



RISK FACTORS FOR CERVICAL CANCER IN IRAQI WOMEN

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Summary

Cervical and breast cancers are the most common causes of cancer-related death in women worldwide and are linked to a number of risk factors, including low parity, infertility, early menarche and late menopause. The purpose of this cross-sectional study was to investigate the risk factors for breast and cervical cancers. In addition, the study aimed to determine whether or not women had a positive outlook on cancer screening. Two hundred women that attended the Iraqi National Center for Cancer Research between July and October 2022 participated in the study. Sixty women with breast and cervical cancer were selected and were tested for malondialdehyde (MDA), reduced glutathione (GSH) and vitamin D3 (Vit D3). A questionnaire was used to gather the information from the patients in the National Iraqi Cancer Research Center. The results showed a highly significant ($p=0.0001$) association for MDA, GSH and Vit D3 and also the receiver operating characteristic ROC curve demonstrated that the (MDA) level had exhibited an effective method for discriminating between control group and the patients with breast and cervical cancers. The breast and cervical cancers were associated with common risk factors, disordered MDA, GSH and Vit D3.

KEYWORDS: *breast and cervical cancers, epidemiological factors, MDA, GSH and Vit D3*

INTRODUCTION

Cancer is now considered one of the main causes of mortality all over the world. It is estimated that cancerous illnesses were responsible for the deaths of 8 million people in 2008, and by 2030, this figure is projected to 11 million(1). Breast cancer (BC) is the most prevalent cancer in Iraqi females and cervical cancer is the second most common. It is the same in the rest of the world. These two cancers are virulent with a chronic coars(2). The worldwide epidemic of breast cancer in women continues to have an effect on every country. The risk factors for breast cancer include menarche before the age of 12, menopause at an advanced old age (>55), first delivery after the age of 35 or being nulliparous woman, hormone replacement therapy, prolonged use of oral contraceptives for more than 5

years, obesity, sedentary lifestyle, smoking, and old age(3). Adenocarcinoma and squamous cell carcinoma are the two subtypes of cervical cancer that are abundantly observed in patients. Data estimated 24.6 million new cancer patients diagnosed throughout the globe(4). There were 600,000 new cases of cervical cancer and 340,000 deaths globally in 2020(5).

Cancer of the cervix is more common in women over the age of 50 in developing countries, but it is also getting more prevalent among women between the ages of 15 and 49. In Ethiopia, cancer of the cervix ranks as the second most common cancer(6).

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In the context of oxidative stress, the term *excessive formation of reactive oxygenated/nitrogenated species* (ROS/RNS) refers to the situation in which the activity of antioxidants is unable to neutralize the effects of the excessive production of ROS/RNS(7).

Malondialdehyde (MDA) is a by-product of the complex oxidative breakdown process known as lipid peroxidation (LPO). LPO occurs/produces when polyunsaturated fatty acids are exposed to oxygen. These by-products are created when lipids become unstable as a result of a chain reaction that is set off when unstable free radicals steal electrons from lipids. This renders the lipids themselves unstable. They are capable of causing cancer as well as mutations, and they are the ones that initiate the structural changes and functional alterations in proteins, lipids, and nucleic acids(8).

MDA is produced as a by-product of the lipid peroxidation process. When MDA combines with glutathione and residues of cysteine, histidine, and lysine in proteins found in cells, it results in a detrimental functional alteration. Additionally, this alteration's influence on DNA promotes the development of cancer(9).

Glutathione (GSH) is a non-protein thiol that is present in all mammalian tissues in the millimolar quantities at the highest frequency. It regulates the redox state of cells and is a vital intracellular antioxidant, protecting cells from damage caused by reactive oxygen, and lipid peroxides(10). Enhanced GSH level in tumor cells is linked to tumor growth and increased resistance to chemotherapy(10).

The primary form of circulating vitamin D3 (Vit.D3) is generated, which is 25-hydroxyvitamin D (25-OHD), via the first hydroxyl reaction, which occurs in the liver. Subsequent hydroxylation takes place in cancer cells and kidneys. The primary organs in which vitamin D works are the bones, intestines, and kidneys, which are important in maintaining calcium homeostasis. However, most tissues, including the mammary glands, express vitamin D receptors and interact with vitamin D(11). Thus, we put our aim to evaluate the previously mentioned biochemical markers in cancer patients.

MATERIALS AND METHODS

This is a cross-sectional study on patients who attended the Iraqi National Center for Cancer

Research between July and October 2022. The data were collected from 200 cancerous women, 100 women with breast cancer and 100 with cervical cancer, who applied to the centre between these dates, aged 30 and over, who were accepted to participate in the study. Then, 60 affected women, 30 women with breast cancer and 30 women with cervical cancer, were selected and their blood was drawn for biochemical tests.

