Oncology and Radiotherapy ©
Vol.17 Iss.11: 001-005 • RESEARCH ARTICLE

Associations of vitamin D, calcium, magnesium and phosphorus with pre and postmenopausal Breast Cancer patients in Iraqi woman

Nasr Afit Alobaidy, Hameed Hussein Ali, AbdulKarim-Talaq Mohammad
Department of chemistry, College of Science, University of Anbar, Anbar, Iraq

Abstract:
The objective of this study was to evaluate the association of serum vitamin D, serum Calcium, serum Phosphorus and serum Magnesium levels with Breast Cancer risk in Iraqi women. In current study, participated 100 women's, 60 women's with Breast Cancer and 40 women healthy. The status divided to two group's pre-menopausal and post-menopausal group. Concentration of Calcium, Phosphorus and Magnesium were measured using Semi-Auto Analyzer and level of vitamin D were determined by the enzyme-linked fluorescence assay (ELFA) technique. In pre and post-menopausal patients, the mean serum vitamin D, Calcium and Magnesium levels was significantly lower than in control, while serum Phosphorus level in case was higher than in control. A negative correlation was observed between vitamin D, Calcium, Magnesium and Phosphorus with pre-menopausal patients. In post-menopausal patients was observed a negative correlation between vitamin D and Magnesium, while observed a positive correlation between Calcium and Phosphorus with breast cancer. Based on these findings, it can be concluded that vitamin D, Magnesium and Calcium deficiency and high levels of Phosphorus can be considered as risk factors for women's with breast cancer. Therefore, routine screening of these parameters in womans with Breast Cancer is recommended to reduce the incidence of disease. .

Key words: Vitamin D deficiency; Calcium; Magnesium; Phosphorus; Breast cancer.

Address for correspondence:
Nasr Afit Alobaidy, Department of chemistry, College of Science, University of Anbar, Anbar, Iraq; Email: Nasr91er@gmail.com

Word count:3758 **Tables:** 02 **Figures:** 00 **References:** 42

Received:-22 August, 2023, Manuscript No. OAR-23-110964
Editor assigned:-18 September, 2023, Pre-QC No. OAR-23-110964(PQ)
Reviewed:-03 October, 2023, QC No. OAR-23-110964 (Q)
Revised:-10 November, 2023, Manuscript No. OAR-23-110964 (R)
Published:-15 November, 2023, Invoice No. J-110964

INTRODUCTION

Breast Cancer is the most frequently occurring tumor among the female population; diagnoses are rising steadily each year and it has become the second leading cause of death in women [1]. In Worldwide; BC accounts for about 1 in 4 cancer cases among women's. It is the more frequently diagnosed cancer in the vast majority of the countries [2]. In both developing and developed countries, with about 2.3 million new cases in 2020, comprising 25% of all cancers diagnosed in women [3-5]. In Iraq BC appear more than 24% of each all cancer cases making it a great problem to the health system in our country [6]. Breast Cancer is extremely rare before the age of 30, after which it becomes more common as get older, peaking around the age of fifty [7].

Vitamin D is a group of fat-soluble secosteroids responsible for increasing the body's absorption of calcium, magnesium and phosphate and many other environmental influences. Vitamin D exerts its job through the VDR, a nuclear receptor that regulate transcription of target genes and is to be found in lobule and ductal epithelial cells in normal mammary glands [8]. The main function of Vitamin D is to maintain calcium and phosphate homeostasis in the body [3]. Vitamin D has potent antiproliferative, prodifferentiative, and immunomodulatory effects as well as a role in DNA repair, these effects could be the cause that decrease vitamin D levels might lead to development breast cancer, and vitamin D deficiency is associated with an increased incidence of advanced cancer stage, recurrence and lymph node metastasis in these type of cancer [9,10]. The anti-carcinogenic potential of vitamin D comes from the active, hormonal form of vitamin D, 1, 2, 5$(OH)_2$D [11,12]. Some studies have found that Breast Cancer is associated with low levels of vitamin D [13]. Believed that vitamin D3 deficiency is much spread and there is growing evidence of an association between vitamin D deficiency and the risk of breast cancer. Also the levels of vitamin D between the pre-menopausal and post-menopausal woman Breast Cancer patients were significantly different compere with healthy woman's [14]. Breast cells can produce vitamin D by participating in the formation of 1, 2, 5 OH vitamin D and may cause apoptosis in the breast cells through Vitamin D Receptors (VDR). It is also that vitamin is effective in prevention and treatment cancer with its immunomodulatory effect and prevents cell differentiation, growth, and angiogenesis by affecting the gene expression related to Breast Cancer (BC) [15].

