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A Comparative study of serum and salivary levels of HER2 and ER in breast cancer

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ABSTRACT

Circulating Human Epidermal Growth Factor Receptor (HER-2/neu) receptor protein concentrations in breast cancer patients seem to be as helpful as predictive indicators of survival as age, tumor size, Progesterone receptor and Estrogen receptor expression. Estrogen receptor is a protein molecule that specifically binds to estrogen in cells, it is one of the effective tumor markers for breast cancer, and Estrogen receptor has an important role in the cellular growth and differentiation of cells and their proliferation. The current study aims to examine and assess changes in serum and salivary Human Epidermal Growth Factor Receptor (HER2), Estrogen Receptor (ER.) and how they affect breast cancer. A total of 130 females within the ages of 17, 75 underwent tests, with 90 of them constituting a clinical group of women with early-stage breast cancer. Of them, 45 had malignant breast cancer and 45 had benign tumors in their breasts and 40 healthy women they represent the control group disease-free, healthy women and paired samples from women with benign breast illness and women with malignant breast cancer were used to compare the serum and salivary levels of the Human epidermal growth factor receptor and the Estrogen Receptor. The results of this investigation showed a favorable association between the levels of Estrogen Receptor (ER) serum with levels of Human epidermal growth factor receptor salivary and serum with (r=0.720, 0.775) these differences statistically were highly significant (p-value=0.000, 0.000) The findings of this study also showed a positive correlation between the levels of Human epidermal growth factor receptor salivary and Human epidermal growth factor receptor serum with (r=0.618) with highly significant differences (p-value=0.000) among malignant and benign groups. Women with benign and malignant tumors have higher levels of estrogen receptor and human epidermal growth factor receptors in their serum and saliva compared with healthy women. The study demonstrated that saliva samples can be used to investigate immunological indicators of breast cancer.

Keywords: breast cancer, ER, HER2, saliva, malignant, benign

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INTRODUCTION

Breast Cancer (BC) is the most prevalent type of cancer in women, results in over 520,000 deaths each year worldwide. and still the second most common cause of cancer death in women, it comes after lung cancer [1]. BC develops when a few breast cells start to grow erratically. These cells continue to create the mass (creating a lump or mass) by dividing more quickly than regular cells do. The breast, lymph nodes, and other regions of the body are all possible sites for cell dissemination (metastasis) [2]. Cells in the milk producing ducts (invasive ductal carcinoma) are where BC most frequently starts. Invasive lobular carcinoma, along with other types of breast cancer, can start in the glandular tissue known as lobules.) or in other cells or tissue within the breast [3]. As a result of variables like earlier discovery, a novel customized strategy to therapy, and a better understanding of the disease, BC survival rates have grown and the number of deaths linked to this di sease is continuously falling. It is one of the diseases that has a potential of being healed when found in its early stages. This is because early disease detection stops the disease from spreading to other bodily parts [4]. Interest has become very great in use of saliva as an auxiliary test that enhances the routine of examinations in the detection of dangerous systemic and cancerous diseases [5]. With the advancement of technology and the development of research, saliva has become an excellent method, due to the ease of obtaining it and a simple Friday method without surgical intervention [6].

The salivary biomarker will be an easily determined diagnostic test with accurate biomarkers and using clinical samples collected non-invasively high volume collection is optimal for early detection of breast tumour, monitori ng and screening of tumour progression and spread. Saliva compared to blood has biochemical properties being they are a filtrated fraction of the blood and thus reflects the physiological conditions of the body, and therefore can be used in monitoring the patient (clinical condition) and monitoring the progress of the disease and its response to treatment and predicting the incidence of systemic diseases [7, 8]. In addition to that, because the collection method is safe and does not cause inconvenience to the patient, such as without the use of needle punctures, biopsies, and surgi cal intervention, it can be collected many times, In breast cancer diagnosis there are many biomarkers used such as HER2 (human epidermal growth factor receptor), CA 15-3 (Cancer Antigen) Progesterone Receptor (PR), Human MUC1 mucin, Ki-67 Antigen, Tumor Protei n P53, Estrogen Receptor (ER) that have a role in the formation, growth, progression, and spread of cancer cells [9, 10].

AIM OF THE STUDY

The current study aims to assess HER2 and ER levels in patient saliva and serum and compare them to controls, as well as to discover any correlations between immunological markers in each of the study groups. and potential application as biomarkers for the early detection of breast cancer.

