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# Vitamin D deficiency in postmenopausal Ecuadorian women with diabetes mellitus type 2

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## Summary

**Objectives:** To know the prevalence of vitamin D insufficiency in Ecuadorian postmenopausal women with type 2 diabetes mellitus, and to investigate the correlation between serum levels of vitamin D, variables of metabolic control of type 2 diabetes mellitus, markers of bone metabolism and bone mineral density.

**Design, materials and methods:** Epidemiological study descriptive and cross-sectional design, carried out between January 2012 November 2015. In 124 postmenopausal women, 96 with type 2 diabetes mellitus and 28 without diabetes, we measured serum levels of vitamin D, glycosylated hemoglobin, HOMA-IR, parathyroid hormone, ionic calcium, osteocalcin, urinary deoxypyridinoline and bone density. Premenopausal women, kidney disease, type 1 diabetes, secondary osteoporosis, and those who received treatments that affect bone metabolism, were excluded.

We separate patients with type 2 diabetes mellitus in 2 groups: group sufficiency vitamin D (>30 ng/mL) and group insufficiency vitamin D (<30 ng/mL). The latter group was subdivided into insufficiency (<30 ng/mL), deficiency (<20 ng/mL) and severe deficiency (<10 ng/mL). An analysis of linear correlation between vitamin D and all variables was performed.

**Results:** We found a significant reduction in serum levels of vitamin D in patients with type 2 diabetes mellitus compared with the controls ( $p<0,034$ ). The group of patients with diabetes mellitus had the following characteristics: age, 66 (13) years; body mass index, 28.5 (6.5); vitamin D, 20.9 (8.2) ng/mL; and parathyroid hormone, 34 (21) pg/mL; 12.5% had sufficiency and 87.5% insufficiency of vitamin D; among these, 44 had insufficiency, 36 deficiency and 4 severe deficiency. There is a significant correlation between VD, age ( $p=0,036$ ) and lumbar bone density ( $p=0,031$ ). We found no correlation between vitamin D and the variables of metabolic control of diabetes.

**Conclusions:** We found a high prevalence of vitamin D insufficiency in the Ecuadorian postmenopausal women with type 2 diabetes mellitus.

**Key words:** diabetes, hypovitaminosis D, parathyroid, densitometry, postmenopausal, prevalence..

## Introduction

Type 2 diabetes mellitus (T2DM) is a worldwide epidemic. The International Diabetes Federation (IDF) predicts that the current figure of 415 million patients affected with diabetes will increase to 642 million by 2040<sup>1</sup>. In Ecuador, the prevalence of T2DM in the age-adjusted population is 9.2%, according to 2015 IDF estimates<sup>1</sup>.

Vitamin D deficiency has been linked to a wide range of health problems, including various cancers and autoimmune or metabolic diseases, such as type 1 diabetes mellitus and T2DM<sup>2</sup>.

Current studies confirm that the prevalence of vitamin D deficiency in the general world population is actually as high as 50-80%<sup>3</sup>, even occurring in countries located in geographical areas which receive sunshine year-round.

Although the high prevalence of hypovitaminosis D has been considered a serious public health problem in Latin America and the Caribbean, the precise extent of the problem is not known due to the lack of information in the general population<sup>4</sup>.

Previous studies have described a high rate of vitamin D deficiency in the general population<sup>5</sup>. However, few have reported the status of vitamin D in patients with T2DM. The prevalence of vitamin D deficiency or insufficiency in patients with T2DM varies from 70 to 90%<sup>6-8</sup>, depending on the threshold used to define vitamin D deficiency or insufficiency.

In Ecuador, the status of serum vitamin D levels in the general population has recently been described<sup>9</sup>, but not in patients with T2DM. This study was conducted to determine the prevalence of vitamin D insufficiency in Ecuadorian postmenopausal women with T2DM and to investigate whether there is a correlation between serum levels of vitamin D, markers of bone metabolism, bone density, and metabolic control variables of T2DM.

## Material and methods

*Population group and study design:* a descriptive and cross-sectional epidemiological study was carried out to determine the prevalence of hypovitaminosis D in the period from January 2012 to November 2015 at the Teaching Hospital of the Guayaquil National Police N° 2 (HDPN-G2).

The city of Guayaquil, located on the Pacific coast (2°11'00"S), encompassing an area of 345 km<sup>2</sup>, is the most populated city in Ecuador. According to the most recent (2010) Census of Population and Housing data, provided by the National Institute of Statistics and Censuses of Ecuador, Guayaquil has 16% of the country's total population<sup>10</sup>.

