RESEARCH ARTICLE

Editorial Process: Submission:11/20/2017 Acceptance:10/07/2018

Low Levels of Vitamin D in a Cohort of Women with Impalpable Breast Lesions from Rio de Janeiro/Brazil

Lucas Delmonico[1,2]*, Maurício Augusto Silva Magalhães Costa[3], Carolina Maria de Azevedo[4], Rafaele Tavares Silvestre[1], Luciano Rios Scherrer[5], Maria Helena Faria Ornellas[1,2], Gilda Alves[1,2]*

Abstract

Background: Low levels of vitamin D have been described as a risk factor for the development of breast cancer. The aim of this study was to evaluate the serum levels of vitamin D (25OHD) in patients with impalpable breast lesions comparing with a control group. **Methods:** Vitamin D quantification (25OHD) was assessed in the plasma of 65 patients with impalpable breast lesions and from 20 health controls using a chemiluminescent microparticle immunoassay. Pearson's chi-square test and nonparametric t-Student were used to evaluate statistical significance between the clinical variables and the means of quantification of vitamin D. The receiver operating characteristic (ROC) curve was used to evaluate the correlation between age and vitamin sufficiency for the cases and the controls. **Results:** The prevalence of vitamin D deficiency and/or insufficiency in women with malignant lesions was 84% and 60% for the control group. Using the chi-square or Fisher's exact test, the relationship between vitamin D levels and age presented significant association only for the control group (P=0.002). Using ROC curve, the plot area (0.778) for the control group defined a cut-off value of 45 years to age, with specificity and sensitivity of 60% and 50%, respectively. Thus, the odds ratio for vitamin D insufficiency in women over 45 years was 1.37 (P=0.011). For the case group, clinical characteristics, histological grade, and lymph node involvement did not show any significant association. **Conclusion:** The prevalence of vitamin D deficiency/insufficiency is high in women with impalpable breast lesions, as well as in the control group, even in a tropical city. According to the results the age advancement may be involved with the decrease in vitamin D levels in plasma, but there was no statistical association between low levels of Vitamin D and breast cancer.

Keywords: Impalpable breast lesions- 25OHD deficiency- hypovitaminosis D- aging

Asian Pac J Cancer Prev, **19 (11)**, 3087-3092

Introduction

Vitamin D is a pre-hormone synthesized mainly following the skin's exposure to solar UV radiation (UV-B), or alternatively found naturally in some foods and ingested from supplementation (Tagliabue et al., 2015). On the skin, it is synthetized as 7-dehydrocholesterol, so this compound is converted by UV into cholecalciferol, which is then transported to the liver associated with DBP (vitamin D carrier protein). The product of hydroxylation in the liver is termed 25-hydroxyvitamin D (25OHD), which is the most abundant form of the vitamin and is the circulating marker used to determine its sufficiency (Bikle, 2014). Circulating 25OHD is transported to the kidneys by vitamin D binding (DBP), where conversion to calcitriol or 1,25-dihydroxyvitamin D [1,25(OH)2D] occurs. This metabolite, due to its liposolubility, is associated with the vitamin D receptor (VDR - nuclear cell receptor group), which will consequently trigger and mediate genomic effects at the cellular level (Bandera et al., 2017). Due to its genomic role, in the last 10 years vitamin D has been identified as a possible therapeutic target for cancer, since it influences the transcription of genes involved in the process of cell growth and differentiation (Richards et al., 2015; Moukayed and Grant, 2017; Rosen et al., 2012).

More recently, low levels of circulating vitamin D in the population have been identified as a risk factor for tumors in general, especially breast cancer, but this association of risk is still controversial (Eliassen et al., 2016; Acevedo et al., 2016). On the other hand, high levels of vitamin D have contributed to better prognosis and overall survival for breast cancer cases (Yao et al., 2017; Villaseñor et al., 2013), and have even

*[1]Circulating Biomarkers Laboratory, [2]Medical Sciences Graduation Program (PGCM), Faculty of Medical Sciences, Rio de Janeiro State University, [3]Americas Medical City, Barra da Tijuca, [4]Radiology Service, Gaffrée e Guinle University Hospital, Rio de Janeiro, [5]Kennedy Faculty, Belo Horizonte, Minas Gerais, Brazil. *For Correspondence: lucasdelmonico@gmail.com, galvesbrown@gmail.com*

reduced the ability of metastasis in in vitro and in vivo assays (Wilmanski et al., 2016; Williams et al., 2016).

