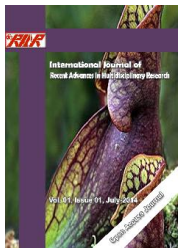

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Full Length Research Article

VITAMIN D STATUS IN SAUDI WOMEN WITH TYPE 2 DIABETES MELLITUS: A CASE-CONTROL STUDY

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ABSTRACT

Background: Vitamin D deficiency is a risk factor for type 2 diabetes mellitus (DM). Both hypovitaminosis D and Type 2 DM are prevalent health problems among Saudi population. Ethnic and gender differences in the association between vitamin D status and type 2 DM were reported. Therefore, the aim of the present study was to determine vitamin D status in Saudi diabetic women as compared to that of age and BMI matched healthy women.
Methods: A total of 120 women, 60 diabetic and 60 age and BMI matched control, were enrolled for this study. Fasting blood samples were collected from all participants and serum was stored at -80ºC until assayed. 25- hydroxyvitamin D [25(OH)D] was measured using chemiluminescent immunoassay.
Results: Hypovitaminosis D was prevalent among both diabetic and control groups. However, mean 25(OH)D level was lower in the diabetic group (30.45nmol/L) as compared to the control group (34.36nnmol/L) although not statistically significant. Vitamin D deficiency (defined as 25(OH)D level < 25 nmol/L) was more common among the diabetic group, but this did not reach statistical significance (P= 0.708).
Conclusion: Although the diabetic women had lower levels of 25(OH)D, vitamin D deficiency was prevalent in both groups. Larger longitudinal studies are required to reveal any relation between hypovitaminosis D and type 2 DM among Saudi subjects.

INTRODUCTION

Hypovitaminosis D is a risk factor for many chronic diseases including type 2 diabetes mellitus (DM) (Wacker *et al*., 2013). Both Type 2 DM (Alhowaish *et al*., 2013), and vitamin D deficiency (Ardawi *et al*., 2010, Ardawi *et al*., 2012), are common health problems among the Saudi population. Diabetes mellitus is a chronic disease with major cause of significant morbidity and mortality and its prevalence in Saudi Arabia is increasing (Al-Daghri *et al*., 2011). Therefore, identifying risk factors that can be easily modified is of paramount importance in reducing the incidence of the disease or at least hampering its development. Increasing evidence support the fact that low vitamin D status may play a role in the development of type 2 DM (Pilz *et al*., 2013). The presence of vitamin D receptors on pancreatic β-cell suggests a direct action on these cells (Johnson *et al*., 1994). Several mechanisms of action of the active form of vitamin D on beta cells of the pancreas had been described (Pittas *et al.,* 2007). These include stimulation of insulin secretion, enhancing insulin sensitivity or indirectly through the role of vitamin D in regulating extracellular calcium. Several observational studies reported low vitamin D level in patients with type 2 DM as reviewed by (Pittas *et al.,* 2007*)*. Moreover, evidence from clinical trials with vitamin D/calcium supplementations suggests a possible role in prevention of the DM development Pittas *et al*., (2007). However, ethnic (Scragg *et al*., 2004) as well as gender (Stadlmayr *et al., 2014*) differences in the association between vitamin D deficiency and type 2 DM were reported. Since few data is available on the extent of vitamin D deficiency in Saudi women with type 2 DM, the aim of this study was to determine vitamin D status in women with type 2 diabetes as compared to that of healthy, age and BMI matched women.

MATERIALS AND METHODS

A total of 120 women, 60 with type 2 diabetes mellitus and 60 age and BMI matched controls, were enrolled for this study. Diabetic subjects were referred from the Diabetes clinic at "King Abdulaziz University Hospital" (KAUH) to the "Center of Excellence for Osteoporosis Research" (CEOR) for the evaluation of bone health. An informed consent was obtained from all participants and the study was approved by the Human

