Int J Biol Med Res.2016;7(2):5473-5476

Contents lists available at BioMedSciDirect Publications

International Journal of Biological & Medical Research

Journal homepage: www.biomedscidirect.com

Original Article

Serum 25-Hydroxyvitamin D in relation to Parathyroid Hormone, and Calcium Intake In Saudi Healthy Premenopausal Women. Short Title: Vitamin D, Parathyroid Hormone, and Calcium Intake

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ARTICLE INFO

Keywords:

ABSTRACT

Introduction: No information is available on dietary calcium intake among Saudi premenopausal women in relation to vitamin D status. Thus, the objective of the present study is to assess the inter-relations between dietary calcium intake, 25-hydroxyvitamin-D [25(OH)D] and PTH among Saudi healthy premenopausal women. Subjects and Methods: A total of 138 Saudi healthy premenopausal women living in the Jeddah area were studied. Each woman completed a questionnaire on life-style factors, anthropometric data and dietary calcium intake. Fasting blood samples were collected for the measurements of serum 25(OH)D, parathyroid hormone (PTH), calcium, phosphate and magnesium. Bone mineral density (BMD) was measured by a dual-energy X-ray absorptiometry. Results: All women showed vitamin-D deficiency (serum 25(OH)D < 50 nmol/L). Stratifying women by tertiles of daily dietary calcium intake showed that women with the lowest tertile exhibited significantly lower serum 25(OH)D (P<0.026), as compared with the group with the highest tertile. Stepwise multiple linear regression analysis showed that changes in serum 25(OH)D contributed to the variation in daily dietary calcium intake. Conclusions: Vitamin-D deficiency is common among Saudi healthy premenopausal women and such was associated with low daily dietary calcium intake. 3

1. Introduction

Adequate supply of cutaneous and/or dietary vitamin D is considered essential for bone health even though, it remains controversial how much of the vitamin is required for the maintenance of bone strength and prevention of osteofragility and/or fractures [1-3]. Vitamin D status can be determined by means of serum 25-hydroxyvitamin D [25(OH)D] measurements, however, a universal serum value constituting deficiency, insufficiency and/or sufficiency is still debatable [4,5]. A further difficulty in assigning a universal reference value arises from the multitude of contributory factors to calcium homeostasis. However, no consensus exists as to define the recommended vitamin D intake; this is partly due to considerable variation in serum 25(OH)D levels associated with any given serum PTH values and also the variations in the threshold levels [3,6]. Such variations could be related to: 1) the use of different methods for the measurements of both serum 25(OH)D and parathyroid hormone (PTH) as well as, defining baseline values [7]; 2) different dietary calcium intakes [8]; and 3) the characteristics of the population under investigation [9]. The interrelationship between calcium intake and vitamin D requirements has been recently documented but it was shown that calcium intake was not related to the maintenance of normal PTH values among individuals with serum 25(OH)D > 25 nmol/L [10,11]. The interrelationship between calcium intake and vitamin D requirements among Saudi women has not been studied previously. Thus, the main objective of the present study was: 1) to evaluate the relationship between dietary calcium intake, serum 25(OH)D and serum intact-PTH in relation to calcium homeostasis; and 2) to define the level of serum 25(OH)D associated with raised serum intact-PTH among the subjects studied. 4

SUBJECTS AND METHODS

Study design:

This is a cross-sectional study. A total of 138 healthy Saudi premenopausal women living in the Jeddah area were recruited from the pool of women attending the clinics at the Center of Excellence for Osteoporosis Research (CEOR) who were randomly selected during a health survey from 40 primary health care center scattered around the city of Jeddah. Women studied were medically examined and interviewed using a locally developed and validated standardized questionnaire to collect information on anthropometric parameters, life style habits, and level of physical

