DOI: https://doi.org/10.53350/pjmhs211592741

ORIGINAL ARTICLE

Association between Vitamin D levels and Breast Cancer at Mosul Nuclear Oncology Hospital: Case - Control study

SARA YOUNIS MAHMOUD AL-RUBIAE[1], SALWA HAZIM ALMUKHTAR[2]
[1]*M.Sc. MCHN. College of Nursing, University of Mosul, City of Mosul, Iraq*
[2]*Professor, PhD.MCHN, College of Nursing, University of Mosul, City of Mosul, Iraq*
**Correspondence to Dr. Salwa HazimAlmukhtar, E mail: dr.salwa@uomosul.edu.iq.*

ABSTRACT

Breast tumor is the most common type of cancer found in women. The issue of whether levels of vitamin D are associated with an increased risk of breast cancer has been brought up. The study's goals are to learn whether low levels of vitamin D are linked to a greater risk of breast cancer. A case-control study was conducted in Mosul Nuclear Oncology Hospital to see how blood vitamin D concentrations, vitamin D supplementation, and sunlight exposure relate to breast cancer among women in Mosul. There were a total of 66 newly diagnosed histologically confirmed primary breast cancer cases among the samples that were newly diagnosed during the time of the study, 66 matched controls, neither of whom had breast cancer nor any other diseases, who were at least 11 years old and who lived in the same geographic area and study site. Personal information, medical history, and exposure history were collected for each participant. The results reveal that women with insufficient vitamin D had a higher risk of breast cancer than those with enough vitamin D. Supplementing with vitamin D decreased the risk of breast cancer among women who had done so in the past. There appears to be a link between decreased 25(OH)D blood levels and an increased risk of breast cancer in this research. Women with lower serum 25(OH)D levels had a greater chance of developing breast cancer as a result of the association between low levels of 25(OH)D and dose-dependent disease. While the opposite association is depending on the amount of vitamin D received, the negative relationship between total supplementary vitamin D consumption and breast tumor risk is not Vitamin D insufficiency is common in Mosul, Iraq, and raising and maintaining serum vitamin D at a population level is a safe and affordable option. Inadequate access to early detection, diagnosis, and treatment as a result of poverty may help prevent breast cancer in women who are deficient in vitamin D. Proving that there is a link between the optimal amount of vitamin D and cancer prevention will need doing the first-of-a-kind research.
Keywords: Association, Breast Cancer, Vitamin D levels.

INTRODUCTION

According to the World Health Organization, breast cancer is the most prevalent disease in the world and can develop in both men and women. However, cancer remains the most widespread, and among women, the most common deadly disease, in the United States and in the United States population [(1)]. As a result, the rate of survival from breast cancer has improved. Thanks to early identification, a more tailored strategy to therapy, and a greater knowledge of the condition, the number of fatalities caused by this illness is reducing. Age, family history of breast cancer, ethnicity, weight, use of hormone replacement treatment, and insufficient Vitamin D consumption are risk factors for breast cancer [(2).] Various kinds of human malignancies, including breast cancer, might be staved off by supplements of Vitamin D and its analogs [(3).] research in the laboratory and epidemiological studies both suggest that vitamin D's potential anti-cancer effects [(4, 5)]. Fat-soluble vitamins include vitamin D. UV exposure is the major source of skin production, while food intake is the secondary source. Vitamin D is also found in fatty fish and vitamin D tablets [(6-8).] The most pressing worldwide health concerns are vitamin D shortage and inadequacy. Obese children and adults who abstain from sun exposure are very vulnerable. [(9)] Of the moms, 76% were deficient in vitamin D and, of the infants, 81% were too [(10, 11)]. A deficiency in vitamin D is associated with poor bone health, and may influence numerous characteristics of cancer. The anticancer effects of vitamin D include suppression of cell proliferation, invasion, and metastasis [(12)] Vitamin D controls cell proliferation and cell differentiation, which can both have an impact on cancer growth and progression. Vitamin D has regulatory effects on cell death, tumor invasion, and angiogenesis, and it is critical to many metabolic processes, including the immunological responses. VDR, which is expressed in the normal mammary gland, plays a crucial role in the development and function of the mammary gland [(13)]. of the over 1 million new instances of breast cancer identified each year, and the vast majority of breast cancer-related fatalities — over 55 percent — occur in low- and middle-income nations [(14).] A case-control study at Mosul Nuclear Oncology Hospital examined the link between vitamin D levels and breast cancer.

