast cancer patients compared to control samples.

4. CONCLUSION

According to the study's findings, breast cancer patients have elevated levels of the indicator CK7, while their concentrations of CLDN7 and CD117 are lower than they are in control samples. This imbalance in biomarker concentrations also becomes more pronounced as the disease progresses. In people who have breast cancer, we may describe a panel as CK7/Hight, CD117/Low, and CDLDN7/Low.

Conflict of Interest: no conflict of interest.

Acknowledgments: to all participants in this study.

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