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Potential association between the incidence of breast cancer in female Iraqi patients and the rs861539 polymorphism, vitamin D, and antioxidant vitamins

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Abstract

Breast cancer is the main cause of mortality for females. Variations in DNA repair capacity and consequent hereditary predisposition to certain malignancies may be attributed to polymorphisms in DNA repair genes. There have been few and inconclusive studies on the relationship between blood levels of vitamins and minerals and food and the genesis of breast cancer. We explored correlations between polymorphisms (rs861539) and vitamin D. In addition, the effects of vitamins D, E, C, and iron on breast cancer were examined. The study population consisted of thirty healthy normal persons and sixty breast cancer patients. For the purpose of estimating vitamins (D, E, C), as well as minerals and iron, venous blood was drawn from all samples utilizing standard procedures. The single nucleotide polymorphism (rs861539) were determined by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) technique. It was discovered that, the mean concentrations of vitamins D, E, and C were lower in female patients compared to healthy controls, but that the serum iron concentration was significantly greater in patients with breast cancer. Also the current study showed a strong correlation between vitamin D, antioxidant vitamins (vitamins A, E, C, and β-carotene), and selenium with breast cancer in the female population of Iraq. Nonetheless, no meaningful correlation was discovered between the polymorphism of rs861539 and the breast cancer risk. Additionally, it implies that increased oxidative stress caused by elevated serum iron levels may increase the risk of breast cancer.

Keywords: Antioxidants, Breast Cancer, Iron, Vitamin D, XRCC3.

Introduction

Globally, breast cancer is the highest prevalent cancer form to harm females. In countries in East Asia where the prevalence of breast cancer was historically low, the rate of the disease is rising quickly[1, 2]. According to an Iraqi registry-based study, the number of individuals with breast cancer between the ages of 20 and 50 grew from 1.46 per 100,000 people in 2000 to 4.36 per 100,000 people in 2019, caused by chemical contamination[2,3]. In another study, the cancer early detection rate in 1,000 women was 11.53, while the general mammography diagnosis rate was 24.96, and the greatest rate was recorded in 2018 (42.2). The overall proportion for positive core biopsies was 31.34 percent. The biggest percentage of biopsy cases occurred in 2017 (43.84%). From 2016 to 2021, the percentage of diagnostic examinations climbed progressively, from 9.5% to 28.6%[4]. Breast cancer risk factors include circulating estrogen levels, obesity, family history, and certain diets. It has been suggested that consuming more meat may be one of the causes iron overload that could promote the growth of cancer[5]. It is estimated by the American Cancer Society that known risk factors contribute for around 25% of instances of breast cancer[6]. High intakes of carotenoids, vitamins A, C, E, and selenium may be protective for individual women, according to epidemiological studies that have yielded

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questionable and conflicting results[7]. These have the potential to operate as a cellular defense against reactive oxygen species, which can damage DNA and start processes like lipid peroxidation. Since they are strong antioxidants, they may also have an impact on the development and spread of breast cancer[8, 9]. The most prevalent transition metal in our bodies and a vital micronutrient is iron. It performs a variety of vital physiological tasks, such as energy production, DNA synthesis, and oxygen transport[10, 11]. Yet, iron's outer shell contains loosely bound electrons that make it a transition metal and promote the creation of reactive oxygen species (ROS), which ultimately results in oxidative stress, the activation of oncogenes and, DNA single breaks[8, 9]. Molecular damage buildup has been connected to a number of clinical disorders, including the development of cancer[10]. Aggressive breast cancers have been reported to contain elevated DNA adducts and DNA strand breaks[11]. Numerous effective DNA repair pathways address various forms of damage, with nonhomologous end-joining pathways being or homologous recombination repair (HRR) the means of correcting double strand breaks (DSB)[12]. Cancer is susceptible to damage to its DNA, but it can be repaired, and this is crucial for the initiation, growth, and spread of the disease. The DNA repair genes is X-ray repair cross-complementing group 3 (XRCC3) of the human retinoid plexus (HRR) that carries out homologous recombination to repair DNA double strand breaks (DSBs) and interstrand cross-links brought on by ionizing radiation exposure and normal metabolic processes[13]. Physically and functionally linked to the XRCC3 gene is the RAD51 gene, that has been demonstrated to be involved in the catalytic dissemination of DSB broken ends throughout the whole sister chromatid. Furthermore, XRCC3 contributes to DSB repair by delaying DNA synthesis and attracting RAD51 to repair sites[14]. The most often investigated XRCC3 gene polymorphism is rs861539 G/A (also known as Thr241Met), which has been the focus of several research assessing its association with cancer risk[15]. Despite conflicting results from a number of XRCC3 association studies, analysis indicates that prevalent XRCC3 polymorphisms are related to the breast cancer risk. Additionally, a different meta-analysis indicates that the Thr241Met polymorphism increases the risk of BC somewhat[16]. The study's objectives were to evaluate the associations between polymorphisms in the XRCC3 gene and vitamin D, as well as the correlations between iron, selenium, vitamin D, C, and E and breast cancer risk.