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activity in leisure time, and the use of vitamins and medications. Dietary calcium intake was calculated based on a locally validated food frequency questionnaire (FFQ) and included pictures of portion sizes with approximately 40 food items containing calcium included in the FFQ. Women with cancer or chronic diseases including osteoarthritis or established osteoporosis or with evident endocrine disorders (diabetes mellitus, hyperthyroidism, hyperparathyroidism, etc.) or on any form of drug treatment with possible effect on bone metabolism (e.g., calcitonin, glucocorticoids, anticonvulsants and/or thyroid hormones) were excluded from the final analysis. Women who reported a recent clinical fracture (within 2 years) were also excluded. In addition, all healthy women included in the present study exhibited: 1) normal blood counts; 2) normal values for renal creatinine; and 3) normal values for liver function tests. Accordingly, a total of 138 healthy premenopausal Saudi women (age range 20–39 years) living in Jeddah area, participated in the present study.

The study protocol was in agreement with CEOR ethical standards and the Helsinki D_e_c_l_a_r_a_t_i_o_n_ _o_f_ _1_9_7_5_,_ _a_s_ _r_e_v_i_s_e_d_ _i_n_ _1_9_8_9_._ _T_h_e_ _s_t_u_d_y_ _w_a_s_ _a_p_p_r_o_v_e_d_ _b_y_ _C_E_O_R_'s_ _H_u_m_a_n_ _R_e_s_e_a_r_c_h_ _&_ _Ethics Committee and informed written consent was obtained from all women participated in the present study. 5

Determination of Bone Mineral Density

Bone mineral density (BMD) (g/cm2) was determined for the anteroposterior lumbar spine (L1-L4) and mean of proximal right and left femur by dual-energy X-ray absorptiometry (DEXA) using LUNAR Prodigy Model, Lunar Corp., Madison, WI), according to standard protocol as described by the manufacturer.

Determination of Serum 25(OH)D, PTH and other analytes

Overnight fasting blood samples were collected in the morning between 8:00 – _11:00 hrs. under standardized conditions. Serum samples were stored at -85°C within 30 min after centrifugation at 2500 g for 10 min. The samples were stored until analyzed for the determinations of serum 25(OH)D, intact-PTH, minerals [serum calcium, phosphate and magnesium] and other biochemical analytes according to the manufac_t_u_r_e_r_'s_ _i_n_s_t_r_u_c_t_i_o_n_s_.__

Statistical Analysis

Results are presented as means (± SD) and categorical variables are expressed as frequencies. Data were analyzed using SPSS-Statistical Package (version 15.0 for Windows Smart Viewer) supplied by SPSS Inc. 2000, Mapinfo Corp. Tokyo, NY, USA. Results that were not normally distributed were log-transformed before analysis. Associations between continuous variables were e_x_a_m_i_n_e_d_ _b_y_ _P_e_a_r_s_o_n_'s_ _c_o_r_r_e_l_a_t_i_o_n_ _c_o_e_f_f_i_c_i_e_n_t_._ _A_N_O_V_A_ _w_a_s_ _u_s_e_d_ _t_o_ _e_x_a_m_i_n_e_ _d_i_f_f_e_r_e_n_c_e_s_ _a_m_o_n_g the groups for different variables. Independent relationships between vitamin-D status or dietary calcium intake and other variables were assessed by multiple regression and partial correlation analysis. Women were stratified by tertiles of dietary calcium intake (mg/day) and various variables were compared according to the tertiles for trending. 6