In Brazil, breast cancer is the most common tumor affecting women, comprising about 28% of all tumors diagnosed annually, excluding skin tumors (non-melanoma) (INCA, 2017). With the improvement of breast cancer screening, more impalpable breast lesions suspicious of cancer have been detected (Delmonico et al., 2015; Romeiro et al., 2016). The aim of this study was to evaluate the serum levels of vitamin D (25OHD) in patients with impalpable breast lesions comparing with a control group.

Materials and Methods

Study population

Patients were recruited from 2008 to 2016 at Hospital Gafrée-Guinle University Hospital (HUGG) and at Americas Barra Medical City (Maurício Magalhães Costa Clinic), in the city of Rio de Janeiro, Brazil. All patients provided written informed consent. The study was conducted according to the guidelines of the Declaration of Helsinki. This study was approved by the ethics committee of both institutions (HUGG-07/2007-80/2012 and Rio de Janeiro State University 43560115.5.0000.5259). All patients were diagnosed with impalpable lesions BIRADS (Breast imaging-reporting and data system) grade 4. Following biopsy or surgery, the lesion was classified as malignant (N =58) or benign (N=7). Data on age, tumor classification, grade, size, nodal involvement, and immunohistochemical profile were obtained from participating institutions. Histologic classification was graded according to current (2012) World Health Organization criteria (Lakhani et al., 2012), and nuclear grade was defined as grades I to III according to Elston and Ellis (Elston and Ellis, 1991). The histologic classification and the nuclear grading were performed by a medical pathologist. Peripheral blood of 20 eligible healthy women (controls) was collected in Rio de Janeiro.

Laboratory analysis

Four mL of blood was collected in EDTA and centrifuged at room temperature for 10 minutes at 2,000 g and plasma was stored at -80°C. We measured serum 25-hydroxyvitamin D (25OHD) using the Roche Elecsys Vitamin D Total assay (Roche Diagnostics, Mannheim, Germany). The measurements were performed on the Modular Cobas E601 Analyzer according to the manufacturer's protocol. Serum concentrations below 20 ng/mL (50 nmol/L) were classified as deficiency, ≥20 ng/mL (50 to 74 nmol/L) as insufficiency, and ≥30 ng/mL (≥75 nmol/L) as sufficiency (Holick, 2006; Holick et al., 2011).

Statistical Analysis

Calculation of the sample size

The calculation of the sample size required to establish the chi-square test depends on the specification of the following parameters, described in the literature according to Cohen (1988): a) Level of significance is 5% ($\alpha = 0.05$ two-sided); b) for the measurement of the effect, the value described in the literature, according to Cohen (1988), was considered the following reference value: medium effect = 0.30; c) test power ($1-\beta$): $\beta = 0.25$; d) degree of freedom equal to 1, since each variable has two categories. These parameters showed that the sample size is 77 individuals.

Analysis of vitamin D levels

Initially, an exploratory analysis was carried out to characterize the patients' sample, using frequency distributions and descriptive measures for the clinical variables.

For a bivariate analysis, individuals with vitamin D deficiency and insufficiency were grouped into a single group (I/D) due to the number of cases evaluated here. The Fischer chi-square or Pearson test was used for the evaluation of differences between the benign/malignant lesions and control group regarding the vitamin D levels. It was calculated the odds ratio for significance chi-square test.

For the associations between deficient and insufficient in control group and cases, the parametric t-Student test was used to determine differences of 25(OH)D concentrations.

The optimal cut-off point for sensitivity and specificity to evaluate the correlation between vitamin sufficiency and the age was done using the receiver operating characteristic (ROC curve). A contingency table was used to associate the age variable with the presence of sufficient amount of vitamin D. The chi-square or Fisher's Exact test was used to test the statistical significance of the association between these variables. The odds ratio for the occurrence of clinical events was calculated by comparing the age groups. The 95% confidence interval was obtained for the odds ratio.

The data were processed in the statistical program Predictive Analytics Software (PASW 18). A level of significance of 5% was considered in all the statistical tests used. Statistically significant data were considered as those whose P value was less than 0.05.

Results

Our study quantified vitamin D in 58 women with malignant breast lesions, which included 45/58 (77%) Luminal A/B, 8/58 (14%) HER positive, 5/58 (9%) triple negative, and 7 cases with benign breast lesions. The mean age was 59 years (SD 12.66), 62 (SD 12.58), 43 (SD 3.07), and 46 (SD 6.96) for the Luminals A/B, HER2, triple negative, and benign lesions, respectively. The mean age of the control group was 37 years (SD 11.31). Clinical-pathological variables of cases are summarized in Table 1.