MATERIALS AND METHODS

Subjects

Samples were gathered and the study was completed between January 12, 2021, and January 30, 2023. Samples were obtained in the Baghdad Governorate from Al-Alwiyya Maternity Teaching Hospital by the Women's Health Department Unit of Early Detection of Breast Cancer after the Ethics Committee authorized the study plan. 130 women between the ages of 17 and 75 who visited the center for routine examinations or because of abnormal symptoms in the breast were included in this study. A signed consent form was provided to the patient, requesting their approval for the study's use of their medical history, test results, and samples. Through the use of a systematic questionnaire that sought in-depth information on the patient's life, medical history, family history, lifestyle, and demographics, the patient group and the healthy control group were chosen in accordance with a number of predetermined criteria. Accordingly, samples were divided into two groups of individuals for each benign and malignant tumor category. The patient group consisted of 90 Iraqi patients. After performing a number of diagnostic tests, including a clinical examination, ultrasound, mammography, and many laboratory tests, samples (blood and saliva samples) were taken from women who had been diagnosed with a tumor in the early stages. to diagnose the tumor Histological analysis (biopsy) was used. Women who met the exclusion criteria were those who were pregnant or recently delivered. Patients with advanced breast cancer, anyone who has a history of cancer, and those with anybody tumors. Women with chronic diseases, those receiving radiation or chemotherapy, immunotherapy, hormonal treatments, and those undergoing surgery to remove bodily parts, glands, or fibrosis in the body, breast, or uterus were all prohibited from participating. as well as those who suffer from allergies, asthma, tooth and gum disease, TB, and digestive disorders. There were 40 participants in the healthy control group, ranging in age from 17 to 60. To make sure there isn't a breast tumor, they were verified by performing a clinical examination, ultrasound, and mammography in the early detection of breast tumors unit.

Specimens

Saliva and venous blood samples were collected. Unstimulated saliva was obtained in morning, within the hours of 8 am to 12 pm at least two hours after the last meal was consumed. Prior to collection, the mouth was thoroughly rinsed five times with distilled deionized water. Next, with the head bowed and the mouth slightly open, saliva was allowed to drip into a test tube from the lower lip. A sample of 5 ml of saliva was taken, put in a test tube that was dry, clean, and anticoagulant-free for 10 minutes, and then centrifuged for 10 minutes (at 2000 rpm–3000 rpm) then two sterile tightly-capped Eppendorf tubes, one for each biomarker were filled with the separated saliva to prevent recurrent cycles of freeze-thaw, each tub was code-labeled and kept frozen at (-30° C) for a considerable amount of time prior to the serological test. Individuals did not brush their teeth or have any oral surgery done within 24 hours of the sample collection in order to avoid saliva being contaminated with blood and debris [11]. in a sterile tube that does not contain any substances a blood sample (4 ml) was deposited and then centrifuged for 10 minutes (at 2000 rpm–3000 rpm) the serum divided one ml in Eppendorf tubes for each biomarker with code for all Individuals and kept frozen at (-30°C) for assay ELISA testing of ER and HER2 concentrations.

Methods

The Estrogen Receptor (ER) (ZellBio GmbH, Germany Cat. No. ZB-11044C-H9648) and Human epidermal growth factor receptor (HER2), (ZellBio GmbH, Germany Cat. No. ZB-10224C-H9648) assay kits use the Enzyme-Linked Immunosorbent Assay (ELISA)-based Biotin double antibody sandwich technique.

After two hours of stop solution application, the absorbance of each well was assessed at 450 nm. On graph paper, the absorbance of the standards was plotted against the standard concentration to produce the standard curve. For unknown samples and controls, the standard curve had been used to measure the levels of ER and HER2 with assay ranges for ER and HER2 of 0.5 ng/mL to 16 ng/L and 2 ng/mL to 64 ng/L, respectively.

Statistical analysis

PSS version 25 was used for statistical analysis and data presentation. To look for differences between research groups, descriptive statistics, an ANOVA table, the chi-square test, the t-test, the mean, were all used.