The study protocol was approved by the HDPN-G2 Ethics and Research Committee. All patients signed informed consent before participating in the study.

The study included 2 groups of postmenopausal women residing in Guayaquil. One group included those who were undergoing their T2DM

check-up in the endocrinology office. The other group was comprised of those who attended for a routine review for non-diabetes related medical problems in the Internal Medicine practice of HDPN-G2 (control group: Non T2DM). Serum levels of 25(OH) were measured as well as total vitamin D (including D3+D2), glycosylated hemoglobin (HbA1c), parathyroid hormone (PTH), ionic calcium in 96 postmenopausal women with type 2 diabetes mellitus and in 28 non-DM2 controls, osteocalcin, and deoxypyridinoline in urine. We also conducted basic biochemistry tests in serum: creatinine, complete blood count, fasting blood glucose, liver enzymes, serum lipids, and proteinogram.

Premenopausal patients with a history of ketoacidosis, type 1 diabetes mellitus and nephropathy, and those receiving medications that affect bone metabolism (bisphosphonates, estrogens, calcium, anabolic steroids or other male or female hormones) were excluded.

### *Diagnosis of type 2 diabetes*

We followed the international criteria for diagnosing T2DM<sup>11</sup>, which considers the disease to be present if at least one of the following criteria are met: (1) FPG (fasting plasma glucose)  $\geq 126$  mg/dL; (2) HbA1  $\geq 6.5\%$ . Patients with T2DM received various combinations of treatments for their metabolic control: metformin, insulin, DPP4 inhibitors, and diet. The duration of T2DM was established based on the dates recorded in the patient's clinical history and/or self-referral.

### *Classification of vitamin D levels*

Normal values of serum vitamin D are defined as those from 30 to 76 ng/mL<sup>2</sup>. Patients were divided into 2 groups according to the serum vitamin D level: sufficiency group ( $\geq 30$  ng/mL) and failure group ( $< 30$  ng/mL)<sup>5</sup>.

The latter group was divided into 3 subgroups: insufficiency ( $< 30$  ng/mL), deficiency ( $< 20$  ng/mL) and severe deficiency ( $< 10$  ng/mL)<sup>6</sup>.

Serum ionic calcium was measured after 12 hours of fasting and without tourniquet, under anaerobic conditions, by direct measurement with selective ion electrode (NOVA-8 equipment), with reference values 4.5-5.6 mg/dL.

Parathyroid hormone PTH (intact molecule) was measured with SIEMENS Immulite 2000 (enzyme-labeled two-site solid-phase chemiluminescent immunometric assay), whose reference value is 12-72 pg/mL. The intra-assay precision performance had a coefficient of variation of 5.7, 4 and 4.2% for concentrations of 72, 258 and 662 pg/mL, respectively, and an inter-assay coefficient of variation of 6.3 and 8.8% for 54 and 387 pg/mL concentrations, respectively. The limit of detection is 3.0 pg/mL and a linearity up to 500,000 pg/mL without Hook effect.

Serum level of total 25(OH) vitamin D (D3+D2) was measured by chemiluminescence, with reference values 30-70 ng/mL (Centaur kit; competitive 1-step assay with fluorescein-marked anti-

body). Total precision performance had a coefficient of variation of 11.1, 9.6, 9.8, 8.2, 7.8, 4.8% for concentrations of 11.7, 18.0, 32.4, 49.9, 55.8, 132.1 ng/mL respectively, a detection limit of 3.2 ng/mL and a linearity up to 150 ng/mL. Renal function integrity was recorded in all cases by measuring serum creatinine levels and calculating endogenous creatinine clearance expressed in ml/ml (formula corrected for age, sex, weight and serum creatinine):

$$[(140 - \text{age in years}) \times \text{weight (kg)}] / [(72 \times \text{serum creatinine (mg/dL)} \text{ and in women } \times \text{correction factor } 0.85)].$$

Glycosylated hemoglobin in EDTA whole blood was measured by HPLC assay (diagnostic value, >6.5%). Osteocalcin, by electrochemiluminescence, ROCHE MODULAR E-170 (reference values for postmenopausal women: 20-48 ng/mL). Deoxypyridinoline (DPD) in urine, by chemiluminescence, whose total precision performance shows a coefficient of variation of 12.0, 11.0, 7.1, 6.3 and 4.3% for concentrations of 25, 32, 78, 120 and 275 nM, respectively (reference values: 3-7.4 nM DPD/mM creatinine).