Materials and Methods

Area of study

Ninety women, ages twenty to sixty, participated in the study. Between July 2022 and September 2023, 60 patients with breast cancer and 30 identically aged controls were selected from breast cancer treatment clinics in Baghdad, Iraq. Patients with breast cancer who had not yet had chemotherapy or radiation therapy were eligible to take part in the research. According to Table 1., there were 10, 20, 19, 7, and 4 patients categorized as stage 0, I, II, III, and IV, respectively. This study did not include participants having a history of diabetes mellitus, liver illness, cardiovascular disease, or respiratory disorders.

Nutritional evaluation

A 100-question semi-quantified frequency of food questionnaire was used to measure dietary consumption. Participants answered questions about the average frequency (all day, all week, all month, all year, or not ever) and intake (small: half the median size, median, and large) of each food item from the interviewer. The accuracy of portion size predictions was increased by using a color photo of food substances that were the median size. CAN-Pro 3.0, APAC Intelligence, Seoul, South Korea, is a computer-aided nutritional analysis tool that was used to code and analyze the food frequency questionnaire. The percentage of iron obtained from MFP (fish, meat, and poultry) that is absorbed as heme iron is 40%; non-heme iron was calculated for the remaining iron[17, 18].

Blood analysis

Ninety female subjects, comprising sixty preoperative cases of breast cancer and thirty healthy controls, had fasting venous blood samples taken; age, weight, height, BMI, and hemoglobin status were noted. The process of obtaining serum and collecting blood samples was previously described[19]. The conventional methods were used to estimate the amounts of vitamins C, E, and selenium[20-22]. High-performance liquid chromatography was used to measure serum β-carotene and vitamin A. After H_2O_2 and nitric acid were dissolved in a microwave (Ethos touch control, Milestone Inc., Italy), the quantities of iron in serum were measured using an ICP-Atomic

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Emission Spectrometer (Vista-PRO, Varian, Australia). Using auto-analyzer a Cobas Integra 400 plus (Roche Diagnostics, Basel, Switzerland) in compliance with the guidelines provided by the manufacturer, the amounts of calcium and zinc were determined in serum samples. Using an automated immunological analyzer Cobas e411 (Roche Diagnostics, Basel, Switzerland), the serum concentration of vitamin D was determined. PTH kit the Immulite 2000 intact (Siemens, Los Angeles, CA, USA) was used to measure serum PTH levels.

DNA Extraction

All individuals had their 5mL of blood specimen drawn into Vacutainer tubes. Following the manufacturer's instructions, Zymo Research Corporation, Valencia, CA, catalogue nos. Quick-gDNA MiniPrep kit was used to extract DNA genomic material. The extracted DNA was kept for later use at ≤–20ºC[13].

XRCC3 Genotyping

SNP in XRCC3 was identified using RFLP-PCR. Using these primers: F: 5′-GCTGTCTCGGGGCATGG CTC-3′ and R: 3′-TTTAGCCAGGATGCGGAAGC-5′. The thermal cycling protocol was as follows: Thirty amplification cycles including 30 sec. of denaturation at 95°C, 30 seconds of annealing at 64°C, 1 minute of extension at 72°C, and a final 10 minutes of extension at 72°C ensued after a 12-minute initial activation at 95°C. After heat cycling, the result of PCR was prolong a three percent agarose gel with a 50 bp ladder. For rs861539, RFLP was carried out utilizing the NlaIII specific restriction endonuclease. The enzyme doses utilized were 1 μL buffer with 5 μL PCR product and 0.5 μL BSA with 0.5 μL NlaIII. The following were the conditions for digestion: three hours at 37°C incubation, after that twenty minutes at 65°C. Following digestion, the digested products underwent a 3% agarose gel electrophoresis process. The size of the PCR products for (rs861539) SNP was 331pb and the size of the allele genotypes and fragments obtained after incubation with restriction enzymes were G:331 and A: (110+210+11pb) as well as GG (231,12pb), AA (110,210,11 pb),and GA (331,110,210, 11pb)[23].