RESULTS

The results of the research showed thatthere had been a highly significant differences between the number and percentages of BMI (Kg/m^2) among the studied groups with predominant overweight and Obese-Mild BMI (Kg/m^2) among malignant groups (n=45) more than benign groups (n=45) with 16 (35.4%),21 (46.7%),15 (33.3%), 10 (22.2%) respectively, the results of this study documented the number of Obese-Sever cases more among malignant groups more than benign groups with 4(8.9%),0 (0.0%) respectively, These differences statistically were highly significant (F.E.P=21.9, p-value=0.008) as arranged in Table 1.

¢l-õ◊ м◊ Distribur̲gon of studied group according to age range groups (years), bmi (kg/m^2), family history and tumor mass (cm)

Studied group	Malignant tumor (n=45)	A benign tumor (n=45)	Healthy (n=40)	Total	p-value
Age range (Years)	48.27 ± 2.045	36.83 ± 2.583	28.60 ± 1.764	-	F-test=18.36
Mean ± SE					p-value ≤ 0.001
(16-25)	2 (9.5%)	7(33.3%)	12 (57.1%)	21 (100.0%)	Chi-sequare=35.8
(16-25)	3 (7.30%)	16 (39.0%)	22 (53.6%)	41 (100.0%)	
(36-45)	15 (53.5%)	8 (28.6%)	5 (17.9%)	28 (100.0%)	p-value ≤ 0.001
(46-55)	10 (50.0 %)	9 (45.0%)	1 (5.0%)	20 (100.0%)	
(56-65)	12 (85.7%)	2 (14.3%)	0 (0.0%)	14 (100.0%)	
>65	3 (50.0%)	3 (50.0%)	0 (0.0%)	6(100.0%)	
BMI (Kg/m^2)	30.22 ± 6.36	29.08 ± 4.87	26.60 ± 6.45	--	F-test=2.36
Mean ± SE					p-value=0.1
Weak	1 (2.2%)	2 (4.4%)	0 (0.0%)	3 (2.3%)	F.E.P=21.9
Normal weight	6 (13.3%)	5 (11.1%)	22(55.0%)	33 (25.4%)	p-value=0.008
overweight	16 (35.6%)	21 (46.7%)	6 (15.0%)	43(33.1%)	H.D
Obese-Mild	15 (33.3%)	10 (22.2%)	6 (15.0%)	31 (23.8%)	
ObeseModerate	3 (6.7%)	7 (15.6%)	4 (10.0%)	14(10.8%)	
Obese-Sever	4(8.9%)	0 (0.0%)	2 (5.0%)	6(4.6%)	
Total	45 (100.0%)	45(100.0%)	40(100.0%)	130 (100.0%)	
Family history	**23 (51.5%)**	**22 (48.3%)**	**18 (45.0%)**	**45 (50.0%)**	**Chi-sequare=0.21**
Positive					
Negative	**22 (48.5%)**	**23(51.7%)**	**22 (55.0%)**	**45 (50.0%)**	**p-value=0.86 (N.S)**
Total	**45(100.0%)**	**45(100.0%)**	**40 (100.0%)**	**130 (100.0%)**	
tumor masss (cm)	10.85	5.66	--	--	0.3 (N.S)
Mean					
SE	4.26	2.6	--	--	
T-test	1.03				

H.S =High-significant at p-value ≤ 0.001

The study's findings revealed that there were a highly significant differences in the levels of ER Salivary and ER serum between the malignant tumor groups, benign tumor groups and control groups (0.24 ± 0.009, 0.23 ± 0.009, 0.176 ± 0.042) respectively, (0.33 ± 0.01, 0.32 ± 0.01, 0.131 ± 0.01) respectively (p-value= ≤ 0.001, ≤ 0.001) as arranged in Table 2. The study's findings revealed that there were a highly significant differences in the levels of HER Salivary and HER serum between the malignant tumor groups, benign tumor groups and control groups (0.36 ± 0.01, 0.33 ± 0.01, 0.172 ± 0.009) respectively, (0.206 ± 0.006, 0.201 ± 0.010, 0.11 ± 0.007) respectively (p-value= ≤ 0.001, ≤ 0.001) as arranged in Table 2.