Bone mineral density (BMD) in the lumbar spine (L2-L4) and femoral neck were determined by dual energy X-ray absorptiometry (DXA: Hologic Discovery), and the data were expressed as T-score units. As no reference values were available for the Ecuadorian population, the NHANES North American reference values were used.

#### Data analysis

Data on demographic and biochemical variables are expressed as median and interquartile range. To compare the clinical and biochemical characteristics between groups, the Wilcoxon signed-rank test was used. A linear correlation analysis (Spearman's coefficient) between vitamin D and all other variables was performed. Statistical significance was considered with values of  $p < 0.05$ . The prevalence of hypovitaminosis D was calculated as the number of existing cases divided by the total population screened and expressed as a proportion of every 100 adults. All analyzes were carried out using Epidata software version 4.2. The confidence intervals of the Spearman correlation coefficient were calculated using the Stata software version 14.2 (2016).

## Results

### Demographics of cases and controls

There were no differences between the two groups (T2DM versus non-T2DM) in terms of age, body mass index (BMI), intact PTH, osteocalcin, urinary deoxypyridinoline, and BMD in the lumbar region or femur. The groups presented significant differences in the variables of metabolic control: the HOMA-IR index ( $p = 0.002$ ) and glycosylated hemoglobin ( $p < 0.001$ ). Serum vitamin D levels were significantly lower ( $p < 0.034$ ) in the T2DM group.

Demographic data and characteristics of cases and controls are presented in table 1.

### Severity and extent of vitamin D deficiency

In the T2DM group we found a significant reduction in serum vitamin D levels: 12.5% (95% CI=5.3-19.6) of the cases had vitamin D sufficiency ( $n = 12$ ) and 87.5% (95% CI=80.3-94.6) had vitamin D insufficiency ( $n = 84$ ), of which 52% (95% CI=51.1-63.6) ( $n = 44$ ) had insufficiency; 42% (95% CI=31.7-54) ( $n = 36$ ), moderate deficiency and 4.8% (95% CI=1.3-11.7) ( $n = 4$ ) severe deficiency. In the non-T2DM group, 67.8% (95% CI=48.8-87) ( $n = 19$ ) had vitamin D sufficiency and 33% (95% CI=13-51) ( $n = 9$ ) had insufficient vitamin D. Figure 1 shows the frequency distribution of vitamin D levels in postmenopausal women with DM2.

There were no differences in the T2DM group between subgroups of patients with adequacy and that of patients with vitamin D insufficiency in terms of age, BMI, HbA1c, PTH, ionic calcium, osteocalcin, urinary deoxypyridinoline, or bone mineral density. The subgroup with vitamin D insufficiency presented a higher HOMA-IR than that with sufficiency, although it did not reach statistical significance ( $p = 0.093$ ). Table 2 shows the demographic data, metabolic variables, bone density and vitamin D status in patients with T2DM.

### Correlation between vitamin D, markers of bone metabolism and variables of metabolic control of T2DM

We found a slight but significant correlation between vitamin D and age ( $r = -0.21$ ,  $p = 0.03$ ) but not with BMI and the metabolic control variables of T2DM (glycosylated hemoglobin, HOMA-IR index), nor with markers of bone remodeling (PTH, ionic calcium, osteocalcin, deoxypyridinoline). There is a slight ( $r = 0.22$ ) but significant correlation between vitamin D and bone density in the lumbar region ( $p = 0.03$ ), but not with femoral neck BMD. Table 3 shows the correlation coefficients between vitamin D, markers of bone metabolism and metabolic control variables of DM2.

## Discussion

The high incidence of T2DM worldwide<sup>1</sup> and the accumulated evidence on the status of vitamin D under different conditions<sup>2</sup> make it extremely important to determine the relationship between vitamin D and diabetes mellitus.

To our knowledge, this is the first study conducted in Latin America, which establishes the prevalence of hypovitaminosis D in postmenopausal women with T2DM.

Hypovitaminosis D appears to be a prevalent phenomenon in populations around the world, in which they influence the type of ethnicity, sex, body mass index, traditional dress, nutrition, consumption of vitamin supplements and level of urbanization<sup>3</sup>.