Trace elements play important roles in biological processes relevant to breast cancer, especially those elements that are essential components of antioxidants [16]. Magnesium is one of the most important element micronutrients for the human body, is involved in many

physiological pathways and is essential for the maintenance of normal cell and organ function [17]. Magnesium also plays a role in the progression of breast cancer, and the inherent physiological changes of the disease induce disturbances in the homeostasis of this element, which favors tumorigenesis [18-20].

Calcium is a mineral involved in a large number of vital functions [21, 22]. Many studies has reported an inverse association between dietary calcium intake and risk of breast cancer. This relation was stronger among pre-menopausal than post-menopausal women [23]. Other studies reported the protective effects of calcium against post-menopausal Breast Cancer [24-26].

MATERIALS

Collection of blood sample

This is a case control study which was proceeding in 2022. After informing all infected and healthy participants to allow samples to be taken for laboratory and clinical examinations. This study was approved by the ethics and research committees of Iraqi Ministry of Health, Anbar Health Directorate. There are hundred female participants in this study. Samples were collected from Anbar cancer center in Anbar, Iraq. Hundred studied women were divided in tow groups including; 1-Pre- menopausal Breast Cancer (BC) group (n=25) and healthy women group (n=23), 2-Post menopausal Breast Cancer (BC) group (n=35) and healthy women group (n=17). Measurement of serum Vit.D3 was done by mini VIDAS instrument (Enzyme Linked Fluorescent Assay (ELFA) method using suitable kits. The data was analyzed using Statistical Package (SPSS) for windows version 16.0 (2018).

Blood Sampling

The venous blood sample was collected and placed in a gel tube for the serum separation (centrifugation at 3000 r.p.m for 10 min.). Serum samples were stored in the freezer at -20°C until use

Evaluation of Serum Biochemical Parameters

Phosphorus, Magnesium and Calcium were measured using Semi-Auto Analyzer kit (AGAPPE, Switzerland). Human Vitamin D were measured using mini VIDAS instrument kit (France)

RESULTS

The results of the measured different biochemical parameters in the research were listed below for Breast Cancer patients and control.

The (Table 1) showed comparison of biochemical parameters in women's with Breast Cancer in pre-menopausal and the control. The results showed significant difference ($p<0.05$) in Serum Magnesium and Serum Calcium and significant difference ($p<0.01$) in Serum Phosphorus and Serum Vitamin D camper with control. No significant difference ($p>0.05$) found in BMI (Body Mass Index) and Age in pre-menopausal Breast Cancer patients and control.

Tab. 1 Clinical characteristics of Iraqi women's in pre-menopausal (cases + control)

Variables	Case (n=25) (Mean ± SD)	Control (n=23) (Mean ± SD)	P-Value
Age	38.42 ± 5.21	36.80 ± 6.42	0.11
BMI	27.94 ± 4.33	28.45 ± 5.06	0.71
S.Magnesium	1.99 ± 0.01	2.24 ± 0.15	0.02
S.Calcium	8.74 ± 0.64	9.36 ± 0.53	0.03
S.Phosphorus	6.01 ± 1.08	3.18 ± 0.31	0.001
S.Vit.D3	13.08 ± 3.78	33.72 ± 6.84	0.002

(Table 2) showed comparison of biochemical parameters in women's with Breast Cancer in post-menopausal and the control. The results showed significant difference ($p<0.01$) in Serum Magnesium, Serum Phosphorus and Serum Vitamin D and significant difference ($p<0.05$) in Serum Phosphorus comparison with control. No significant difference ($p>0.05$) found in BMI (Body Mass Index) and Age in post-menopausal Breast Cancer patients and control.