Methodology of statistics

IBM Corp., Armonk, NY's SPSS version 23.0 was worked for the statistical analysis. The standard deviation and mean was worked to express continuous values. For analysis, the student's t-test was employed. Using Pearson's chi-squared test, the variances in genotypic frequencies between the study groups were calculated.

Results

The patient population's baseline characteristics are shown in Table 1. On average, females diagnosed with breast cancer were 4 years older than those who did not get a cancer diagnosis. In addition, the BMI of females with breast cancer was somewhat greater than that of those without the disease. The differences in PTH serum and 25(OH) D concentrations were not statistically significant between the two groups. The levels of hemoglobin, calcium, and selenium in the patients and controls did not differ significantly. Nonetheless, there was a noticeable variation in the zinc levels between the two groups.

Table 1. Distribution of some parameters in study groups.

Items	Breast cancer (No. = 60)	Healthy controls (No. = 30)	P value
Age	59.021±8.56	55.23±5.42	<0.001
BMI(kg/m2)	31.111±4.32	30.215±6.41	0.002
25-(OH) vitamin D (ng/ml)*	19.854±8.10	20.847±7.64	0.071
PTH (pg/ml)**	98.784±42.52	75.765±14.99	0.092
Selenium (µmol/l)	3.32 ± 0.41	3.45 ± 0.74	0.081
Hemoglobin (g/dL)	11.9 ± 0.51	12.1 ± 0.61	0.121
Zinc	0.82 ±0.25	0.93±0.14	0.002
Calcium	7.52 ± 1.21	8.56±1.81	0.19
Stage	**NO. of patients**		
0	10		
I	20		
II	19		
II	7		
IV	4		

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Table 2. displays the consumption of antioxidant vitamins. Vitamin A, β-carotene, C, and E intakes in the patients were considerably lower (p<0.01) than those in the control group.

Table 2. Antioxidant vitamins in the study groups.

Factors	Control Mean ± SD.	Cases Mean ± SD.	p-value
Vitamin A (ug RE)	920.61 ± 270.215	684.21 ± 225.180	0.001
β-carotene	4678.75 ± 2612.32	3215.14 ± 1556.22	0.002
Vitamin C (mg)	163.24 ± 63.77	125.89 ± 48.52	0.000
Vitamin E (mg)	16.01 ± 4.62	12.99 ± 5.76	0.03

Table 3. presents a comparison of serum iron levels and dietary iron intake between patients with BC and those without it. When compared to the control group, the BC group consumed considerably less non-heme iron and total iron (p<0.001). Heme iron intake did not show any differences. On the other hand, BC patients had considerably higher serum iron levels and iron-overloaded subjects than the healthy group (p<0.001).

Table 3. Serum iron levels and dietary iron intake in the study groups.

Parameters	Control / Mean ± SD.	Cancer patients / Mean ± SD.	p-value	X^2 test
Iron intake (mg)	16.01 ± 5.10	14.13 ± 3.55	0.000	—
Heme iron	0.39 ± 0.12	0.61 ± 0.22	0.411	—
Serum iron (mg/L)	1.65 ± 0.52	3.78 ± 0.99	0.000	
Non-heme iron	13.98 ± 3.95	11.91 ± 5.11	0.000	—
Iron overload (%)	40.22	76.21	—	X^2 = 4.2401
Normal (%)	50.12	30.11		(df = 1) 0.040

Table 4. indicates that of the 60 female patients and 30 controls, the GG genotype was shared by 33 female patients and 20 healthy controls, the GA genotype was shared by 12 female patients and 8 controls, and the AA genotype was shared by 5 female patients and 2 controls. Additionally, the risk of breast cancer was significantly higher for females who were homozygous for alleles AA and heterozygous for alleles GA (OR, 1.75; 95% CI, 0.45-1.98 and OR, 1.20; 95% CI, 0.39-1.62).