Regarding vitamin D dosage, 49/58 (84%) of patients with malignant tumors presented deficiency and/or insufficiency, of which 30/58 (65%) were Luminals A/B. All patients with HER2 (n=8) and triple negative (n=5) tumors had insufficiency and/or deficiency as well.

Using the chi-square test, the vitamin D levels were compared between groups, malignant and benign lesions versus control, and between subtypes of breast cancer versus control. These associations are summarized in

Table 1. Clinical Data of the Cases with Malignant Impalpable Lesion Evaluated in This Study

Age	Mean (years)	
Luminal A/B	59 (SD 12.66)	
HER2	62 (SD 12.58)	
Triple Negative	43 (SD 3.07)	
	Patients N=58	%
Histopathologic grade		
I	13	22%
II	28	49%
III	17	29%
Molecular classification		
Luminal A/B	45	77%
HER2	8	14%
Triple negative	5	9%
Histopathologic classification		
IDC	36	62%
DCIS	5	9%
IDC-DCIS	6	10%
ILC	2	3%
Other malignant lesions (LCIS, Mucinous carcinoma, micropapillary carcinoma, and others)	9	16%

IDC, infiltrative ductal carcinoma; DCIS, ductal carcinoma *in situ*; ILC, infiltrative lobular carcinoma; LCIS, infiltrative carcinoma *in situ*

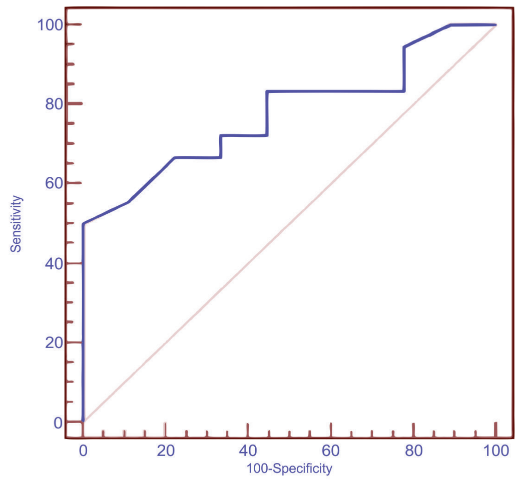

Figure 1. ROC Curve of Association between Age and Vitamin D Quantification for the Control Group

Table 2.

The results of associations between deficient and insufficient 25(OH)D concentrations and case and control are described in Table 3. There was no statistical association of deficiency and insufficiency between groups.

The relationship between vitamin D levels and age presented significant association only for the control group (P=0.002). For this reason, according to the ROC plot area (0.778) of the control group, a cut-off value of 45 years old for women was determined, with specificity and sensitivity of 60% and 50%, respectively (Figure 1). Once the 45-year cutoff point was determined, the odds ratio for vitamin D insufficiency in women over 45 years of age was 1.37 (P=0.011).

The statistical relationship between sufficiency and deficiency/insufficiency of vitamin D for different types of histological grade (P=0.102), and lymph node involvement (P=1.00) did not show any significant association, according to the chi-square test.

Discussion

This study revealed low levels of vitamin D in a heterogeneous group of women with impalpable breast lesions and in the controls as well. Although vitamin D deficiency is a widespread health problem, it has been gaining prominence in regions where sunshine prevails all the year (Schoenmakers et al., 2008). Indoor lifestyles, urban living, and nutrition may explain this finding (Arabi et al., 2010). Nevertheless, low levels of vitamin D were positively associated with aging only in the control group.

Based on our previous study, the vitamin D-binding protein level was considered a candidate to differentiate patients with breast impalpable lesions from controls. A nano-liquid chromatography-quadrupole-time-of-

Table 2. Association of the Control Group with the Benign and Malignant Lesions Regarding the Levels of Vitamin D

Variable	Vitamin D		P value
	I+D (%)	S (%)	
Controls (N=20)	12 (60%)	8 (40%)	0.363
Benign lesions (N=7)	6 (86%)	1 (14%)	
Controls (N=20)	12 (60%)	8 (40%)	0.255
Malignant lesions (N=57)	49 (86%)	8 (14%)	
Controls (N=20)	12 (60%)	8 (40%)	0.779
Luminals A/B (N=45)	30 (67%)	15 (33%)	
Controls (N=20)	12 (60%)	8 (40%)	0.063
HER2 (N=8)	8 (100%)	0 (0%)	
Controls (N=20)	12 (60%)	8 (40%)	0.140
Triple negative (N=5)	5 (100%)	0 (0%)	

I, insufficient; D, deficient; S, sufficient. *The probability of significance (P-value) refers to the chi-square test.