Most epidemiological information on hypovitaminosis D in the world population comes from studies in Europe, the Middle East, India, and Asia<sup>3,5</sup>, with few studies in our region<sup>4,9</sup>.

Choosing the cut-off point to define vitamin D deficiency in the population remains a controver-

sial issue. Some consider levels >30 ng/mL to define sufficiency, while others set adequate levels of 20 ng/mL. According to the definition of the Endocrine Society (USA), vitamin D values below 20 ng/mL are considered deficient, and values between 21 and 29 ng/mL are insufficient<sup>2</sup>. According to these cut-off points, it is estimated that 20 to 100% of elderly men and women have vitamin D deficiency in the United States, Canada and Europe<sup>13</sup>.

In 3 studies conducted in Latin America, a cutoff point of <20 ng/mL<sup>14,16</sup>; and in another <20 and <30 ng/mL for deficiency and insufficiency, respectively<sup>9</sup>.

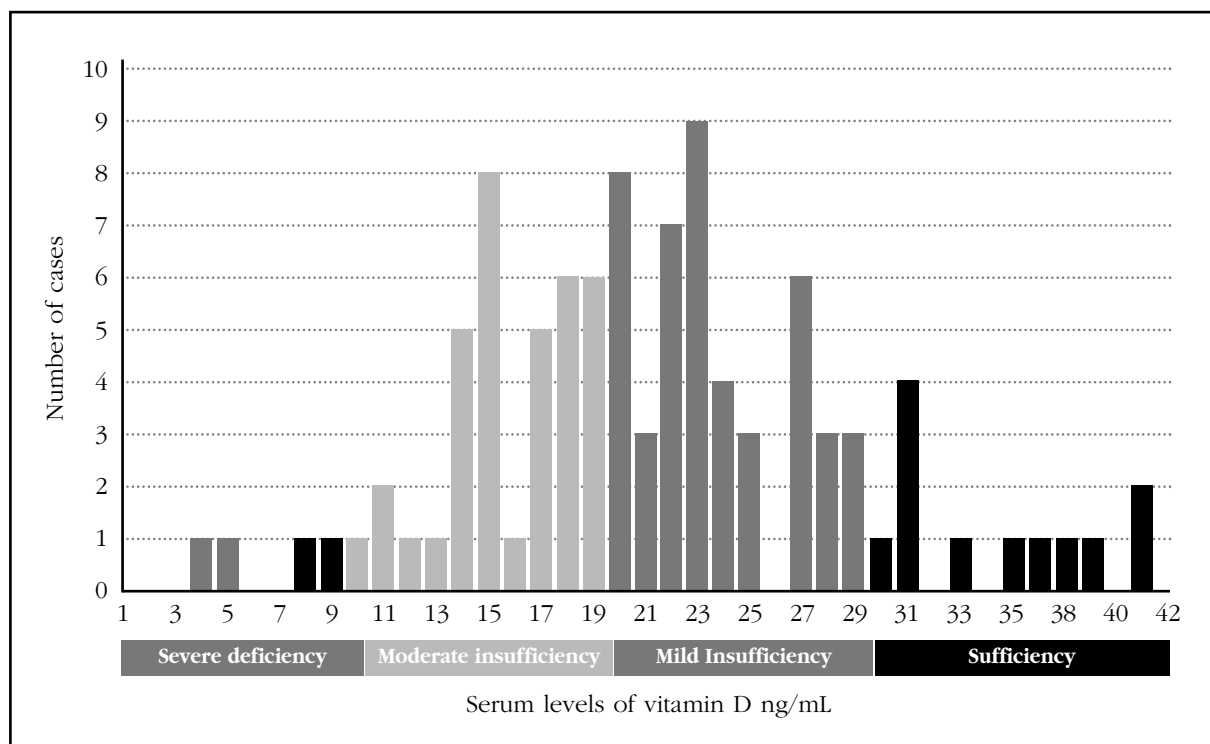
With a cutoff <20 ng/mL, the prevalence of vitamin D deficiency among women in Santiago de Chile is 60%<sup>14</sup>. In Argentina, the prevalence of vitamin D deficiency varies from 73% in southern cities to 50% in northern cities<sup>15</sup>, and in Brazil it is 17%, much lower than in previous series<sup>16</sup>.