Table 4. Genotype frequencies of (rs861539) SNP in study groups.

Genotype	Cases No. (%)	Controls No. (%)	OR and (95% CI)	χ 2	P-value
GG	33 (66 %)	20 (66.67%)	Ref.		
AA	5 (10%)	2 (6.66 %)	1.75 (0.45–1.98)	2.01	0.041
GA	12 (24%)	8 (26.67%)	1.20 (0.39–1.62)	1.23	0.016
GA+AA	12 (24%)	9 (30 %)	1.16 (0.37–1.43)	1.52	0.45
GA+GG	38 (76%)	21 (70%)	2.71 (0.48–2.15)	2.14	0.62

In our investigation, SNP does not correlate with 25(OH) D concentration Table 5. The XRCC3 (rs861539) polymorphism was shown to have a significantly lower correlation with vitamin D3-related breast cancer risk in the female study groups (OR 0.91, 95% CI 0.32–1.25), (OR 0.83, 95% CI 0.30–1.20).

Table 5. Relation between (rs861539) SNP and vitamin D-related gene.

Genotype	Cases No. (%)	Controls No. (%)	OR and (95% CI)	P-value
G/G	22 (44%)	13 (43.33%)	Ref.	
G/A	17(34%)	10(33.33%)	0.91 (0.32-1.25)	0.06
A/A	11(22%)	7(23.34%)	0.83 (0.30-1.20)	0.08

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Discussion

In its broadest sense, nutrition is related to breast cancer since the multistage process of carcinogenesis can be significantly modified by dietary deficits in poor nations. Breast cancer has a complex etiology, with several risk factors being proposed. We assessed serum levels of iron, 25(OH) vitamin D3, vitamins E, C, selenium, and markers of blood oxidative stress in Iraqi females with breast cancer and healthy in order to look into the possibility that iron may be linked to increased oxidative stress and a higher chance of breast cancer. A number of analyses have demonstrated a correlation between low serum concentrations of vitamin D and a higher chance of developing breast cancer[24-26]. Serum vitamin D levels over 30 ng/mL are thought to be adequate for normalcy. In this investigation, the level of vitamin D in serum was (19854±8.10). This was less than the median of a different study conducted in Brazil on postmenopausal women (25.8 ng/mL)[27].There is a 12% preventive benefit against breast cancer for levels of vitamin D between 35 and 27 ng/mL; however, serum vitamin D concentrations over 35 ng/mL did not show any extra protective impact[28]. The results of this investigation showed a substantial correlation between vitamin C and breast cancer. When compared to the controls, the patients' serum levels of vitamin C were noticeably lower. Analogous results were noted in a further Iraqi investigation, which discovered that breast cancer patients' vitamin C levels were considerably lower than those of controls[29]. Vitamin C concentration were found to be significantly lower in women with breast cancer compared to controls in another Indian case-control study ($P<0.01$)[30]. It has been demonstrated that vitamin C, an antioxidant, prevents nitrosamines from forming. Additionally, it affects the immune system, which lowers the chance of developing breast cancer[5-7] Additionally, a strong link was discovered in the current study between vitamin E level and breast cancer. In another Indian investigation, vitamin E concentration were found to be lower in breast cancer cases than in another healthy group ($P<0.01$)[8]. The highest quintile levels of vitamin E have been found to have an OR of 0.8 and 4.2 in two further case-control studies that looked at blood levels of the nutrient. Two more investigations' results have also shown that cases' plasma, erythrocytes, and leucocytes had slightly to significantly greater levels of vitamin E than controls' [9]. Via its antioxidant properties and possible effects on selenium, vitamin E may play a part in preventing cancer. It lowers nitrite, which prevents the expression of several oncogenes and the synthesis of carcinogenic nitrosamines and nitrosoamides[10, 11]. Reactive oxygen species can be neutralized by vitamin E, which also improves host immune responses and may lessen oxidative DNA damage and genetic alterations. These responses could provide protection against the development of breast cancer[10]. The current study's findings showed that breast cancer patients had lower selenium levels than the controls, however the difference was not statistically significant. Serum selenium levels in breast cancer cases were shown to be lower than in controls in case-control studies[13-15].According to a Spanish case-control research, women with breast cancer had mean blood selenium concentrations of 61.1 µg/l, while women without tumoral disease had mean values of 98.5 µg/l ($p<0.001$)[16]. A different case-control study carried out in the Netherlands showed that the mean plasma selenium concentrations in the cases were lower (89 µg/l) than in the controls (93 µg/l). Selenium and breast cancer, however, did not significantly correlate[31].