Tab. 2. Mean levels of ER and HER2 in salivary and serum of studied groups

Studied group	Malignant tumor (n=45)	A benign tumor (n=45)	Healthy(n=40)	*P*-value
HER2 Salivary	0.36 ± 0.01	0.33 ± 0.01	0.172 ± 0.009	≤0.001
(M ± SE)				(H.S)
HER2 serum	0.206 ± 0.006	0.201 ± 0.010	0.11 ± 0.007	≤0.001
(M ± SE)				(H.S)
ER Salivary	0.24 ± 0.009	0.23 ± 0.009	0.176 ± 0.042	0.05
(M ± SE)				(H.S)
ER serum	0.33 ± 0.01	0.32 ± 0.01	0.131 ± 0.01	≤0.001
(M ± SE)				(H.S)

H.S =High-significantly

The study's findings revealed that there were a positive correlation between the levels of ER –ER-salivary and ER-serum HER2-salivary with (r=0.379, 0.371) these differences statistically were highly significant (p-value=0.002, 0.003), while the levels of ER-salivary were inversely correlated with the levels of HER-2 serum (r=-0.31), These differences were non-significant (p-value=0.809). The results also documented there were weak positive correlations between the levels of ER-serum with levels of HER-2 salivary with (r=.072) these differences had (p-value=0.577). The results of the research showed that there was a positive correlation between the levels of HER-2 salivary of HER- serum with (r=0.356) with highly significant differences (p-value=0.004) among malignant and benign groups as arranged in Table 3.

Tab 3. Correlation Between the Levels of ER and HER-2 in Serum and Saliva Samples Among Malignant and Benign Group

Parameters		Malignant and Benign group			
		ER- salivary	ER-serum	HER 2-salivary	HER 2-serum
ER –salivary	r	1	0.379	0.371	-0.031
	p		0.002	0.003	0.809
	N	62	62	62	62
ER- serum	r	0.379	1	0.072	0.373
	p	0.002		0.577	0.003
	N	62	62	62	62
HER2- salivary	r	0.371	0.072	1	0.356
	p	0.003	0.577		0.004
	N	62	62	62	62
HER2 serum	r	-0.031	0.373	0.356	1
	p	0.809	0.003	0.004	
	N	62	62	62	62

N.S =non-significant at p-value ≥ 0.05, H.S =High-significant at p-value ≤ 0.001

The study's findings revealed that there werea positive correlation between the levels of ER –salivary and ER-serum HER2-salivary with (r= 0.286, 0.322) these differences statistically were highly significant (p-value= 0.038, 0.019) The results also documented there were positive correlations between the levels of ER-serum with levels of HER-2 salivary and serum with (r= 0.720, 0.775) these differences statistically were highly significant (p-value= 0.000, 0.000) Results of the research also showed a positive correlation between the levels of HER-2 salivary of HER- serum with (r=0.618) with highly significant differences (p-value=0.000) among malignant and benign groups as arranged in Table 4.

Tab. 4. Correlation Between the Levels of ER and HER-2 in Serum and Saliva Samples Among Malignant and Control Group

Parameters		Malignant and Control group			
		ER salivary	ER serum	HER2 salivary	HER2 serum
	r	1	0.286	0.322	0.243
ER salivary	p		0.038	0.019	0.08
	N	53	53	53	53
	r	0.286	1	0.72	0.775
ER serum	p	0.038		0	0
	N	53	53	53	53
	r	0.322	0.72	1	0.618
HER2 salivary	p	0.019	0		0
	N	53	53	53	53
	r	0.243	0.775	0.618	1
HER2 serum	p	0.08	0	0	
	N	53	53	53	53

Results of the research showed a non-significant differences in the levels of HER-2 serum and salivary and ER-salivary and serum among malignant (n=45) for patients who had a positive family history of breast cancer or those who hadn't family history (negative family history) with p-value ≥ 0.05, The study's also findings revealed that there were a non-significant differences in the levels of HER-2 serum and salivary and ER-salivary and serum among benign (n=45) for patients who had a positive family history of breast cancer versus significant differences for those patients who hadn't family history (negative family history) with p-value ≤ 0.05 the results of the research showed that significant correlation between family history of breast cancer and levels of ER serum (p-value = 0.001)) as arrange in Table 5.