METHODOLOGY

In order to meet the study goals, a case-control study design was employed from December 1, 2020 to March 1, 2021. The research was conducted in Mosul City in Nineveh province in northern Iraq, around 400 kilometers north of the city. On the northern border of the city of Baghdad. At this hospital, we give financial support for cancer diagnosis and treatment to more than 75% of our patients from all around Mosul on a welfare basis. Women who have newly diagnosed primary histologically confirmed breast cancer and have been treated at the Mosul Nuclear Oncology Hospital are the target audience for this campaign. The research sample was selected at random from all (n=120) people to be included in the study. In order to participate in the study, the patient had to be at least 11 years of age, and there had to be a total of 66 newly diagnosed histologically confirmed primary breast cancer

cases that met eligibility requirements. This research did not include women who had adjuvant or neoadjuvant chemotherapy or radiation. In the control group, we selected 66 women, who are similar to the sample under investigation in terms of age, geographic location, and study site, but had no previous breast cancer diagnosis or any other cancer matched by age, residency, and study site. In order to discover if there is a relationship between Vitamin D levels and breast cancer, these people were studied. The questionnaire is an important instrument in educational and social research, particularly in the field of science. The researcher gathers knowledge and data pertaining to the study topics by doing research. To assist the researcher in carrying out scientific research, the demographic variables are frequently employed to identify and understand the study populations' tendencies, interests, and needs. To see if vitamin D serum concentrations, vitamin D supplementation, and sunlight exposure were all associated with breast cancer, a matched case-control research was undertaken in Mosul Oncology Nuclear Hospital. The ladies of Mosul Among the 60 newly diagnosed histologically confirmed primary breast cancer cases, 60 individuals matched by age, residency, and study site were recruited and allocated randomly to either the control group or the case group. No one was left out; all willing participants were questioned using a pre-determined questionnaire that took 15 minutes to complete. Detailed sociodemographic history, past medical and obstetrical history, and past sun exposure history were taken into consideration, as well as family history of breast cancer, as well as anthropometric measurements, including height and weight, as well as a blood sample to measure the level of 25(OH)D. This questionnaire was designed to investigate several aspects of the sociodemographic makeup of the respondents, such as gynecological and obstetric history, cancer history, history of any vitamin D supplementation, and history of sun exposure. Clinical notes and pathology reports were reviewed for relevance when applicable. People who are older, who are minorities, who are less educated, who are single, who have fewer dependents, and who are employed are more likely to get selected for job postings. Participants self-reported their family history of breast cancer in one of three ways: whether or not they had a first-degree family history, or if they had a first-degree relative who had the disease, or if they had many relatives who had the disease. The following factors were examined to try to discover information on previous reproductive histories, BMI, and previous breast illness history: determining the serum 25(OH)D concentration Venous blood samples (2.5 ml) were taken from all registered individuals, who then received them in yellow-topped gel tubes. For breast cancer patients, the dataset included of breast cancer patients who had received primary histologically confirmed diagnoses and had not yet started chemotherapy, and pre- and post-treatment form controls. The blood was taken on the same day as the Vitamin D to the Section of Clinical Chemistry, Department of Hormones at the Department of Clinical Chemistry. The serum was centrifuged to separate it, and it was kept until the analysis was completed. Solid-phase enzyme-linked immunoassay (Biomerieux SA Biotechnology firm established and headquarter:376 Chemin del Orme 69280 Marcy-l Etoile-France) was used to assess the serum 25(OH)D concentrations utilized by Minividas Machin. Serum 25(OH)D concentration was classified as 12-19 ng/ml as inadequate, 20-30 ng/ml as insufficient, and 30-50 ng/ml as sufficient. To measure the efficacy of vitamin D supplementation, people were asked if they'd taken vitamin D supplements on a regular basis (at least weekly), infrequently (every few months), or not at all throughout their lives, with delivery method as either a vitamin D injection, tablets, or ampoules. measurement of the level of sunlight exposure Maintaining appropriate 25(OH)D concentrations throughout the year is made possible by the environment of Mosul, where sunshine is abundant all year long. To see how many cases and controls have been exposed to the sun. Estimating long-term exposure to sunlight is crucial to illnesses like breast cancer, which take several years to develop. The questionnaire examined skin tone, different regions of the body's exposure to the sun, and whether or not the person avoids it. Quantitative data were examined using version 25 of SPSS. Information on all associated variables was gathered and descriptive statistics were produced. To investigate the relationship of 25(OH)D, sun Vitamin D, and vitamin D supplements with breast cancer, researchers used methods ratios (ORs) and 95% confidence intervals (CIs) to analyze 25(OH)D, sun Vitamin D, and vitamin D supplements' effects on breast cancer. The following factors were evaluated as categorical variables for confounding: socioeconomic position, education, parity, BMI, whether or not there is a first-degree family history of breast cancer, whether or not women have given birth, and whether or not they are postmenopausal. For all statistical tests, a p-value < 0.05 was acceptable when using SPSS 25 program.