RESULTS

The main anthropometric and clinical characteristics of studied women are presented in Table 1. The mean age was 29.52 ± 5.79 years with a range of 20-39. About 26.8% of participants were obese (BMI > 30 kg/m2)__w_i_t_h__4_2_._1_%_ _c_l_a_s_s_i_f_i_e_d_ _a_s_ _o_v_e_r_w_e_i_g_h_t_ _(_B_M_I_ _≥_2_5_ _-< 30 kg/m2). Of participants studied, 14.2% performed high physical activities compared to 58.0% with sedentary lifestyle and 13.5% had v_i_t_a_m_i_n_ _D_ _s_u_p_p_l_e_m_e_n_t_a_t_i_o_n_ _(_≥ 4_0_0_I_U_/_d_a_y_)_._ _T_h_e_ _m_e_a_n_ _d_a_i_l_y_ _d_i_e_t_a_r_y_ _c_a_l_c_i_u_m_ _intake in the studied women was 431.9 ± 110.1 mg/day (Table 1), and when data were analyzed by class of dietary calcium intake (<600, 600-1_0_0_0_ _a_n_d_ _≥ 1_0_0_0_ _m_g_/_d_a_y_)_,_ _t_h_e_ _p_e_r_c_e_n_t_a_g_e_ _o_f_ _s_u_b_j_ects with a low calcium intake (<600 mg/day) was 90.6%. The overall mean (± SD) calculated sun exposure index was 3.58 ± 2.57. The overall mean (± SD) serum 25(OH)D level was 30.34 ± 6.18 nmol/L. All women studied exhibited serum 25(OH)D levels < 50.0 nmol/L. However, none of the women had severe vitamin D deficiency [serum 25(OH)D < 12.5 nmol/L)] but 36 (26.1%) women were with moderate vitamin D deficiency (_≥ 1_2_._5_ _-<25.0) and 73.9% were considered to be with mild vitamin D deficie_n_c_y_ _[_≥2_5_._0_ _-<50.0 (25(OH)D)], respectively.

When stratifying participants by tertiles of daily dietary calcium intake, the group with the lowest intake (< 380 mg/day) showed significantly lower serum 25(OH)D (P<0.026), compared with the group with the highest dietary calcium intake (>1000 mg/day), respectively (Table 2).

Significant positive correlations were evident between serum 25(OH)D levels and dietary calcium intake (r=0.268; P<0.000); serum intact-PTH showed significant positive correlations with age (r=0.263; P<0.010) and negative correlations with serum 25(OH)D (r=-0.111, not significant), respectively.

Stepwise multiple linear regression analysis was performed including all participants (n = 138) in the analysis. When daily dietary calcium intake (mg/day) was the dependent variable, only serum 25(OH)D significantly contributed to the variation. Conversely, when serum 25(OH)D was the dependent variable, dietary calcium intake, serum intact-PTH, and age contributed significantly to the changes in serum 25(OH)D levels. 7

Table 1: Demographic and anthropometric characteristics of the studied healthy premenopausalwomen

Variables	Number =138
Age(yrs)	29.52 –5.80
Parity	3.06 –2.59
Body mass index(Kg/) m^2	27.37 –5.17
Calcium intake(mg/day)	431.9 –110.1
Sun exposure time(h/day)	0.77 –0.53
Sun exposureindex	3.58 –2.57
Serum FSH(U/L)	3.40 –1.26
Serum LH(U/L)	7.31 –1.78
Serum E_2(pmol/L)	394.9 –77.6
Serum 25(OH)D(nmol/L)	30.34 –6.18
Serum intact-PTH(pmol/L)	2.66 –0.69

Serum calcium(mmol/L)	2.38 –0.11
Serum phosphate(mmol/L)	1.24 –0.15
Serum magnesium(mmol/L)	0.805 –0.095
BMD(g/cm^2):	
Lumbar spine (L_1-L_4)	1.034 –0.288
NeckFemur	0.922 –0.256

Data are presented as mean ± SD, BMI = body mass index; BMD = bone mineral density; sun exposure index was calculated using the number of hours per week spent outside without sun protection multiplied by the percentage of the body service area exposed tosunlight.

Table 2: Age, body mass index, dietary calcium intake and other variables stratified by tertiles of daily dietary calcium intake among healthy premenopausal womenstudied.