Tab 5. Comparative Mean Values of HER-2 Serum and Salivary and ER-Salivary and Serum Between Malignant Groups (n=45) and Benign Groups (n=45) According to Family History

	Family history	N	Malignant groups (n=45)				Benign groups (n=45)	
Test			Mean ± SE	P-value	Family history	N	Mean ± SE	P-value
HER-2 salivary	Positive	23	0.35 ± 0.01	0.46 (N.S)	Positive	22	0.23 ± 0.015	0.68 (N.S)
	Negative	22	0.37 ± 0.01		Negative	23	0.24 ± 0.010	
ER-salivary	Positive	23	0.24 ± 0.01	0.61 (N.S)	Positive	22	0.30 ± 0.022	0.15 (N.S)
	Negative	22	0.23 ± 0.008		Negative	23	0.35 ± 0.026	
HER-2 serum	Positive	23	0.32 ± 0.008	0.35 (N.S)	Positive	22	0.30 ± 0.016	0.1(N.S)
	Negative	22	0.34 ± 0.023		Negative	23	0.33 ± 0.016	
ER-serum	Positive	23	0.19 ± 0.010	0.07 (N.S)	Positive	22	0.17 ± 0.013	0.01 (S)
	Negative	22	0.21 ± 0.007		Negative	23	0.22 ± 0.012	

N.S =non-significant at p-value ≥ 0.05

DISCUSSION

Breast cancer is the second most common cancer-related death in women worldwide [12]. The rate of mortality rises whenever the tumor is discovered at a later time Age, breastfeeding, gender, family history, and other demographic factors are the risk factors and factors that influence the occurrence and development of breast cancer [13, 14].

Age is a significant risk factor for breast cancer, it is associated with age. The risk of breast carcinoma increases with age and peaks at menopause age as the body is exposed to more internal and external hormones, such as estrogen, which is produced by the ovaries prior to menopause or through treatments, over time. After menopause the risk of breast cancer gradually decreases or remains constant [15]. Present statistical analysis of the collected information showed that breast cancer had a high prevalence within the age group (36-65) years. The age stages in women are one of the factors that have an impact on the incidence of breast cancer, as the risk of breast cancer increases in the premenopausal age stages less than 50 years compared to younger women (18 years to 35 years) [16].

Obesity is one of the important factors that have a direct impact on human health and the incidence of serious diseases, as there is a close link between the risk of breast cancer and body mass index in women, where the link between breast cancer and obesity depends on the microenvironment generated by adipose tissue and changes that occur in the systemic endocrine glands such as an increase in estrogen and hypersecretion of the hormone insulin in the blood and potassium Which are the main and important factors in promoting the growth of tumors [17]. And after menopause, adipose tissue resulting from obesity acts as a source of estrogen synthesis, as the rate of risk of developing breast cancer after menopause in obese women increases with increasing body mass index [18].

In this study, the results of the data showed that there are significant statistical differences between the body mass index and the studied groups indicating that the number of cases of excess and excessive obesity among women with malignant breast cancer is higher than among women with breast cancer with benign lesions as well as in the case of dangerous obesity, as the cases of dangerous obesity in women with malignant lesions is much higher than benign lesions in women with breast cancer (p-value=0.008)

In previous studies, the research results have shown that the percentage of patients with malignant breast cancer who suffer from excessive obesity is higher than patients with benign breast cancer lesions study by Serdar E. Bulun showed that the risk of developing breast cancer in overweight obese women increases by almost three times compared with women of normal weight [19, 20].

Early diagnosis of breast cancer plays an important and decisive role in improving the chances of survival and obtaining an easy and appropriate treatment method for patients [21]. Saliva has many biological characteristics compared to blood, including the ease of obtaining it in good quantities and frequently, and the method of collecting it is considered non-surgical. the use of saliva in laboratory diagnostics such as breast cancer diagnosis has the potential to be more effective in the early stages [22].

Recently, the use of saliva as a biomarker has spread in the diagnosis and monitoring of various diseases, including some types of cancers, chronic or acute infections, autoimmune diseases and systemic diseases compared to blood or other body fluids, because saliva contains 99% of water, organic and inorganic substances and many types of proteins and enzymes produced by the salivary glands such as histatin, isozyme, mucin and plasma derivatives (albumin and laclobulin an immune) contains foreign biomaterials circulating in the blood and thus reflects the physiological physical conditions of the body It can be used to monitor the patient's bed condition, monitor the progress of the

disease and predict systemic diseases of many diseases, including breast cancer, it can be used to detect RNA, DNA of cancer cells, proteins made by cancer cells and proteins resulting from the tumor microenvironment the CA 15-3 by and HER2 antigen is one of the first biomarkers examined in saliva in breast cancer patients [23]. Biomarkers ER, PR, Her2, and Ki-67 are important biomarkers for diagnosing breast cancer, understanding the nature of the disease and the microenvironment of the disease and predicting it [24].