RESULTS

Table 1: shows that 50.8% Menarche Age was between (10-13) years old, 75% Menses Duration was between (3-6) days, and 77.5% of mothers didn’t use Contraceptive. Table 2: shows that 48.3% of Gestational age was between (38-42) weeks, 74.2% of congenital anomalies didn't discovered during pregnancy, 91.7% of pregnant women were examined twice or more with an ultrasound, 61.7% of Gravida was between (1-4) once, 63.3% the Number of Children a life was between (1-3) child, 71.7% the History of Stillbirths did not exist for pregnant women, 72.5 % of pregnant women didn't have History of Abortions, 92.5% of pregnant women didn't birth twins, and 70.8% of pregnant women did not use Medication. Table 3: shows that 70.8 % of pregnant women used Folic acid in 2nd and 3rd month, 56.7% of pregnant women didn’t vaccinated, 68.3% of Maternal nutrition was Variety food, 84.2% of pregnant women didn’t have History of chronic disease, 52.5% of pregnant women didn't have fever during gestation, and 67.5% of pregnant women didn't have UTI during gestation, 83.3% of pregnant women didn't have History of congenital anomalies,77.5% of pregnant women didn't have Family history of CA. Table 4 shows that mean of Mother Age (27.12) and SD. (6.856), that mean of Gravidity (3.85) and SD (2.186), that mean of Parity (3.39) and SD (2.186), that mean of Newborn Weight (2975.42) and SD (857.713).

Table (1): Association between vitamin D levels in women with breast cancer and healthy women (N= 132).

Variable		Deficiency		Normal	
		F	%	F	%
Vit. D	No cancer	12	17.1	54	87.1
	With cancer	58	82.9	8	12.9
$X^2 = 64.358^a$ Df= 1 , sig=0.000					

*Deficient 25(OH)D ≤12 ng\ml; *Normal :25(OH)D ≥30 ng\ml.