Tab 2. Clinical characteristics of Iraqi women's in post-menopausal (cases + control)

Variables	Case (n=35) (Mean ± SD)	Control (n=17) (Mean ± SD)	P-Value
Age	57.50 ± 8.18	56.12 ± 7.33	0.24
BMI	27.84 ± 5.04	27.83 ± 5.23	1.0
S.Magnesium	1.37 ± 0.44	2.22 ± 0.13	0.00
S.Calcium	8.06 ± 0.70	9.29 ± 0.60	0.03
S.Phosphorus	6.23 ± 1.10	3.60 ± 0.45	0.00
S.Vit.D3	13.05 ± 2.94	30.22 ± 14.06	0.00

A significant difference ($p<0.01$) was found between patients pre-menopausal and post-menopausal with regard to serum Magnesium level and significant difference ($p<0.05$) with regard to serum Calcium level. No significant difference ($p>0.05$) found in serum Phosphorus level, serum Vitamin D level and BMI (Body Mass Index) in pre-menopausal and post-menopausal Breast Cancer patients, as in (Table 3).

Tab 3. Comparison of Biochemical parameters (Mean ± SD) between pre-menopausal and post-menopausal woman with breast cancer

Variables	pre-menopausal (n=25) (Mean ± SD)	post-menopausal (n=35) (Mean ± SD)	P-Value
Age	38.42 ± 5.21	57.50 ± 8.18	0.01
BMI	27.94 ± 4.33	27.84 ± 5.04	0.93
S.Magnesium	1.99 ± 0.01	1.37 ± 0.44	0.00
S.Calcium	8.74 ± 0.64	8.06 ± 0.70	0.02
S.Phosphorus	6.01 ± 1.08	6.23 ± 1.10	0.44
S.Vit.D3	13.08 ± 3.78	13.05 ± 2.94	0.72

(Table 4) showed the correlation coefficient (r) between Body Mass Index (BMI) and other parameters used in this study. In Pre-menopausal patients our results showed that a middle negative correlation at ($p<0.05$) between (Magnesium and Vitamin D) and BMI, while a weak negative correlation at ($p>0.05$) for Phosphorus with BMI and ($p<0.05$) for Calcium with BMI. In Post-menopausal patients found that a weak negative correlation at ($p<0.05$) between (Magnesium and Vitamin D) and BMI, while found a weak positive correlation at ($p<0.05$) for Calcium and ($p<0.01$) for Phosphorus with BMI.

Tab 4. Correlations between BMI and Biochemical Parameters

Parameters	Correlation (r) of BMI				
	Groups				
		Pre-menopausal		Post-menopausal	
		Patient (n.25)	Control (n.23)	Patient (n.35)	Control (n.17)
S.Magnesium	r	-0.6	0.014	-0.14	-0.28
	p	0.01		0.033	
S.Calcium	r	-0.057	-0.4	0.28	0.76
	p	0.01		0.027	
S.Phosphorus	r	-0.12	-0.1	0.18	-0.73
	p	0.79		0.00	
S.Vitamin D	r	-0.67	-0.63	-0.38	-0.51
	p	0.04		0.012	

DISCUSSION

This study showed that level of Magnesium, Calcium, Phosphorus and Vitamin D associated with Breast Cancer risk. This study focused on the association between dietary Magnesium, Calcium, Phosphorus and Vitamin D intake and Breast Cancer risk because diet is an easy target for intervention. The results in this study showed a low level of (Magnesium, Calcium and Vitamin D) and high level of Phosphorous in pre and postmenopausal women's with Breast Cancer risk compared to healthy women's.

Our results showed statistically significant low of Magnesium level in Breast Cancer patients in pre and postmenopausal, but the levels are more decreased in post-menopausal patients. Our finding agrees with Huang W.Q whom found a decrease in Magnesium level at patients with Breast Cancer (BC) compared to the control group [27]. Deheinzelin pointed out to the low serum magnesium level in Breast Cancer patients and these findings agree with our results [28]. There are many studies have linked Magnesium deficiency to the development and prognosis of Breast Cancer [29-31]. Our findings showed that a weak negative correlation between Magnesium and Breast Cancer according BMI these results agree with results Huang W.Q pointed out to the revealed a negative relationship between dietary magnesium intake and Breast Cancer risk among premenopausal women [27]. In similar studies, Feng found a negative correlation between reduced serum magnesium concentrations and Breast Cancer patients [32].