Table 3. Associations between Deficient and Insufficient 25(OH)D Concentrations in Control Group and Cases

Groups*	Number of cases	Mean (ng/mL)	SD	t-student test	P-value**
Benign lesions	6	17.83	7.60	0.336	0.741
Controls	12	18.88	5.84		
Luminal A/B	30	20.29	5.66	0.751	0.457
Controls	12	18.88	5.84		
HER2	8	17.13	7.26	0.621	0.542
Controls	12	18.88	5.84		
Triple Negative	5	17.60	5.03	0.433	0.670
Controls	12	18.88	5.84		
Luminal	30	20.29	5.66	0.908	0.371
Benign lesions	6	17.83	7.60		
HER2	8	17.13	7.26	0.177	0.862
Benign lesions	6	17.83	7.60		
Triple Negative	5	17.60	5.03	0.059	0.955
Benign lesions	6	17.83	7.60		
Luminal A/B	30	20.29	5.66	0.990	0.330
Triple Negative	5	17.60	5.03		
Luminal A/B	30	20.29	5.66	1.308	0.200
HER2	8	17.13	7.26		
Triple Negative	5	17.60	5.03	0.127	0.901
HER2	8	17.13	7.26		

SD, standard deviation, * Only deficiency and insufficiency cases of vitamin D, ** The probabilities of significance (P-value) refer to the t-Student test for independent samples

flight (nLC-Q-TOF) technology was used, and vitamin D-binding protein was found down expressed in the plasma of cases with benign and malignant breast lesions in comparison with controls´ plasmas (Delmonico et al., 2016). In view of these findings, vitamin D-binding protein should be validated as a putative biomarker in a future study.

With regard to the Brazilian population, two reports evaluated breast cancer and vitamin D deficiency (de Lyra et al., 2006; Oliveira et al., 2016). Lyra (2006) studied the levels of 1,25(OH)2D3 and 25OHD in 88 women with breast cancer and 35 controls (submitted to mammoplasties or resection of benign lesions) in the city of São Paulo. These authors found no significant difference between the groups (P= 0.722). Further, when they evaluated the differences in vitamin D levels according to the histological grade of the tumor, no significant difference was found between grade tumors I/II (P=0.329) and III/IV (P=0.256). These results were similar to those of our study, in which no significant difference was detected for the different degrees of tumors (P=0.102) and lymph node involvement (P=1.00). On the other hand, the second Brazilian study, conducted in Belo Horizonte city, evaluating 181 women with breast cancer and 197 controls, determined that the levels of vitamin D sufficiency (P=0.012) and the moderate practice of physical activity (P=0.037) were protective variables for breast cancer (Oliveira et al., 2016).

Considering population studies from other countries, Acevedo (2016) reported that 98/105 (93.3%) Chilean women with breast cancer and 88/93 (94.6%) of cases with Luminal A/B tumors had vitamin D insufficiency/deficiency (≤29.9 ng / mL). Further, 51/53 (96%) of histological grade 3 tumors showed levels of vitamin D in the same range of insufficiency. In our study, these values were lower, with 30/45 (67%) of the Luminal tumors A/B and 15/17 (88%) from grade 3 tumors (see Table 3). In the study by Bilinski and Boyages (2013), 217 Australian women with breast cancer and 852 controls had vitamin D insufficiency with rates of 39.7% (85/214) and 32.3% (275/852), respectively. We found a higher value, being 49/65 (75%) and 12/20 (60%) for malignant tumors and controls, respectively.

The low levels of Vitamin D herein presented for the control group, as well as for the other studies (Oliveira et al., 2016; Bilinski et al., 2013; Unger et al., 2010), are alarming. These values become more evident in countries whose sun incidence is low or that have periods of rigorous winter (Nouri et al., 2017; Shirazi et al., 2016). Consequently, we believe that a part of the global population may be experiencing hypovitaminosis D, increasing the susceptibility to development of the carcinogenic process and other diseases. In relation to the carcinogenic process, the studies with larger numbers of evaluated cases have highlighted low levels of vitamin D as a risk factor for breast cancer (Rose et al., 2013), colorectal cancer (Maalmi et al., 2014), and haematological tumors (Wang et al., 2015). In addition, low levels of vitamin D were associated with the lower overall survival rate (OS) and the lower rate of disease-free survival (RFS) in these tumors.