Variable	Tertiles of calcium intake(mg/day)			P-value (fortrending)
	T_1 (n=46)	T_2 (n=44)	T_3 (n=48)	
Age(yrs)	28.59 –5.71	30.41 –5.89	29.60 –5.78	0.329
Parity	2.87 –2.53	3.32 –2.97	3.00 –2.30	0.704
Body mass index(Kg) m^2	28.02 –5.19	26.71 –5.74	27.35 –4.61	0.491
Calcium intake(mg/day)	329.4 –30.6	413.6 –16.7	547.1 –100.1	0.0001
Serum FSH(U/L)	3.15 –1.07	3.45 –1.21	3.59 –1.43	0.215
Serum LH(U/L)	7.25 –1.70	7.28 –1.89	7.40 –1.83	0.918
Serum E$_2$(pmol/L)	399.1 –80.7	372.9 –77.1	411.1 –71.7	0.061
Serum 25(OH)D(nmol/L)	28.30 –5.87	31.69 –6.63	31.04 –5.65	0.026
Serum intact-PTH(pmol/L)	2.61 –0.69	2.58 –0.61	2.78 –0.74	0.311
Serum calcium(mmol/L)	2.39 –0.09	2.35 –0.11	2.39 –0.10	0.092
Serum phosphate(mmol/L)	1.24 –0.14	1.23 –0.18	1.23 –0.15	0.949
Serum magnesium(mmol/L)	0.783 –0.087	0.813 –0.103	0.818 –0.094	0.166
BMD(g/cm^2):				
Lumbar spine (L_1-L_4)	1.029 –0.258	1.01 –0.298	1.06 –0.309	0.728
NeckFemur	0.911 –0.227	0.199 –0.275	0.935 –0.270	0.903

DISCUSSION

The present study examined the extent of vitamin deficiency and/or insufficiency together with dietary calcium intake and serum 25(OH)D levels in relation to changes in serum intact-PTH among Saudi healthy premenopausal women. It is known that PTH is a major regulator of calcium and phosphate levels and is considered to be the most reliable marker of inadequate calcium availability, and itself is modulated by calcitriol and serum calcium [8,9]. Thus, vitamin-D deficiency or insufficiency or calcium deficiency are generally associated with an increase in PTH levels, however, the relative contribution of each nutrient to these processes are still under investigation and has not been studied previously in Saudi premenopausal women.

In Saudi healthy premenopausal women, vitamin D deficiency and insufficiency were common: all participants exhibited serum 25(OH)D levels that are commonly considered to represent deficiency (< 50.0 nmol/L), and with no women studied s_h_o_w_i_n_g_ _l_e_v_e_l_s_ _o_f_ _s_u_f_f_i_c_i_e_n_c_y_ _(_≥ _7_5_._0_ _nmol/L). These results have several important implications and demonstrate the deleterious effects of vitamin D deficiency on bone health among the studied premenopausal women. In addition, the present results are concurrent with previous studies in Caucasians [12-15], Asians [16,17] and others [18] confirming the observation that vitamin D deficiency and/or insufficiency is endemic among populations of the world, and countries with sunny climates throughout the year are no exception.

In the present study, daily dietary calcium intake is low, reflecting the common dietary pattern among Saudi healthy premenopausal women: this is consistent with the few studies published previously in Arabian populations showing inadequate intake of this nutrient [19,20] which is much lower than that observed in Caucasian [21] or Asian, (e.g. [16,22]) populations. Further, the dietary calcium intake of the present study failed to meet the recommended daily intake for calcium in the majority of subjects [21].

The results of the present study are similar to those described by Adami et al [11], but contrast from that described by Steingrimsdottir et al [10] with some relevant differences: some 8

interaction was evident with age and the effect of calcium intake was more obvious at all serum 25(OH)D levels. Such differences are possibly explained by: 1) the low dietary calcium intake obtained for Saudi women which was much lower than that described for Icelanders [10], and other European [3] populations; and 2) the high prevalence of vitamin-D deficiency and/or insufficiency among Saudi women.

The strengths of the present study include its very strict detailed inclusion criteria including BMD measurements. Furthermore, both serum 25(OH)D and intact-PTH levels were determined independently by laboratory services at CEOR in a blinded manner. The main limitations of the present study were, its cross-sectional design, and hence not sufficient to demonstrate casualty and was based on a single assay of 25(OH)D and intact-PTH levels. The possibility of selection bias also arises. Finally, the accuracy of self-reported data related to lifestyle factors may have been subject to report bias, such that these may be unrecognized confounding.