Our findings showed that serum Calcium level low in pre and post-menopausal Breast Cancer patients compare with control group, but the levels are more decreased in post-menopausal patients. The results showed a negative correlation with Breast Cancer in pre-menopausal, while a positive correlation with Breast Cancer in post-menopausal according Body Mass Index (BMI). Our results agree with Khan M.T. and Viala M. whom pointed out the low serum calcium level in pre and post-menopausal Breast Cancer patients [33,34]. Ebrahimpour K. S. pointed out an inverse association between dietary calcium intake and risk of breast cancer. This relation was stronger among premenopausal than post-menopausal women [35].

The concentration of serum Phosphorus levels shows significant difference in between patients and control. The serum Phosphorus levels are significantly increased in pre and post-menopausal patients. Our findings showed a negative correlation with Breast Cancer in pre-menopausal and a positive correlation with Breast Cancer in post-menopausal according body mass index (BMI). Our findings agree with Singh M. M. and Dimou, N. L. pointed out revealed that the estimated and mean values of serum phosphorous increased significantly in pre and postmenopausal patients compare with control [36,37].

Deficiency of Vitamin D has become a major health concern after the discovery of great extent of peoples suffering from its various health consequences. Reports showed that the most humans are not getting sufficient amount of Vitamin D due to the current lifestyle and environmental factors that limit sunlight exposure [14].

The current study showed that most Breast Cancer participants were vitamin D deficiency with a significant difference in the mean serum level of Vitamin D between Breast Cancer (BC) cases and healthy cases. The results indicated Vitamin D concentration in the both pre and

postmenopausal Breast Cancer (BC) groups showed significantly lower than the healthy group.

Our finding are consistent with several studies that have demonstrated similar results. Vrieling A. reported that serum level of Vitamin D in the postmenopausal Breast Cancer (BC) group was significantly lower than in the control group [38]. The same was also reported by Al-Al-Saigh, T. H. who found that Vitamin D level in the Breast Cancer (BC) patients was significantly lower than in the control group in Iraqi females [39]. Most studies indicate that obesity and higher Body Mass Index (BMI) may increase the risk of Breast Cancer in females and this corresponding with our findings [40]. Experimental studies showed that Vitamin D inhibits the development of Breast Cancer and metastasis by inducing apoptosis, reducing cell growth and angiogenesis [41, 42].

CONCLUSION

The present study has shown significant differences in the biochemical parameters in the Breast Cancer patients in pre and post-menopausal compared with control group. This study showed that vitamin D, Magnesium and Calcium deficiency and high Phosphorus in women's is associated with a greater risk of Breast Cancer in pre and post-menopausal. Serum vitamin D, Magnesium, Calcium and Phosphors status in women should be routinely assessed. In addition, casual sun exposure and take dietary supplementation are recommended to correct vitamin D, Magnesium, Calcium and Phosphorus level in women's.