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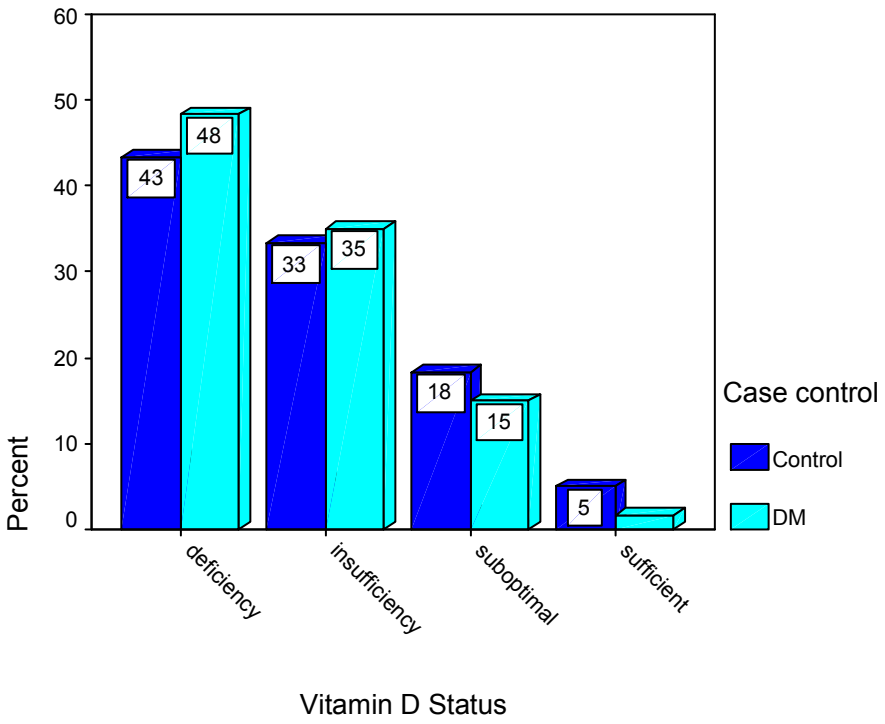

Figure 1. Categories of vitamin D status in the diabetic and control groups (n=120). Vitamin D deficiency is defined as 25(OH)D level <25 nmol/L, insufficiency as a level between 25-<50 nmol/L, suboptimal as a level between 50-<75 nmol/L and sufficient as a level ≥75 nmol/L.

Ethics Research Committee at CEOR. Those with any diabetic complications, or with any medical illness other than diabetes, and patients on any medications that may affect bone metabolism (e.g. corticosteroids, antiepileptic, or calcitonin) were excluded from the study. The control group was randomly selected from apparently healthy women attending CEOR for routine screening. Demographic data were collected for all subjects. Weight, height, hip circumference and waist circumference were recorded. Body mass index (BMI) in Kg/m^2 and waist: hip ratio (WHR) values were calculated. Fasting blood samples (12 hours) were collected from all participants and serum was stored at -80ºC until assayed. Twenty five- hydroxyvitamin D [25(OH)D] was measured using chemiluminescent immunoassay system (DiaSorin Inc., Stillwater, MN, USA).

Statistical analysis

Data are presented as means ± SD. Categorical variables are expressed as frequency and percentage. Comparison between groups was done using independent student T-test for continuous variables. Chi-square or Fisher's exact test was used to examine association between categorical variables. For all comparisons, P values of <0.05 were considered as statistically significant. Statistical analyses were carried out using SPSS (version 20.0; SPSS, Chicago, IL, USA).

RESULTS

Demographic and anthropometric characteristics of the study groups are presented in Table 1. BMI values in both groups were in the obese range. Mean 25(OH)D levels were lower in the diabetic group as compared to the control group (30.45±17.96 nmol/L vs. 34.36±21.68 nmol/L, respectively) but this did not reach statistical significance (p>0.05). Women in both groups were classified according to their 25(OH)D status. Vitamin D deficiency was defined as 25(OH)D level <25 nmol/L, insufficiency as a level between 25-<50 nmol/L, suboptimal as a level between 50-<75 nmol/L and sufficient as a level ≥75 nmol/L. Figure (1) shows vitamin D status in both diabetic and control groups. Levels less than 50 nmol/L were prevalent among 83% of the diabetic women as compared to 76% in the control group. Although vitamin D deficiency (25(OH)D<25 nmol/L) was more common among the diabetic group (48% vs. 43%), this did not reach statistical significance (P= 0.708).

Table 1. Clinical characteristics of the study group with and without diabetes

Variables	DM N=60	Control N=60	P value
Age (year)	55.2 (8.0)	55.3 (8.2)	NS
Weight (kg)	78.0 (13.9)	79.2 (13.6)	NS
Height (m)	1.53 (0.1)	1.55 (0.1)	NS
BMI (kg/m^2)	33.1 (5.6)	32.8 (5.2)	NS
WC (cm)	97.0 (10.6)	93.0 (12.1)	NS
HC (cm)	109.3 (9.6)	110.8 (11.8)	NS
WHR	0.89 (0.06)	0.84 (0.08)	NS

Values are means (S.D.); BMI, body mass index; WC, waist circumference; HC, hip circumference; WHR, waist to hip ratio; NS, non significant.