Table 1. Demographic data and characteristics of the 2 study groups

	T2DM n=96	No T2DM n=28	p
Age (years)	66 (13)	65 (15.5)	0.569
Body mass index (kg/m <sup>2</sup> )	28.5 (6.5)	28.4 (1.8)	0.909
HOMA-IR	4.22 (5.7)	3 (2.3)	0.002*
Glycosylated hemoglobin (%)	6.4 (2.2)	5.8 (0.6)	0.0001*
Vitamin D (ng/mL)	20.9 (8.1)	25.18 (12.3)	0.034*
PTH intact (pg/mL)	34 (21.5)	36 (30.7)	0.445
Ionic calcium (mg/dL)	4.9 (0.32)	4.91 (0.21)	0.792
Osteocalcin (ng/mL)	15.34 (10.26)	15.34 (10.3)	0.171
Deoxypyridinoline (nM DPD/mM Cr)	6.5 (2.7)	5.5 (3.07)	0.28
Lumbar spine BMD (T-score)	-1.5 (2.2)	-1.4 (1.8)	0.971
BMD femoral neck (T-score)	-1.5 (1.5)	-1.4 (2.2)	0.692

\*p<0.05 (Wilcoxon Signal Range Test). Data are expressed as medians and interquartile range. T2DM: type 2 diabetes mellitus; HOMA-IR: Homeostasis Model of Assessment-Insulin Resistance Index; PTH: parathyroid hormone; BMD: bone mineral density.

Figure 1. Distribution of vitamin D frequency frequencies in postmenopausal women with T2DM



In Ecuador, a recent study<sup>9</sup> in the elderly population has described a prevalence of vitamin D insufficiency and deficiency of 68 and 22%, respectively. Despite the abundant natural light throughout the year, this condition varies considerably among the different regions and zones of our country. It is more frequent in older women, the inhabitants of the Andean region and the indigenous race<sup>9</sup>.

The prevalence of vitamin D deficiency or insufficiency in patients with T2DM also depends on the threshold used to define it. In our study, vitamin D insufficiency was defined as a vitamin D level <30 ng/mL, which is in accordance with the

recommendation of the International Osteoporosis Foundation<sup>5,17</sup>.

In general, the prevalence of hypovitaminosis D in patients with T2DM reported in international series is high. In a previously published study, 74.6% of patients with T2DM had D hypovitaminosis<sup>8</sup>. In another, prevalence (cutoff <20 ng/mL) was more frequent in diabetics compared to controls (83% vs 70%,  $p=0.07$ )<sup>7</sup>. In a more recent study, prevalence was greater in diabetic patients than in control subjects (90% vs 83%,  $p<0.01$ )<sup>18</sup>. Data on hypovitaminosis D in patients with T2DM are not available in Latin America.

Table 2. Demographic data, metabolic variables, bone density and vitamin D status in patients with T2DM

	Sufficiency VD (n=12)	Insufficiency VD (n=84)	p
Age (years)	61 (22.5)	66 (11.5)	0.272
Body mass index (kg/m <sup>2</sup> )	26.97 (10.7)	28.69 (5.8)	0.720
HOMA-IR	3.26 (6.7)	4.28 (5.1)	0.093
Glycosylated hemoglobin (%)	7.25 (3.5)	6.4 (2.3)	0.284
Vitamin D (ng/mL)	34.59 (7.1)	20.23 (7.4)	0.002*
PTH intact (pg/mL)	34.5 (20.5)	34 (23)	0.583
Ionic calcium (mg/dL)	4.98 (0.25)	4.9 (0.32)	0.410
Osteocalcin (ng/mL)	13.99 (10.7)	15.3 (10.3)	0.480
Deoxypyridinoline (nM DPD/mM Cr)	6.35 (4.02)	6.56 (2.67)	0.646
BMD lumbar spine (T-score)	-1.40 (2.8)	-1.50 (2.23)	0.724
BMD femoral neck (T-score)	-1.00 (2.85)	-1.50 (1.40)	0.875

\* $p<0.05$  (Wilcoxon Signal Range Test). Data are expressed as medians and interquartile range. T2DM: type 2 diabetes mellitus; HOMA-IR: Homeostasis Model of Assessment-Insulin Resistance Index; PTH: parathyroid hormone; BMD: bone mineral density.