DISCUSSION

Table 1 in this study reveals that there are no significant differences between the BC and control group in regard to age (years), marital status, physical activity, and smoking of the participants. On the other hand, BC users exhibited a very different educational profile, with 88.9% of users having illiterate education. Most of the people in the control group fall below a certain educational level. While the BC unawareness and its harmful effects may be primarily to blame for the worse socio-economic position among the study group, it may be related to poorer socioeconomic status for the control group. The results of another investigation by Sofi et al. revealed comparable evidence [15] This study indicates that 73.2% of the individuals were BCs. The control group consisted of individuals who did not work for an employer. Our findings point to a correlation between occupational status and BC. Primarily, the lower socioeconomic position might be the cause. Cases enrolled in the current case-control research learned about the connection between residing in an area with high levels of either BC or a focus on serum ^{25}(OH)D levels. A new study done by (Malvia et al., 2017) showed that rural women have higher chances of having BC compared to urban women, which is in agreement with other research that have indicated urban women to be better protected against BC [16]. More people in metropolitan regions are aware of the need for preventative testing, which is not readily available in rural areas. In this study, Table 4.1 found that vitamin D insufficiency women in the 41-50, 51-60, and 60 years and older age groups were substantially more likely to be in menopause than were vitamin D normal women. unexpected similarity of the 37.5% of the sample population had serum values less than 20 nanograms per milliliter. Women in the age group (53- 60) of 53 and under, but with a greater concentration than those who are 60 and over [17]. Women with low vitamin D levels were found to be substantially more likely to be women of lower socioeconomic class who avoided exposure to the sun during menopause. In this study, 82.9% of breast cancer cases were found to be deficient in vitamin D, compared to 17.1% of control subjects. Only 12.9% of breast cancer cases were found to be sufficient in vitamin D, compared to 87.1% of control subjects. Fascinating results. A significant incidence of vitamin D insufficiency was found in Saudi Arabia with adjacent nations of India and China, in a research done on women that revealed mean serum 25(OH)D concentrations of 13.1ng/mL for breast cancer. A Western American population revealed that 28.9% of breast cancer cases were associated with low levels of vitamin D. Interestingly, 54.5% of Singaporean women also exhibited vitamin D insufficiency, which may imply that women of Asian descent are predisposed to low vitamin D concentrations. Might be the result of some other factor like reduced sun exposure due to regular monthly sunlight throughout the year, as is seen in this study's discovery of a relationship of lower serum 25(OH)D concentrations with breast cancer, despite the low latitude of Mosul and plentiful monthly sunshine. Because to their Islamic faith, Mosul women cover much of their body for cultural and religious reasons, especially avoiding sunlight and air pollution, and due to air pollution and poor dietary vitamin D consumption, many Mosul women suffer from skin cancer. This study reveals that, regardless of vitamin D insufficiency, the two groups had similar levels of problems associated with nursing, having twins, and timing of their first pregnancy, duration of their menstrual cycle, and duration of their menstrual cycle regularity. The BC group, however, demonstrated a substantial difference in parity, as can be seen from the comparison of the parity to the P. According to these researchers, women with VDD have a substantially greater parity, and they are more likely to be in the 35-44 year age range. An connection between lower blood 25(OH)D concentrations and parity was found in this study, as those women with vitamin D deficiency and insufficiency on average had greater parity. The results from table 4.3 reveal that women who develop breast cancer are more likely to have their menopause after the age of 67.8 years, rather than before the age of 32.2 years. While 35.6% of the breast cancer cases are classified as pre-menopause, 64.4% of the control cases are classified as post-menopause. The incidence of vitamin D insufficiency was greater among post-menopausal breast cancer patients than in healthy controls. Additional research carried out by (Peppone, Rickles, Janelsins, Insalaco, & Skinner, 2012) also returned similar results [20]. This new study reveals that 67.8% of breast cancer patients were in the menopausal period, and that means the remaining 33.2% of patients are premenopausal. It is a fact that women between the ages of 40 and 60 are at increased risk of osteoporosis, as the bone density declines and the bone-resorption process weakens. Also, table 2 reveals that a link exists between 25(OH)D concentration and miscarriage, as almost half of the breast cancer women cases 63.4% had undergone abortion while only a third of the control group women had done so. These results were established in prior research that found an increased risk of BC among women who had previously had an abortion (Sofi et al., 2018). Our research found that vitamin D may help throughout pregnancy. Tables 4.4 and 4.5 present the univariate findings of which reveals a strong positive relationship between some type of influencing factor, such as prior breast cancer, and effect. have any difficulty, have illness, You might look for early detection clinics with VDD if you want to practice breast self-examination. There are notable variations in the history of breast cancer, with few exceptions. Results reported in a recent research are in agreement with a previous study, where Atoum et al. [21] found breast cancer patients lacking in 25(OH)D had 22.7-fold higher risk of the illness. In this study, it was shown that the mean 25(OH)D levels for both breast cancer patients were statistically significant (p=0.000). Our research indicated that new instances of breast cancer with VDD were involved. Since the nation's breast cancer screening program does not operate in

Mosul, and the level of knowledge of symptoms is low, few women will benefit from it. In the prevention and treatment of chronic diseases such as osteoporosis, cardiovascular disease, high blood pressure, and diabetes, vitamin D maintains the balance of minerals in the body, mainly the level of calcium and phosphorous. [23].

Ethical Clearance: The ethical approval was obtained for the Research Ethics Committee at Nineveh Health Directorate, Mosul Region, Iraq, before this study. The purpose was briefly explained to participants, and their consent was obtained. They were informed that they had the full right to withdraw at any time.