The human growth receptor family is HER (EGFR or HER1 or c-erbB-1) HER2 is an important receptor in the process of growth and differentiation of epithelial cells, and it directly dictates the behaviour of epithelial cells, and its importance lies in the diagnosis of breast cancer, knowledge of its types and increased overexpression portends the development of tumors [25].

In this study, the data obtained indicate a higher percentage of ER and HER2 in saliva compared to serum. In both groups, malignant and benign breast cancer, which indicates the possibility of adopting the diagnostic reading of the early stages of the disease and this is consistent with numerous studies [26].

Present data obtained indicate, a highly significant correlation between estrogen levels in saliva and serum estrogen and Human Growth Factor Receptor 2 in saliva among a group of patients with malignant and benign breast cancer (p-value=0.002, 0.003), while the correlation was observed with HER-2 in the blood serum (p-value=0.809). The relationship was positive between estrogen receptor levels in saliva and between serum estrogen receptor and Human Growth Factor Receptor 2 in saliva (r=0.379, 0.371) while the inverse correlation was with HER-2 in the blood serum (r=-0.31). A significant correlation between the levels of HER2 in saliva and the levels of HER2 in serum (p-value=0.004) with a positive correlation (r=0.356) between the group of benign and malignant breast cancer patients. Our findings were consistent with those of other researchers who evaluated a variety of markers for the detection of breast cancer in the saliva of a group of healthy women, women with benign breast lesions, and women who had been diagnosed with breast cancer who found recognized tumour markers HER2, in the saliva of all three groups of women. The levels of HER2 in the cancer patients evaluated, however, were significantly higher than the salivary levels of healthy control subjects and benign tumour patients [26]. The results of this study indicate that there is a high statistically significant correlation between serum ER levels and HER2 levels in serum (P-value=0.003) The relationship was positive (r=0.373), and the results of the current study showed in the data that there was a, a significant correlation between the levels of ER salivary and levels of ER in the blood serum and HER2 in saliva between the group of women with malignant breast cancer and healthy women (P-value=0.038 , 0.019) and there was a positive relationship between the two groups (r=0.286, 0.322) a highly significant correlation appeared between serum ER levels and HER2 levels in Salivary and serum (P-value= 0.000, 0.000) The relationship was positive (r=0.720, 0.775), a highly significant correlation with HER2 levels. Salivary and serum HER2 levels (P-value=0.000)and were positively correlated (r=618) this is confirmed by another study conducted to assay the HER2 in the saliva and serum of women with and without carcinoma of the breast and to determine the diagnostic utility of the soluble form of the HER2 protein was assayed in the saliva and serum using ELISA in three different groups of women [27]. To compare the relative diagnostic utility of the HER2, CA 15-3 was also measured. as a “gold standard” by which to compare the HER2 protein’s diagnostic effectiveness. We found HER2 in the saliva and serum of all three groups of women. The salivary and serological levels of HER2 in the cancer patients, however, were significantly higher (p-value<0.001) than the salivary and serum levels of healthy controls and benign tumor patients. Additionally, the HER2 was found to be equal to or surpass the ability of CA 15-3 to detect patients with carcinoma.

The results of this study observed there were a non-significant differences in the levels of HER-2 serum and salivar and ER-salivary and serum among malignant (n=45) for patients who had a positive family history of breast cancer or those who hadn't family history (negative family history) with p-value ≥ 0.05, The results also observed there were a non-significant differences in the levels of HER-2 serum and salivar and ER-salivary and serum among benign (n=45) for patients who had positive family history of breast cancer versus significant differences for those patients who hadn't family history (negative family history) with p-value ≤ 0.05. the results of the research showed that significant correlation between family history of breast cancer and levels of ER serum (p-value= .001)as arrange in Table 5.

CONCLUSION

In view of the previous results, it could be concluded that: It was observed that a higher body mass index (overweight or obese) more predominant among women with malignant breast cancer is higher than in women with breast cancer with benign lesions. High levels of HER-2 and ER in the blood serum and saliva of women who have malignant and benign tumors compared with healthy subjects. The study also proved that it is possible to adopt saliva samples to investigate immunological indicators in the saliva sample. Research using saliva samples shows promise in identifying or forecasting vulnerability to systemic illness. Saliva is a potential reservoir for researchers to find novel biomolecular markers and might be a useful replacement for blood in diagnostic procedures.

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