Sample collection and preparation: a total of five millilitres of blood were taken from the veins of each individual patient as well as the healthy control subject. Then it was placed in a gel tube and left to coagulate on a bench for twenty minutes. Afterwards, it was centrifuged at three thousand revolutions per minute for ten minutes. The obtained serum was kept in a refrigerator at a temperature of 20° Celsius in order to facilitate a subsequent examination.

Data collection method: researchers gathered the information through an interview with the patients who attended the Iraqi National Center for Cancer Research, after they had given their consent; each interview lasted ten to fifteen minutes. Afterwards, 60 patients were identified and blood samples were taken for MDA, reduced GSH and Vit D3.

Statistical analysis: descriptive statistics using t-test. The obtained results were stated using a formula consisting of the mean plus the standard error (SE). The data analysis for this work was generated using the Statistical Package for the Social Sciences software, version 22. The statistical tests were highly significant at p 0.01, and a confidence interval of 95% was used for graphing the data in Excel 2016.

RESULTS AND DISCUSSION

The demographic criteria are shown in Table 1, the highest rates of breast and cervical cancer were found in patients over the age of 50 (47%) and (42%), respectively. The highest percentage of cervical cancer were in the uneducated, single group (69%) and (43%) respectively. Those patients who had family history of cervical and breast cancer were (83%) and (77%) and being overweight (89%) and (87%) respectively. Regarding smokers, the percentage of women with breast cancer was higher (46%) than the percentage of women with cervical cancer (35%).

Percentages were given for the clinical characteristics of the periodic examination of breast and cervical cancer patients (22%) and (19%), and this is shown in Table 1.

The calculated mean ± SE values for MDA, GSH, and Vit D3 in control and patients with

breast and cervical cancers are summarized in Table 2 and Figure 1, the results revealed highly significant differences when comparing groups with each other (control, breast, and cervical cancers).

The area under the curve (AUC) values with MDA were given in Table 3 and Figure 2, the ROC curve demonstrates that the (MDA) level had exhibited a reasonable method for discrimination between control patients and patients with breast and cervical cancers (AUC=1.000, S.E=0.0001, 95%CL=1.000 to 1.000 and p≤ 0.0001(AUC=1.000, S.E=0.0001, 95%CL=1.000 to 1.000and p≤ 0.0001) respectively.

Breast and cervical cancers can be avoided by screening programs and early detection(12). Breast cancer is a disease which is both the most common cancer in Iraq and the one responsible for the greatest number of deaths from cancers. Mammography is the recommended screening tool in Iraq. Our findings are comparable with a study done in Germany which found that the incidence of BC is 100/100,000 women annually, with the highest incidence reported between the ages of 45 and 75(13).

While cervical cancer affects 9 out of every 100,000 women annually, peak incidence occurring at the age of 53, (between 40 and 59 years of

Table 1. Social traits of participating women (n=200).

Variables	Categories	Cervical cancer.	Breast cancer
		%	%
Age (years)	30-39	8	5
	40-49	28	38
	50-59	42	47
	60-69	22	10
Educational status	Educated	26	31
	Uneducated	74	69
Marital status	Single	43	39
	Married	19	15
	Divorced	23	30
	Widowed	6	16
Family history		83	77
Overweight		87	89
Smoking		35	46
If regular breast examination was performed?		19	22

Table 2. The levels of MDA, GSH, and Vit D3 in the study groups.

Parameters	Mean ±S.E			G1&G2	G1&G3	G2&G3
	G1 N.O=30	G2 N.O=30	G3 N.O=30			
MDA (nmol/ml)	4.17±0.04	12.67±0.11	10.05±0.25	0.0001	0.0001	0.0001
GSH (mg/dl)	±0.06 3.87	6.53±0.08	2.90±0.09	0.0001	0.0001	0.0001
Vit D3(ng/ml)	±0.4739.75	9.76±0.15	4.72±0.52	0.0001	0.0001	0.0001