Table 3. Correlation between vitamin D, markers of bone metabolism and variables of metabolic control of DM2

	r	IC 95%	p
Age (years)	-0.215	-0.4 a -0.015	0.036*
Body mass index (kg/m <sup>2</sup> )	-0.113	-0.313 a 0.098	0.294
HOMA-IR	0.097	-0.124 a 0.309	0.388
Glycosylated hemoglobin (%)	-0.024	-0.245 a 0.200	0.838
Ionic calcium	-0.042	-0.245 a 0.156	0.654
PTH intact (pg/mL)	0.18	-0.021 a 0.368	0.079
Osteocalcin (ng/mL)	-0.052	-0.25 a 0.15	0.617
Deoxypyridinoline (nM DPD/mM Cr)	-0.149	-0.353 a 0.069	0.179
BMD lumbar spine (T-score)	0.221	0.021 a 0.404	0.031*
BMD femoral neck (T-score)	0.155	-0.047 a 0.345	0.131

\* $p<0.05$ ; r: Spearman correlation coefficient; 95% CI: 95% confidence interval; T2DM: type 2 diabetes mellitus; HOMA-IR: Homeostasis Model of Assessment-Insulin Resistance Index; PTH: parathyroid hormone; BMD: bone mineral density.



The results of the present study are similar to those of recent studies in non-Latin American populations, which demonstrated a high prevalence of hypovitaminosis D in patients with T2DM<sup>6,19,21</sup>.

It is unclear whether vitamin D deficiency and poor glycemic control are causally related or represent two independent features of T2DM. Previous studies have reported inconclusive results regarding the association between vitamin D status and HbA1c<sup>22</sup>. In our study, vitamin D-deficient women had lower levels of HbA1c compared to those who had sufficiency, although this did not reach statistical significance. This adds to the evidence that the vitamin D status is not associated with the metabolic control variable HbA1c.

An inverse association has been reported between serum vitamin D levels and BMI >30, and therefore, obesity would be associated with vitamin D deficiency<sup>23</sup>. In postmenopausal women with T2DM, obesity is also considered a risk factor for vitamin D deficiency<sup>20</sup>. However, our data do not confirm previous reports of a negative association between vitamin D and BMI. In contrast, in our sample cases and controls were not different in their BMI, although both groups were overweight.

The main finding of this cross-sectional study is the high prevalence (85.7%) of vitamin D insufficiency (<30 ng/mL) in patients with T2DM, with an average vitamin D level of 22 ng/mL. However, this value is higher than the average vitamin D reported for patients with diabetes and obesity in other series in Africa and Asia (16 to 17 ng/mL)<sup>24,25</sup> and similar to a sample of patients in the United States (23 ng/mL)<sup>26</sup>.

In Ecuador, there is no definite four-season separation as in the northern and southern hemispheres. The city of Guayaquil, where this study was conducted, is located on the coast of the Pacific (2°11'00"S), and its inhabitants enjoy open skies, warm weather and sunlight throughout the year, their garments of clothing are light and expose much of their skin.

The results of this study contradict the assumption that abundant exposure to sunlight throughout the year reduces the risk of hypovitaminosis D. The discrepancy between our results and outcomes in other ethnic groups may reflect racial differences, lifestyle factors (physical inactivity, limited sun exposure) and/or insufficient intake of vitamin D, or all.

Vitamin D deficiency is associated with an increased risk of fracture<sup>27</sup>, and is associated with diffuse muscular pain, muscle weakness and increased risk of falls<sup>28,29</sup>. However, despite the increased risk of fracture, bone mineral density is generally higher in patients with T2DM<sup>30</sup>. In our study, we did not investigate the prevalence of fragility fractures, so we cannot confirm this evidence.

Previous studies indicate that even a slight reduction in serum vitamin D levels may be associated with secondary hyperparathyroidism, increased remodeling, and accelerated bone loss, which increase the risk of bone fractures<sup>31</sup>. In the

present study, intact PTH and ionic calcium levels were within the normal range, so our results do not confirm the association between vitamin D, PTH and calcium that has been described in the literature.

There are some strengths and limitations related to the present study. Although the sample of population was relatively small, we were able to compare it with a control group, which allows us to establish inferences with the general population.

The present study does not provide data that could explain the higher prevalence of hypovitaminosis D in patients with T2DM.

It is generally accepted that vitamin D levels vary with daily activity and exercise level. In our study we do not consider these variables, and although in our country we only have one dry season and one rainy season, we do not know if in our population the measured variables are modified with the time of year.