REFERENCES

1. Miriam DL, Maria AC, María JC, Marta HC, and Luis CY. Vitamin D: And its role in breast cancer. Kaohsiung J Med Sci, 34(2020): 423-427. |
2. Ataollahi MR, Sharifi J, Paknahad MR, Paknahad A. Breast Cancer and associated factors: a review. J Med Life, 8(2015): 6-11. |
3. Vanhevel J, Verlinden L, Doms S, Wildiers H, Verstuyf A. The role of vitamin D in Breast Cancer risk and progression. Endocr Relat Cancer, 29(2) (2022): R33-R55. |
4. Almeida-Filho BS, Omodei MS, Buttros DA, Carvalho-Pessoa E, et al. Negative Impact of Vitamin D Deficiency at Diagnosis on Breast Cancer Survival: A Prospective Cohort Study. Breast J. |
5. Allami ZZ and Dragh MA. Identification of Some Breast Cancer Related Genes by RAPD Technique in Maysan Province, Iraq. J Revis Bionatura, 7(2018): 20. |
6. Ali ZH, Ridha AA, Mosa AU, Sahib AS, and Mohsin KK. Effect of Tamoxifen Therapy on Lipid Profile in Iraqi Postmenopausal Breast Cancer Woman. HIV Nurs, 22(2020): 1373-13. |
7. Albaghdadi AM. Evaluation of lipid profile in postmenopausal Breast Cancer patients and its association with serum level of thyroid hormones, vitamin D, and estrogen. World J Adv Res Rev, 14(2021): 443-45. |
8. Huss L, Butt ST, Borgquist S, Elebro K, Sandsveden M,. Vitamin D receptor expression in invasive breast tumors and Breast Cancer survival. Breast Cancer Res, 21(2019): 1-13. |
9. Hemida MA, AbdElmoneim NA, Hewala T I, Rashad, MM, Abdallah S. Vitamin D receptor in Breast Cancer tissues and its relation to Estrogen Receptor Alpha (ER-α) gene expression and serum 25-hydroxyvitamin D levels in Egyptian Breast Cancer patients: a case-control study. Clin Breast Cancer, 19(2019): e407-e41. |
10. Demircioglu ZG, Aygun N, Demircioglu MK, Ozguven BY, Uludag M. Low Vitamin D Status is Not Associated with the Aggressive Pathological Features of Papillary Thyroid Cancer. Med Bull Sisli Etfal Hosp, 56(2022): 132. |
11. Segersten U, et al. 25-Hydroxyvitamin D3 1alpha-hydroxylase expression in Breast Cancer and use of non-1alpha-hydroxylated vitamin D analogue. Breast Cancer Res, 7(2005): R980-986. |
12. Friedrich M, Rafi L, Mitschele T, Tilgen W, Schmidt W. Analysis of the vitamin D system in cervical carcinomas, breast cancer, and ovarian cancer. Recent Results Cancer Res, 146(1998): 239–246. |
13. Shaukat N, Jaleel F, Moosa FA, Qureshi NA. Association between vitamin D deficiency and breast cancer. Pak J Med Sci, 33(2017): 645-694. |
14. Khedr MI, Sharaf SAF, Aal ANA, Dessouky IS, Soliman M. Serum 25-Hydroxyvitamin D Level and Breast Cancer Risk in Egyptian Females. Asian J Oncol, 8(2022): 76-80. |
15. Ozmen V, Ordu C, İlgun AS, Unal Ç, Soybir G et al. The effects of vitamin D replacement on pathological complete response (pCR) in Breast Cancer patients receiving neoadjuvant systemic chemotherapy (NAC). Breast J, 27(2021): 902–905. |
16. Choi R, Kim MJ, Sohn I, Kim S, Kim I. Serum trace elements and their associations with Breast Cancer subgroups in Korean Breast Cancer patients. Nutrients, 11(2019): 37. |
17. Porri D, Biesalski HK, Limitone A, Bertuzzo L, Cena H. Effect of magnesium supplementation on women's health and well-being. NFS J, 23(2021): 30-36. |
18. De Baaij JH, Hoenderop JG, Bindels RJ. Regulation of magnesium balance: lessons learned from human genetic disease. Clin Kidney J, 5(2012): i15-i24. |
19. Blaszczyk U, Duda-Chodak A. Magnesium: its role in nutrition and carcinogenesis. Rocz Panstw Zakl Hig, 64(2013): 165-171. |
20. Gobato RC, Chaves DFS, Chaim EA. Micronutrient and physiologic parameters before and 6 months after RYGB. Surg Obes Relat Dis, 10(2014): 944-951. |
21. WHO. Vitamin and mineral requirements in human nutrition. World Health Organization (Publication year not available). |
22. Ross AC, Manson JE, Abrams SA, Aloia JF, Brannon PM et al. The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know. J Clin Endocrinol Metab, 96(2011): 53-58. |
23. DeSantis CE, Fedewa SA, Goding Sauer A, Kramer JL, Smith RA, et al. Breast Cancer statistics, 2015: Convergence of incidence rates between black and white women. CA Cancer J Clin. 2016; 66:31-42.

24. McCullough ML, Rodriguez C, Diver WR, Feigelson HS, Stevens VL, et al. Dairy, calcium, and vitamin D intake and postmenopausal Breast Cancer risk in the Cancer Prevention Study II Nutrition Cohort. Cancer Epidemiol Biomarkers Prev. 2005;14:2898-2904.