*G1= Control, G2=Breast cancer, G3=Cervical cancer

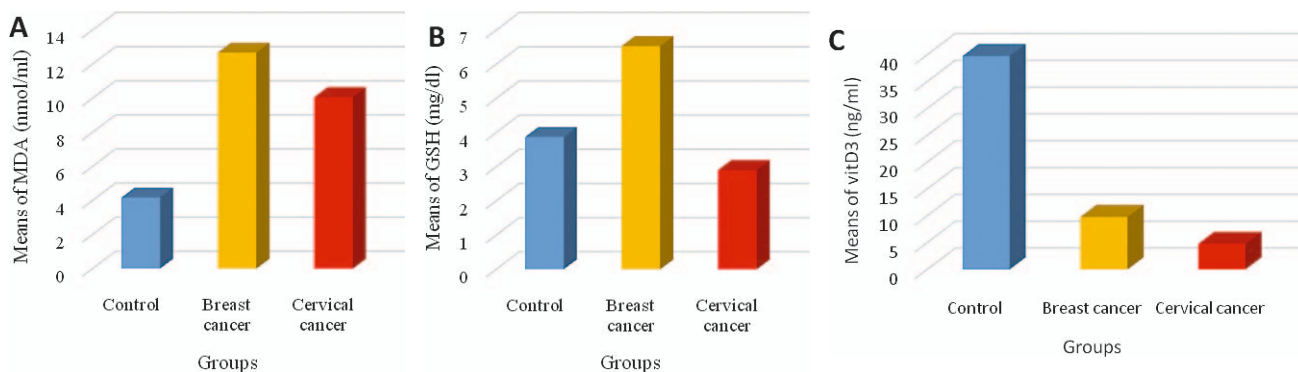


Fig. 1. Means of MDA, GSH, and Vit D3 in comparison with 3 study groups A, B and C

Table 3.

Area under the curve (AUC) ROC curve for analysed biomarker.

Parameter	AUC		S.E		95% Confidence Interval		P-value	
	G2	G3	G2	G3	G2	G3	G2	G3
MDA(nmol/ml)	1.000	1.000	0.0001	0.0001	1.000 to 1.000	1.000 to 1.000	0.0001	0.0001

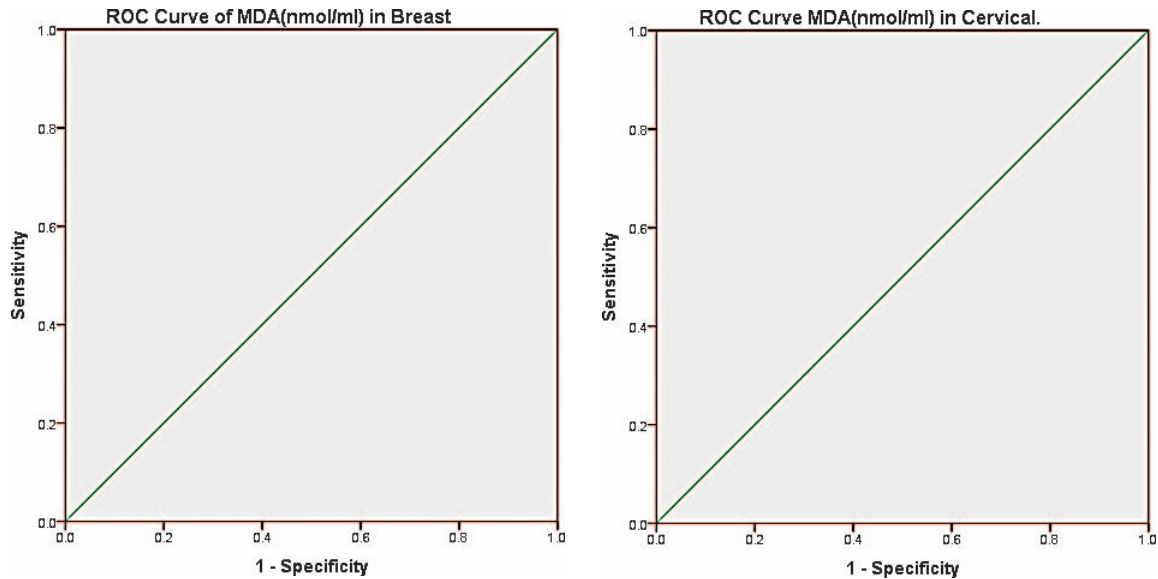


Fig 2: Receiver operating characteristic curves: showing AUC between sensitivity and specificity for studied parameter.

age). At the age of 34, cervical precancerous lesions are found a hundred times more frequently(14) and this is in agreement with our study.

It is difficult to run public health education programs for women in Iraqi society. It might be because of the limited country’s social and educational circumstances which limit their ability to obtain media information so the initiatives of school health education may be quite beneficial. Younger women were more receptive to information on BC and early detection(15).

A research was done by Naz and her colleagues in order to have a comprehensive analysis of the impact of educational interventions on the cervical cancer screening (CCS) on the behaviour of female participants. However, only a small percentage of people who have human papillomavirus (HPV) go on to develop cervical cancer. The study found that a history of unexplained genital tract infection, having a poor income, and having a low educational level all led to an increase in the chance of cervical cancer development(16).