The prevalence of hypovitaminosis D in the general population has been overestimated due to improper use of a high cut-off point for vitamin D. Geographic latitude with a large amount of sunlight exposure or low calcium consumption<sup>9</sup>, which generally occurs in Ecuador, will undoubtedly affect the cut-off point for the development of vitamin D deficiency. In this sense, the cut-off point chosen to define vitamin D insufficiency may not be adequate for our predominantly mestizo population, using the one for predominantly Caucasian populations, as these values vary widely even from region to region<sup>12</sup>.

Considering that in this sample the average vitamin D was very close to 20 ng/mL, further studies are required to evaluate the adequacy of the vitamin D cutoff points chosen in Ecuadorian women with T2DM. In this study, a lower cutoff point for vitamin D normality would undoubtedly have resulted in a much lower prevalence of hypovitaminosis D.

Despite these limitations, the present study is the first to report the prevalence of vitamin D insufficiency among Ecuadorian postmenopausal women with T2DM, and allows us to infer that this prevalence is higher in patients with T2DM than in the population without T2DM.

In conclusion, our study found that vitamin D deficiency was significantly more frequent among Ecuadorian postmenopausal women with T2DM compared to those without T2DM.

Our data indicate that the availability of abundant sunlight is not sufficient for the prevention of vitamin D deficiency. This warns us of the risk of hypovitaminosis D in the diabetic population, regardless of geographical location.

The high prevalence of hypovitaminosis D in postmenopausal women with T2DM highlights the need for prospective studies to evaluate the impact of vitamin D supplementation on glucose metabolism. Additional studies should clarify the relationship between hypovitaminosis D and osteoporosis in patients with T2DM.

The results of our study may help the country's public health authorities implement vitamin D supplementation policies, especially among the population at risk of this condition.