25. Zhang CX, Ho SC, Fu JH, Cheng SZ, Chen YM, et al. Dairy products, calcium intake, and Breast Cancer risk: a case-control study in China. Nutr Cancer. 2011;63:12-20.

26. Kawase T, Matsuo K, Suzuki T, Hirose K, Hosono S, et al. Association between vitamin D and calcium intake and Breast Cancer risk according to menopausal status and receptor status in Japan. Cancer Sci. 2010; 101:1234-1240.

27. Huang WQ, Long WQ, Mo XF, Zhang NQ, Luo H, et al. Direct and indirect associations between dietary magnesium intake and Breast Cancer risk. Sci Rep. 2019;9:1-10.

28. Deheinzelin D, Negri EM, Tucci MR, Salem MZ, Da Cruz VM, et al. Hypomagnesemia in critically ill cancer patients: a prospective study of predictive factors. Braz J Med Biol Res. 2000 ;33:1443-1448.

29. Sartori S, Nielsen I, Tassinari D, Mazzotta D, Vecchiatti G, et al. Serum and erythrocyte magnesium concentrations in solid tumors: relationship with stage of malignancy. Magnes Res. 1992;5:189-192.

30. Yang CY, Chiu HF, Cheng BH, Hsu TY, Cheng MF, et al. Calcium and magnesium in drinking water and the risk of death from breast cancer. J Toxicol Environ Health A. 2000;60:231-241.

31. Tao M, Dai Q, Millen AE, Nie J, Edge SB, et al. Associations of intakes of magnesium and calcium and survival among women with breast cancer: results from Western New York Exposures and Breast Cancer (WEB) Study. Cancer Res. 2015;75:884-884.

32. Feng JF, Lu L, Zeng P, Yang YH, Luo J, et al. Serum total oxidant/antioxidant status and trace element levels in Breast Cancer patients. Int J Clin Oncol. 2012;17:575-583.

33. Khan MT, Ali MA, Obaidullah M, Intekhab M, Rahman NR, et al. Biochemical factors associated with Breast Cancer in Bangladeshi women. Int J Adv Biochem Res. 2022;6:51-54.

34. Viala M, Firmin N, Touraine C, Pouderoux S, Metge M, et al. Changes in vitamin D and calcium metabolism markers in patients undergoing adjuvant chemotherapy for breast cancer. BMC Cancer. 2021;21:1-11.

35. Ebrahimpour-Koujan S, Benisi-Kohansal S, Azadbakht L, Esmaillzadeh A. The Association between Dietary Calcium Intake and Breast Cancer Risk among Iranian Women. Nutr Cancer. 2022;74:1652-1659.

36. Singh MM, Jain MA. Study to assess the role of Biochemical Markers in pre and post-menopausal women at selected Hospitals in Indore. Int J Res Publ Rev. 2015; 3:1445-1446.

37. Dimou NL, Papadimitriou N, Gill D, Christakoudi S, Murphy N, et al. Sex hormone binding globulin and risk of breast cancer: a Mendelian randomization study. Int J Epidemiol. 2019;48:807-816.

38. Vrieling A, Hein R, Abbas S, Schneeweiss A, Flesch-Janys D, et al. Serum 25-hydroxyvitamin D and postmenopausal Breast Cancer survival: a prospective patient cohort study. Breast Cancer Res. 2011; 13:1-9.

39. Al-Al-Saigh TH. Deficiency of Serum 25-hydroxyvitamin D in Patients with Breast Cancer in Iraq. Iraqi J Med Sci. 2018;16:400-404.

40. Chowdary R, Pillarisetti RR, Verma VK, Korabathina R, Beevi SS. Prognostic Significance of Systemic Cholesterol Profile in Patients with Breast Cancer. J Cancer Res. 2022;10:30-33.

41. Negri M, Gentile A, de Angelis C, Montò T, Patalano R, et al. Vitamin D-induced molecular mechanisms to potentiate cancer therapy and to reverse drug-resistance in cancer cells. Nutrients. 2020;12:1798.

42. Wu X, Hu W, Lu L, Zhao Y, Zhou Y, et al. Repurposing vitamin D for treatment of human malignancies via targeting tumor microenvironment. Acta Pharm Sin B. 2019;9:203-21.