According to the results of our research, unmarried and single women have a much higher

chance of developing breast and cervical cancers compared to married women.

A study in Iran investigated the effect of marital status on the stage of the disease at the time of the diagnosis as well as the likelihood of surviving breast and cervical cancer(17).

There was a positive correlation between being single and the risk of cancer diagnosis.

Our findings indicated that more than 75% of cases had family history of cancer. There were greater rates of BC among women whose sisters or mothers had the disease. However, the occurrence rate was lowest among people whose aunts had BC. In a study conducted in Kurdistan, the researchers discovered that there was a greater incidence of BC in Kurdish patients with a positive family history(18).

Few industry professionals had an opinion that certain cases of familial cervical cancer can be traced back to a rare inherited disease that reduces the resistance of some women to the effects of HPV infection in comparison to other women(19).

We found that obese females have a considerably higher risk of acquiring BC. Similarly a study

shows that obesity and being overweight are risk factors for breast cancer(20).

Obese women had a greater risk of developing cervical cancer as well and a lower risk for development of precancer lesion, in comparison to women whose body mass index was normal.

Smoking increases the risk of breast and cervical cancers(21). It could damage DNA, which would make cells more likely to develop malignant alterations. Alternatively, it can hinder the immune system's capacity to eradicate HPV from the body(22).

Women who smoked continuously for more than 10 years seem to have a 10% higher risk of BC than those who have never smoked.

Plasma MDA levels in BC patients were found to be significantly higher than those in control patients(15), and a subsequent study further confirmed that the progressive rise in mean MDA levels with cervical cancer disease is indicative of excessive lipid oxidation and subsequent oxidative stress that take place with worse disease progression(23), this is in agreement with our study.

A decrease in serum GSH may be a predictor of the treatment response for cervical cancer patients receiving radiation therapy(24). According to the previous study, the GSH content drops dramatically following chemoradiation, particularly in patients who achieve complete response (CR), as opposed to patients who experience no response at all. Our study demonstrated the same results.

In breast tumors, the GSH concentration is two times higher than that found in normal breast tissue. Vitamin D has been suggested to have a preventive effect against the development of BC. Contrarily, vitamin D deficiency, a condition that affects a large portion of the USA population, raises the risk of BC(25). Lower serum vitamin D levels were linked to a greater incidence of postmenopausal breast malignancies over a 5-year follow-up(26). Danish study, however, found no correlation between vitamin D levels and the occurrence of breast (or other) cancers(27), this is in disagreement with our study.

The findings of the study by Askandar et al, showed that cervical cancer patients had lower levels of vitamin D than healthy women did. Cervical cancer risk is 2.7 times higher in people with low vitamin D levels(28).

CONCLUSION

Our study found critical and specific gaps in social awareness for the risk factors and symptoms of breast and cervical cancers. In addition, our biochemical scores for MDA, GSH, and Vit D3, also provide an important baseline measure for evaluating future interventions.

CONFLICT OF INTEREST

No conflicts of interest.

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Sažetak

ČIMBENICI RIZIKA ZA RAK GRLIĆA MATERNICE KOD ŽENA U IRAKU

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Rak grlića maternice i rak dojke najčešći su uzroci smrti žena diljem svijeta uzrokovani malignom bolešću i povezani su s nizom rizičnih čimbenika, uključujući nizak paritet, neplodnost, ranu menarhu i kasnu menopauzu. Svrha ove presječne studije bila je istražiti čimbenike rizika za rak dojke i vrata maternice. Osim toga, studija je imala za cilj utvrditi imaju li žene pozitivan stav o programima ranog probira malignih bolesti. U studiji je sudjelovalo dvjesto žena koje su pohađale Irački nacionalni centar za istraživanje raka između srpnja i listopada 2022. Odabrano je 60 žena s rakom dojke i rakom grlića maternice te su testirane na malondialdehid (MDA), reducirani glutation (GSH) i vitamin D3 (Vit D3). Korišten je upitnik za prikupljanje informacija od pacijenata u Nacionalnom iračkom centru za istraživanje raka. Rezultati su pokazali značajnu povezanost ($p=0,0001$) za MDA, GSH i Vit D3, a ROC krivulja je pokazala da je razina (MDA) pokazala učinkovitu metodu za razlikovanje kontrolne skupine i skupine bolesnica s rakom dojke i rakom vrata maternice. Rak dojke i rak vrata maternice bili su povezani s uobičajenim čimbenicima rizika, poremećajem MDA, GSH i Vit D3.

KLJUČNE RIJEČI: *rak dojke, rak vrata maternice, epidemiološki čimbenici, MDA, GSH i Vit D3*