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## Bibliography

1. <http://www.diabetesatlas.org/>. acceso 20 abril 2017.
2. Rosen CJ. Clinical practice. Vitamin D insufficiency. *N Engl J Med*. 2011;1364:248-54.
3. Gind, AA, Liu M. C, Camargo CA Jr. Demographic differences and trends of vitamin D insufficiency in the US population, 1988-2004. *Arch Intern Med*. 2009;169(6):626-32.
4. Brito A, Cori H, Olivares M, Fernanda Mujica M, Cediell G, López de Romaña D. Less than adequate vitamin D status and intake in Latin America and the Caribbean: a problem of unknown magnitude. *Food Nutr Bull*. 2013;34(1):52-64.
5. Mithal A, Wahl DA, Bonjour JP, Burckhardt P, Dawson-Hughes B, Eisman JA, et al. IOF Committee of Scientific Advisors (CSA) Nutrition Working Group. Global vitamin D status and determinants of hypovitaminosis D. *Osteoporos Int*. 2009;20(11):1807-20.
6. Mori H, Okada Y, Tanaka Y. Incidence of vitamin D deficiency and its relevance to bone metabolism in Japanese postmenopausal women with type 2 diabetes *mellitus*. *Intern Med*. 2015;54:1599-04.
7. Tahrani AA, Ball A, Shepherd L, Rahim A, Jones AF, Bates A. The prevalence of vitamin D abnormalities in South Asians with type 2 diabetes *mellitus* in the UK. *Int J Clin Pract*. 2010;64(3):351-5.
8. Miñambres I, Sánchez-Quesada JL, Vinagre I, Sánchez-Hernández J, Urgell E, de Leiva A, et al. Hypovitaminosis D in type 2 diabetes: relation with features of the metabolic syndrome and glycemic control. *Endocr Res*. 2014;40(3):160-5.
9. Orces C. Vitamin D status among older adults residing in the Littoral and Andes Mountains in Ecuador. *Scientific World Journal*. 2015;2015:545297. doi: 10.1155/2015/545297. Epub 2015 Aug 2. <http://www.ecuadorencifras.gob.ec/censo-de-poblacion-y-vivienda/>. Acceso: 17 enero/2017.
10. American Diabetes Association. Diagnosis and Classification of Diabetes Mellitus *Diabetes Care*. 2012;35(Suppl 1): S64-S71.
11. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2011;96(7):1911-30.
12. Lips P, Hosking D, Lippuner K, Norquist JM, Wehren L, Maalouf G, et al. The prevalence of vitamin D inadequacy amongst women with osteoporosis: an international epidemiological investigation. *J Intern Med*. 2006;260:245-54.
13. González G, Alvarado JN, Rojas A, Navarrete C, Velásquez CG, Arteaga E. High prevalence of vitamin D deficiency in Chilean healthy postmenopausal women with normal sun exposure: additional evidence for a worldwide concern. *Menopause*. 2007;14(3 Pt 1):455-61.
14. Oliveri B, Plantalech L, Bagur A, Wittich AC, Rovai G, Pusioli E, et al. High prevalence of vitamin D insufficiency in healthy elderly people living at home in Argentina. *Eur J Clin Nutr*. 2004;58(2):337-42.
15. Arantes HP, Kulak CA, Fernandes CE, Zerbini C, Bandeira F, Barbosa IC, et al. Correlation between 25-hydroxyvitamin D levels and latitude in Brazilian postmenopausal women: from the Arzoxifene Generations Trial. *Osteoporos Int*. 2013;24(10):2707-12.
16. <https://www.iofbonehealth.org/vitamin-d-deficiency-and-insufficiency>. Acceso: 17 enero 2017.
17. Muscogiuri G, Nuzzo V, Gatti A, Zucconi A, Savastano S, Di Somma C, et al. Hypovitaminosis D: a novel risk factor for coronary heart disease in type 2 diabetes? *Endocrine*. 2016;51(2):268-73.
18. Isaia G, Giorgino R, Adami S. High prevalence of hypovitaminosis D in female type 2 diabetic population. *Diabetes Care*. 2001;24:1496.
19. Raška I Jr, Rašková M, Zikán V, Škrha J. high prevalence of hypovitaminosis D in postmenopausal women with type 2 diabetes *mellitus*. *Prague Medical Report*. 2016;117(1):5-17.
20. Zhang FF, Al Hooti S, Al Zenki S, Alomirah H, Jamil KM, Rao A, et al. Vitamin D deficiency is associated with high prevalence of diabetes in Kuwaiti adults: results from a national survey. *BMC Public Health*. 2016;16:100.
21. Al-Timimi DJ, Ali AF. Serum 25(OH) D in diabetes *mellitus* type 2: relation to glycaemic control. *J Clin Diagn Res*. 2013;7(12):2686-8.
22. Cheng S, Massaro JM, Fox CS, Larson MG, Keyes MJ, McCabe EL, et al. Adiposity, cardiometabolic risk, and vitamin D status: the Framingham heart study. *Diabetes*. 2010;59(1):242-8.
23. Alhumaidi M, Agha A, Dewish M. Vitamin D deficiency in patients with type-2 diabetes *mellitus* in southern region of Saudi Arabia. *Maedica (Buchar)*. 2013;8(3):231-6.
24. Suzuki A, Kotake M, Ono Y, Kato T, Oda N, Hayakawa N, et al. Hypovitaminosis D in type 2 diabetes *mellitus*: association with microvascular complications and type of treatment. *Endocr J*. 2006;53:503-10.
25. Kos E, Liszek MJ, Emanuele MA, Durazo-Arvizu R, Camacho P. Effect of metformin therapy on vitamin D and vitamin B<sub>12</sub> levels in patients with type 2 diabetes *mellitus*. *Endocr Pract*. 2012;18(2):179-84.
26. Holvik K, Ahmed LA, Forsmo S, Gjesdal CG, Grimnes G, Samuelsen SO, et al. Low serum levels of 25-hydroxyvitamin D predict hip fracture in the elderly: a NOREPOS study. *J Clin Endocrinol Metab*. 2013;98(8):3341-50.
27. Plotnikoff GA, Quigley JM. Prevalence of severe hypovitaminosis D in patients with persistent, nonspecific musculoskeletal pain. *Mayo Clin Proc*. 2003;78(12):1463-70.
28. Bischoff-Ferrari HA, Dawson-Hughes B, Willett WC, Staehelin HB, Bazemore MG, Zee RY, et al. Effect of vitamin D on falls: a meta-analysis. *JAMA*. 2004;291(16):1999-06.
29. Vestergaard P. Discrepancies in bone mineral density and fracture risk in patients with type 1 and type 2 diabetes a meta-analysis. *Osteoporos Int*. 2007;18(4):427-44.
30. Mezquita-Raya P, Muñoz-Torres M, Luna JD, Luna V, Lopez-Rodriguez F, Torres-Vela E, et al. Relation between vitamin D insufficiency, bone density, and bone metabolism in healthy postmenopausal women. *J Bone Miner Res*. 2001;16:1408-15.