Source of Funding- Self

Conflict of Interest- Nil

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal AJCacjfc. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. 2018;68(6):394-424.
2. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman DJCacjfc. Global cancer statistics. 2011;61(2):69-90.
3. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet- Tieulent J, Jemal AJCacjfc. Global cancer statistics, 2012. 2015;65(2):87-108.
4. Field S, Newton-Bishop JAJMo. Melanoma and vitamin D. 2011;5(2):197-214.
5. Marcinkowska E, Wallace GR, Brown GJIjoms. The use of 1α, 25-dihydroxyvitamin D3 as an anticancer agent. 2016;17(5):729.
6. Chen TC, Chimeh F, Lu Z, Mathieu J, Person KS, Zhang A, et al. Factors that influence the cutaneous synthesis and dietary sources of vitamin D. 2007;460(2):213-7.
7. Lu Z, Chen T, Zhang A, Persons K, Kohn N, Berkowitz R, et al. An evaluation of the vitamin D3 content in fish: Is the vitamin D content adequate to satisfy the dietary requirement for vitamin D? 2007;103(3-5):642-4.
8. Lamberg-Allardt CJPib, biology m. Vitamin D in foods and as supplements. 2006;92(1):33-8.
9. Cannell J. VITAMIN D AND CARDIOVASCULAR RISK Recently published research by Wang et al addresses this issue in a prospective study of over 1700 men and women with a mean age of 59 years. Vitamin D status was ascertained by the blood.
10. Holick MFJRiE, Disorders M. The vitamin D deficiency pandemic: Approaches for diagnosis, treatment and prevention. 2017;18(2):153-65.
11. Dawodu A, Wagner CJP, health ic. Prevention of vitamin D deficiency in mothers and infants worldwide—a paradigm shift. 2012;32(1):3-13.
12. Vuolo L, Faggiano A, Colao AAJFie. Vitamin D and cancer. 2012;3:58.
13. Lopes N, Paredes J, Costa JL, Ylstra B, Schmitt FJBCR. Vitamin D and the mammary gland: a review on its role in normal development and breast cancer. 2012;14(3):1-7.
14. Welsh JJM, endocrinology c. Function of the vitamin D endocrine system in mammary gland and breast cancer. 2017;453:88-95.
15. Haq A, Svobodová J, Sofi NY, Jindrová A, Kába B, Rajah J, et al. Vitamin D status among the juvenile population: a retrospective study. 2018;175:49-54.
16. Malvia S, Bagadi SA, Dubey US, Saxena SJAPJoCO. Epidemiology of breast cancer in Indian women. 2017;13(4):289-95.
17. Engel P, Fagherazzi G, Boutten A, Dupré T, Mesrine S, Boutron-Ruault M-C, et al. Serum 25 (OH) vitamin D and risk of breast cancer: a nested case-control study from the French E3N cohort. 2010;19(9):2341-50.
18. Alzaheb RAJCMIWsH. The prevalence of hypovitaminosis D and its associated risk factors among women of reproductive age in Saudi Arabia: a systematic review and meta-analysis. 2018;11:1179562X18767884.
19. Shamsi U, Khan S, Azam I, Habib Khan A, Maqbool A, Hanif M, et al. A multicenter case control study of association of vitamin D with breast cancer among women in Karachi, Pakistan. 2020;15(1):e0225402.
20. Peppone LJ, Rickles AS, Janelsins MC, Insalaco MR, Skinner KAJAoso. The association between breast cancer prognostic indicators and serum 25-OH vitamin D levels. 2012;19(8):2590-9.
21. Atoum MF, Al-Khatib YMJCmj. Association between serum 25-hydroxy vitamin D concentration and TaqI vitamin D receptor gene polymorphism among Jordanian females with breast cancer. 2017;130(9):1074.
22. Khaw K-T, Luben R, Wareham NJTAjocn. Serum 25-hydroxyvitamin D, mortality, and incident cardiovascular disease, respiratory disease, cancers, and fractures: a 13-y prospective population study. 2014;100(5):1361-70.
23. Pilz S, Zittermann A, Obeid R, Hahn A, Pludowski P, Trummer C, et al. The role of vitamin D in fertility and during pregnancy and lactation: a review of clinical data. 2018;15(10):2241.