A micronutrient called iron is necessary to keep cells functioning normally. On the other hand, oxidative damage resulting from an excessive amount of localized iron buildup in the breast has been proposed as a chance for the development of breast cancer[27]. Nonetheless, there has been inconsistent research on the link between nutritional iron consumption and breast cancer. There is no correlation between nutritional iron intake and the incidence of breast cancer, according to epidemiological research[32, 33]. Additionally, in meals that made up over 95% of the total iron consumption in both groups, Chang et al. found no association between the total iron intake and the amount of non-heme iron intake. It is believed that the variance in non-heme iron intake between two groups did not significantly impact the concentration of iron in serum because non-heme iron has a low bioavailability[33].

There is evidence linking iron to tumor development in the etiology of breast cancer[14]. It has been demonstrated that the iron storage protein ferritin is elevated in breast tumor tissues[33], suggesting that the development of breast cancer requires more iron availability. Although it's unclear if iron overload contributes to or results from carcinogenesis, when compared to normal tissue the iron was also discovered to be substantially more prevalent in

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breast tumor tissue[33]. The development of breast cancer may be intimately linked to the abnormal iron accumulation in breast tissues, according to the scientists. Mechanistic investigations revealed that iron release from ferritin storage was aided by circulating estrogen. It is believed to play a part in the onset of cancer[32]. These findings have led to conjecture that elevated serum iron levels could be somewhat linked to oxidative stressors observed in breast cancer patients. While oxidative stress increases brought on by iron overload have been illuminated to promote formation of tumor by modulating signaling cell pathways that govern proliferation and apoptosis[23], there currently is no proof that cancer formation can increase iron accumulation in breast tissue or that women who have a tendency to store more iron in their bodies are more likely to develop breast cancer. The mismatch between antioxidant capacity and production of reactive oxygen species (ROS) determines the level of oxidative stress, and iron is one of several elements controlling oxidation-reduction equilibrium. Thus, additional elements play a role in maintaining the oxidation-reduction equilibrium in addition to iron. The power to identify a significant correlation between oxidative stress indicators and serum iron may have been weakened by our small number of participation and restricted number of indicators. In conclusion, elevated oxidative stress may be the underlying cause of the correlation between iron overload in serum and risk of breast cancer. The inconsistency of several markers calls for additional research to clarify the elements that lead to oxidative stress and the development of breast tumors.

The current case-control analysis found no evidence of a significant association between Iraqi women's risk of developing breast cancer and the XRCC3 (rs861539) polymorphism. Our findings concur with those of a number of earlier investigations[34, 35]. They were forced to conjecture that ethnic difference exists between XRCC3 polymorphism and the risk of females with breast cancer because they were unable to demonstrate any correlation between the XRCC3 (rs861539) gene and the risk of breast cancer.

However, other research revealed that the XRCC3 (rs861539) gene's AA genotype markedly raised the risk of breast cancer[36,37]. Chai et al. found a correlation between the aforementioned polymorphism and breast cancer risk in analysis of 23 cases with the connection being strongest among Asian populations and in individuals devoid of a family history of the disease[38]. According to a 2019 study, patients with the XRCC3-rs861539 AA genotype were more likely to advance than those with the GA or GG genotypes. This variation has been linked to a reduced ability to repair DNA and has been linked to an elevated danger of breast cancer[39].

According to analysis of studies conducted in different ethnic populations that found rs861539 polymorphisms in the XRCC3 gene were significantly correlated with an elevated danger of breast cancer are unpredictable with our results. This discrepancy may be caused by environmental components, variations in ethno cultural practices, and/or linkage disequilibrium in the variants of the XRCC3 gene[36, 40].