In conclusion, vitamin D deficiency [serum 25(OH)D < 50 nmol/L] is very common among Saudi healthy premenopausal women. Further, the present study, together with previous reports [10-11], indicate that the optimum levels of serum 25(OH)D are influenced by age and dietary calcium intake. With the emerging evidence that vitamin D sufficiency may be linked to the prevention of several health conditions including cardiovascular diseases, autoimmune diseases, common cancers and pregnancy and its outcomes; it is essential that further studies are required to review recommendations for vitamin D nutrition and to identify the appropriate preventive practical measures to remedy vitamin D deficiency among Saudi healthy women. 9

References

1. Holick MF (2004). Sunlight and vitamin-D for bone health and prevention of autoimmune diseases, cancers, and cardiovascular disease. Am J Clin Nutr 80: 1678S-1688S.
2. Holick MF (2009). Vitamin-D status: measurement, interpretation and clinical application. J Am Epidemiol 19: 73-78.
3. Scientific Advisory Committee on Nutrition. Update on vitamin-D (2007), TSO (The Stationery Office), Norwich UK, pp. 1-68.
4. Lips P (2004). Which circulating level of 25-hydroxyvitamin D is appropriate? J Steroid Biochem Mol Biol 89-90: 611-614.
5. Holick MF (2007). Vitamin D deficiency. N Engl J Med 357: 266-281.
6. Dawson-Hughes B, Heancy RP, Holick MF, Lips P, Meunier PJ, Vieth R (2005). Estimates of optimal vitamin D status. Osteoporos Int 16: 713-716.

7. Lips P, Chapuy MC, Dawson-Hughes B, Pols HA, Holick MF (1999). An international comparison of serum 25-hydroxyvitamin D measurements. Osteoporos Int 9: 394-397.

8. Heaney RP (2002). Ethnicity, bone status, and the calcium requirement. Nutr Res 22: 153-178.

9. Heaney RP (2005). The vitamin D requirement in health and disease. J Steroid Biochem Mol Biol 97: 13-19.

10. Steingrimsdottir L, Gunnarsson O, Indridason OS, Franzson L, Sigurdsson G (2005). Relationship between serum parathyroid hormone levels, vitamin D sufficiency, and calcium intake. JAMA 294: 2336-2341.

11. Adami S, Viapiana O, Gatti D, Idolazzi L, Rossini M (2008). Relationship between serum parathyroid hormone, vitamin D sufficiency, age, and calcium intake. Bone 42: 267-270.

12. Lips P, Duong T, Oleksik A, Black D, Cumming S, Cox D, Nickelsen T (2001). A global study of vitamin D status and parathyroid function in postmenopausal women with osteoporosis: baseline data from the multiple outcomes of raloxifene evaluation clinical trial. J Clin Endocrinol Metab 86: 1212-1221.

13. Lamberg-Allardt CJ, Ontila TA, Karkkainen MU, Rita HJ, Valsta MA (2001). Vitamin D deficiency and bone health in healthy adults in Finland: could this be a concern in other parts of Europe? J Bone Miner Res 16: 2066-2073.

14. Kudlacek S, Schneider B, Peterlik M, Leb G, Klaushofer K, Weber K, Woloszczuk W, Willvonseder R (2003). Assessment of vitamin D and calcium status in healthy adult Austrians. Eur J Clin Invest 33: 323-331.

15. Saquib N, vonMuhlen D, Garland CF, Barrett-Connor E (2006). Serum 25-hydroxyvitamin D, parathyroid hormone and bone mineral density in men: the Rando Bernardo Study. Osteoporos Int 17: 1734-1741.

16. Nakamura K (2006). Vitamin D insufficiency in Japanese populations: from the viewpoint for the prevention of osteoporosis. J Bone Miner Metab 24: 1-6. 10