DISCUSSION

Evidence is accumulating on the role of vitamin D in the pathogenesis of type 2 DM (Mezza et al, 2012). In a recent meta-analysis of prospective studies, a significant inverse association was demonstrated between 25(OH)D level and the incidence of type 2 DM (Song et al, 2013). Another study showed that increasing the intake of vitamin D to 8oo IU with adequate calcium intake, lowered the risk of developing type 2 DM by 33% (Pittas et al., 2007).

Moreover, in a longitudinal study with a median of 15 years of follow up, severe vitamin D deficiency (25(OH)D levels <13.9 nmol/L), in type 2 DM patients predicted an increase risk of all-cause mortality (Joergensen et al., 2010). A high prevalence of vitamin D deficiency among both diabetic and control groups was seen in the present study. This is in agreement with the reported high prevalence of hypovitaminosis D among the Saudi population in general (Ardawi *et al*., 2011, Alfawaz *et al*, 2014; Kanan *et al*., 2013). Factors contributing to this high prevalence in a sunny country include limited sun exposure due to high temperatures, conservative clothing, physical inactivity, dark skin, and dietary habits. One of the earliest studies that reported a lower 25(OH)D level among diabetic patients was that by Pietschmann *et al*. (1988). The present study failed to show a statistically significant difference in 25(OH)D level between the diabetic and control groups. Although vitamin D deficiency was common in both groups, its prevalence was higher among the diabetic group (48% vs. 43%) who had lower mean 25(OH)D levels, albeit non-significant. These results are in agreement with other case-control studies conducted on different populations.

Bachali *et al* (2013) reported a significantly lower level of 25(OH)D in diabetic (50.2 nmol/L) as compared to non-diabetic subjects (59.7 nmol/L) of both sexes. Mean 25(OH)D levels for both groups were higher than those found in the present study, despite the fact that Indians are at known risk for vitamin D deficiency due to their dark skin color. These relatively high levels cannot be explained especially that the authors clearly stated that women on vitamin D supplementation were excluded (Bachali *et al*, 2013). Similar findings of lower 25(OH)D level among diabetics as compared to controls were found in a Lebanese (Ahmadieh *et al*., 2013), Chinese (Guo *et al*., 2013) and Iranian (Bayani *et al*., 2014), populations, although in the latest study, this difference was only noted in female subjects. On the other hand, in a Saudi study conducted in the central region of Saudi Arabia, Al-Daghri *et al*., (2010) reported a higher level of 25(OH) D in the diabetic group rather than the non-diabetic, although both groups were in the deficient range. However, in this study the non-diabetic group was not matched to the diabetic group and the non-diabetic women were younger (mean age 39 years, n=106 female) and had lower BMI (mean 29 kg/m2) as compared to the diabetic group (mean age 49 years, n=76 and mean BMI 34kg/m2). The authors suggested that this was probably due to the intake of multivitamins supplementation (containing 400 IU of vitamin D) that diabetic women are routinely prescribed and the intake of lipid lowering medications that are known to increase 25(OH) D levels (Yavuz *et al*., 2009)

The present study has its limitations. The study included a relatively small number of subjects and the failure to detect a statistically significant difference could possibly be due to a low power analysis. Larger longitudinal studies are required to reveal any relation between hypovitaminosis D and type 2 DM among the Saudi population. If such studies proved that vitamin D deficiency is more prevalent among diabetic patients, further intervention studies with vitamin D supplementation given to vitamin D deficient subjects with high risk to develop diabetes e.g. those with insulin resistance or with family history of diabetes, would be worthwhile. If vitamin D supplementation proved to be of value in reducing the risk of developing diabetes, a recommendation of vitamin D supplementation would be sound in subjects with increased risk to develop diabetes. Therefore, our findings may not be generalizable to other populations. To conclude, the present study revealed non-significant and marginally lower 25(OH)D levels among diabetic women as compared to their age and BMI matched control group. Larger scale studies are needed to confirm these findings. Prospective studies are also required to further examine the true association between vitamin D deficiency and the incidence of type 2 DM. If this was the case, repletion of vitamin D status in deficient subjects that are at risk of developing DM, is a simple and cost effective measure to reduce the incidence of such a serious disease.

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