An equally important finding here was the relationship between the low levels of vitamin D and aging. One reason why vitamin D tends to decrease with aging is directly related to the decreasing capacity to produce vitamin D3, due to degeneration in the cutaneous levels of 7-dehydrocholesterol (Bolland et al., 2006; Bolland et al., 2007). Two other reasons associated with decreasing vitamin D in the elderly are the increase of fat mass and the decrease of sun exposure. The first is related to the number of adipocytes that sequester vitamin D naturally, ingested or produced in the skin, before being transported to the liver to be converted to 25(OH)D3 (Bolland et al., 2007); and the second that elderly tend to wear more clothing and spend more time indoors due to reduced walking capacity (Unger et al., 2010).

This study is original in that it shows that vitamin D deficiency is prevalent lower in women with impalpable breast lesions and that vitamin levels are directly related to aging. We emphasize the need for monitoring vitamin D levels especially in the elderly, even in sunny countries, to prevent diseases such as cancer.

Acknowledgments

The authors thank everyone at the Endocrinology Service of Pedro Ernesto University Hospital and MD, PhD Sandra Boiça for advice and assistance. Delmonico L. is a recipient of a graduate fellowship from Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES).

References

Acevedo F, Pérez V, Pérez-Sepúlveda A, et al (2016). High prevalence of vitamin D deficiency in women with breast cancer: The first Chilean study. *Breast J*, **29**, 39-43.

Arabi A, El Rassi R, El-Hajj Fuleihan G (2010). Hypovitaminosis D in developing countries-prevalence, risk factors and outcomes. *Nat Rev Endocrinol*, **6**, 550-61.

Bandera BM, Morcillo S, Martin-Nuñez G, Tinahones FJ, Macías-González M (2017). The role of vitamin D and VDR in carcinogenesis: Through epidemiology and basic sciences. *J Steroid Biochem Mol Biol*, **167**, 203-18.

Bikle D (2014). Vitamin D metabolism, mechanism of action, and clinical applications. *Chem Biol*, **21**, 319-29.

Bilinski K, Boyages J (2013). Association between 25-hydroxyvitamin D concentration and breast cancer risk in an Australian population: an observational case-control study. *Breast Cancer Res Treat*, **137**, 599-07.

Bolland MJ, Grey AB, Ames RW, et al (2006). Determinants of vitamin D status in older men living in a subtropical climate. *Osteoporos Int*, **17**, 1742e8.

Bolland MJ, Grey AB, Ames RW, et al (2007). The effects of seasonal variation of 25-hydroxyvitamin D and fat mass on a diagnosis of vitamin D sufficiency. *Am J Clin Nutr*, **86**, 959e64.

Cohen J (1988). Statistical power analysis for the behavioral sciences. In “Tables and the determination of sample size”, Lawrence Erlbaum Associates, New York, pp 444-5.

de Lyra EC, da Silva IA, Katayama ML, et al (2006). 25(OH) D3 and 1,25(OH)2D3 serum concentration and breast tissue expression of 1alpha-hydroxylase, 24-hydroxylase and Vitamin D receptor in women with and without breast cancer. *J Steroid Biochem Mol Biol*, **100**, 184-92.

Delmonico L, Bravo M, Silvestre RT, et al (2016). Proteomic profile of saliva and plasma from women with impalpable breast lesions. *Oncol Lett*, **12**, 2145-52.

Delmonico L, Moreira Ados S, Franco MF, et al (2015). CDKN2A (p14(ARF)/p16(INK4a)) and ATM promoter methylation in patients with impalpable breast lesions. *Hum Pathol*, **46**, 1540-7.

Eliassen AH, Warner ET, Rosner B, et al (2016). Plasma 25 Hidrodyvitamin D and risk of breast cancer in women folowed over 20 years. *Cancer Res*, **76**, 5423-30.

Elston CW, Ellis IO (1991). Pathological prognostic factors in breast cancer. I. The value of histological grade in breast cancer: experience from a large study with long-term follow-up. *Histopathology*, **19**, 403-10.

Holick MF (2006). High prevalence of vitamin D inadequacy and implications for health. *Mayo Clin Proc*, **81**, 353e73.