In this nested case-control analysis, we verified that there was no correlation between 25(OH)D concentrations and SNP (rs861539) in XRCC3 among Iraqi females with initial primary breast cancer. It is generally known that genetic changes in DNA repair genes might change a person's ability or risk of getting cancer[41]. Numerous polymorphism-exhibiting SNPs have been found in XRCC3, and studies conducted in other populations have demonstrated that the genotype frequencies of these SNPs vary greatly amongst populations[39, 41]. Research on various cancer types has also produced a number of contradicting findings. For example, some studies have linked certain SNPs in XRCC3 to a higher risk of cancers of gastric, lung, colorectal, breast, meningioma and glioma, liver, head and neck[41, 42], while other studies have found no link[42. 43]. The XRCC3 polymorphisms may be utilized as a predictive factor of precancerous lesion for neck and head cancer in a Polish people, according to Sliwinski et al[40]. In this regard, a few investigations on various XRCC3 polymorphisms and their interactions with various malignancies provide conflicting results. However, there was no discernible link between this SNP and the risk of breast cancer. Our study's relatively small sample size and thus low power to identify connections are two of its limitations. In this work, we looked at whether there was a discernible difference between the case and control groups' distributions of rs861539 allele frequencies and XRCC3.

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Conclusion

Breast cancer risk may be significantly correlated with XRCC3 (rs861539). The XRCC3 (rs861539) polymorphism was not found to significantly correlate with any clinically meaningful risk factors for breast cancer in the current investigation. This study looked at the connection between oxidative stress and iron as a potential risk indicator for breast cancer development. We are unable to determine from our data if vitamin D, C, E, and selenium deficiencies happened before the malignancy or as a result of it. Nonetheless, a high correlation was found between Iraqi females and breast cancer, as evidenced by the low mean levels of vitamins D, C, E, and selenium in patients with breast cancer relative to controls.

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Authors' Declaration

- Conflicts of Interest: None.
- We hereby confirm that all the Tables in the manuscript are ours. Furthermore, any Figures and images, that are not ours, have been included with the necessary permission for re-publication, which is attached to the manuscript.
- Authors sign on ethical consideration's approval.
- No animal studies are present in the manuscript.
- Ethical Clearance: The project was approved by the local ethical committee at Middle Technical University's local ethical council.

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الارتباط المحتمل بين حدوث سرطان الثدي لدى المريضات العراقيات وتعدد الأشكال 861539rs وفيتامين د والفيتامينات المضادة للأكسدة

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الخلاصة

سرطان الثدي هو السبب الرئيسي للوفيات بين الإناث. قد تعزى الاختلافات في قدرة إصلاح الحمض النووي وما يترتب على ذلك من استعداد وراثي لبعض الأورام الخبيثة إلى تعدد الأشكال في جينات إصلاح الحمض النووي. كانت هناك دراسات قليلة وغير حاسمة حول العلاقة بين مستويات الفيتامينات والمعادن والغذاء في الدم ونشوء سرطان الثدي. لقد استكشفنا الارتباطات بين الأشكال المتعددة (rs861539)في جين XRCC3 وفيتامين د. في أحد المستشفيات، أجرينا أيضًا تحقيقًا لتقييم علاقات الفيتامينات د، ه، ج، والحديد مع سرطان الثدي. تكون مجتمع الدراسة من ثلاثين شخصا طبيعيا سليما وستين مريضة بسرطان الثدي. لغرض تقدير الفيتامينات د، ه، ج وبعض المعادن والحديد تم سحب الدم الوريدي من المرضى والضوابط وباستخدام الإجراءات القياسية. تم تحديد SNP (rs861539) في جين XRCC3 بواسطة RFLP-PCR. وقد اكتشف أن متوسط تركيزات الفيتامينات D و E وC كانت أقل لدى المرضى الإناث مقارنة بالأصحاء، ولكن تركيز الحديد في الدم كان أكبر بكثير في المرضى الذين يعانون من سرطان الثدي. كما أظهرت الدراسة الحالية وجود علاقة قوية بين فيتامين د والفيتامينات المضادة للأكسدة (فيتامينات أ، ه، ج، وبيتا كاروتين) والسيلينيوم وسرطان الثدي لدى الإناث في العراق. ومع ذلك، لم يتم اكتشاف أي علاقة ذات معنى بين تعدد أشكال XRCC3 (rs861539) وخطر الإصابة بسرطان الثدي. بالإضافة إلى ذلك، فإنه يعني أن ارتفاع مستويات الحديد في الدم يمكن أن يزيد من خطر الإصابة بسرطان الثدي عن طريق زيادة الأكسدة.

الكلمات المفتاحية: مضادات الأكسدة، سرطان الثدي، الحديد، فيتامين د، XRCC3.