Holick MF, Binkley NC, Bischoff-Ferrari HA, et al (2011). Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*, **96**, 1911-30.

Holick MF (2007). Vitamin D deficiency. *N Engl J Med*, **357**, 266e81.

Instituto Nacional de Câncer José Alencar Gomes da Silva. [INCA website] http://www2.inca.gov.br/wps/wcm/connect/tiposdecancer/site/home/mama/cancer_mama. Acessed July, 12, 2017.

Lakhani SR, Ellis IO, Schnitt SJ, Tan PH, van de Vijver MJ (2012). WHO classification of tumours of the breast. 4th ed. Lyon: IARC Press.

Maalmi H, Ordóñez-Mena JM, Schöttker B, Brenner H (2014). Serum 25-hydroxyvitamin levels and survival in colorectal and breast cancer patients: systematic review and meta-analysis of prospective cohort studies. *Eur J Cancer*, **50**, 1510-21.

Moukayed M, Grant WB (2017). The roles of UVB and vitamin D in reducing risk of cancer incidence and mortality: A review of the epidemiology, clinical trials, and mechanisms. *Rev Endocr Metab Disord*, **18**, 167-82.

Nouri Saeidlou S, Vahabzadeh D, Babaei F, Vahabzadeh Z (2017). Seasonal variations of vitamin D and its relation to lipid profile in Iranian children and adults. *J Health Popul Nutr*, **36**, 21.

Oliveira Sediyama CM, Dias MM, Pessoa MC, et al (2016). Lifestyle and vitamin D dosage in women with breast cancer. *Nutr Hosp*, **33**, 584.

Richards SE, Weierstahl KA, Kelts JL (2015). Vitamin deffect on growth and vitamin D metabolizing enzymes in triple-negative breast cancer. *Anticancer Res*, **5**, 805–10.

Romeiro Lopes TC, Franca Gravena AA, Demitto Mde O, et al (2016). Mammographic screening of women attending a reference service center in southern Brazil. *Asian Pac J Cancer Prev*, **17**, 1385-91.

Rose AA, Elser C, Ennis M, Goodwin PJ (2013). Blood levels of vitamin d and early stage breast cancer cancer prognosis: a systematic review and meta-analysis. *Breast Cancer Res Treat*, **141**, 331-39.

Rosen CJ, Adams JS, Bikle DD, et al (2012). The nonskeletal effects of vitamin D: an Endocrine Society scientific statement. *Endocr Rev*, **33**, 456–92.

Schoenmakers I, Goldberg GR, Prentice A (2008). Abundant sunshine and vitamin D deficiency. *Br J Nutr*, **99**, 1171-3.

Shirazi L, Almquist M, Borgquist S, Malm J, Manjer J (2016). Serum vitamin D (25OHD3) levels and the risk of different subtypes of breast cancer: A nested case-control study. *Breast J*, **28**, 184-90.

Tagliabue E, Raimondi S, Gandini S (2015). Meta-analysis of vitamin D-binding protein and cancer risk. *Cancer Epidemiol Biomarkers Prev*, **24**, 1758-65.

Unger MD, Cuppari L, Titan SM, et al (2010). Vitamin D status in a sunny country: where has the sun gone?. *Clin Nutr*,

29, 784-88.
Villaseñor A, Ballard-Barbash R, Ambs A, et al (2013). Associations of serum 25-hydroxyvitamin D with overall and breast cancer-specific mortality in a multiethnic cohort of breast cancer survivors. *Cancer Causes Control*, **24**, 759-67.
Wang W, Li G, He X, et al (2015). Serum 25-hydroxyvitamin D levels and prognosis in hematological malignancies: a systematic review and meta-analysis. *Cell Physiol Biochem*, **35**, 1999-05.
Williams JD, Aggarwal A, Swami S, et al (2016). Tumor autonomous effects of vitamin D deficiency promote breast cancer metastasis. *Endocrinology*, **157**, 1341-7.
Wilmanski T, Barnard A, Parikh MR, et al (2016). 1α,25-Dihydroxyvitamin D inhibits the metastatic capability of MCF10CA1a and MDA-MB-231 cells in an In Vitro model of breast to bone metastasis. *Nutr Cancer*, **68**, 1202-9.
Yao S, Kwan ML, Ergas IJ, et al (2017). Association of serum level of vitamin D at diagnosis with breast cancer survival: A case-cohort analysis in the pathways study. *JAMA Oncol,* **20**, 351-7.