Vitamin D Status among Patients Attending Hussein Medical Center for Diabetes in Jordan

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ABSTRACT

Objective: Vitamin D is a steroid fat soluble vitamin, in which deficiency is highly prevalent world wide and has been linked to many diseases. The aim of this study is to assess vitamin D status, and factors associated with low serum level of vitamin D in a sample of patients attending Al-Hussein Medical Center for Diabetes in Salt Hospital.

Methods: This is a retrospective study which was done on subjects attending Al-Hussein Medical Center for Diabetes during the period between 1st of June 2011 and 30th of October 2012 who were routinely assessed for vitamin D during this period. The total sample size was 590 subjects, divided into two groups, group one (340) subjects with type 2 diabetes and group 2 (250) subjects without diabetes, excluding from the sample pregnant women and all patients with problems related to vitamin D deficiency. A specially designed medical record form was used to collect the relevant data.

Results: Vitamin D level less than 30 ng/mL was found in 71.7% of subjects. Calcium, phosphorous, albumin, parathyroid hormone and cholesterol were normal in the majority of the subjects. Low serum vitamin D level (< 30ng /mL) was seen in 68.2%, and in 76.4% of group 1 and group 2 respectively, (p=0.000). Obese subjects showed low serum vitamin D in both groups (71.1% and 77.2% respectively). About 79% of group 1 and 83% of group 2 with history of infrequent exposure to sun showed low serum vitamin D (p=0.000) and 13.5% in group 1 and 12.8% in group 2 gave history of infrequent intake of milk and dairy product. Subjects wearing hijab or nigab in both groups had low serum vitamin D (80.4%, 82.4%, p=0.000 respectively).

Conclusion: Low serum vitamin D level is highly prevalent among both groups, and the most important risk factors for low serum vitamin D level were the lack of sun exposure and dressing style. National plan for education, screening and control of risk factors associated with vitamin D deficiency is highly recommended.

Key words: Diabetes Mellitus type 2, Dressing style, Sun exposure, Vitamin D

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Introduction

Vitamin D is a steroid fat soluble vitamin that maintains calcium and phosphorus homeostasis and promotes bone mineralization.[1] It is produced endogenously when the skin is exposed to sun light and can be obtained exogenously from food such as fish, eggs, vitamin D fortified milk, cod liver oil and from vitamin supplements. There are two main forms of vitamin D. Vitamin D3 (Cholecalciferol) which is synthesized in the skin through UVB (ultraviolet exposure) and is also presented in some kinds of food such as oily

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fish and fortified dairy products. Vitamin D2 (Ergocalciferol) mainly available in plants after exposure to UVB. Skin production of vitamin D depends on: the time spent outdoors , covering of the skin with clothing and sun screen, skin colour, season of the year, and latitude such that, little or no vitamin D is produced during winter months. Vitamin D, whether endogenous or exogenous, is converted in the liver to 25-hydroxy vitamin D (25(OH) D) which is the best indicator of vitamin D status. Vitamin D deficiency in adults leads to mineralization defect in the skeleton, causing osteomalacia and induces secondary hyperparathyroidism with consequent bone loss and osteoporosis.[2] Vitamin D deficiency is highly prevalent worldwide and affects one billion people worldwide as deduced from several studies.[3,4] Diabetes mellitus is a global problem associated with considerable morbidity and mortality. The incidence of type 2 DM is increasing at an alarming rate both nationally and worldwide. To date, around 250 million people worldwide are living with diabetes and by 2025 this total is expected to increase to over 380 million.[5] There is accumulating evidence to suggest that altered calcium and vitamin D homeostasis may play role in the development of type 2 diabetes.[6] The role of Vitamin D is suggested by cross–sectional studies showing that low serum 25-hydroxy-Vitamin D concentration is associated with glucose intolerance diabetes insulin resistance, and the metabolic syndrome. The role of calcium in the development of type 2diabetes is suggested indirectly by cross – sectional studies in which high calcium intake has been found to be inversely associated with body weight and fatness.[6] Epidemiological research suggests that low Vitamin D intake is associated with greater risk of type 2 diabetes.[7] Vitamin D may reduce disease risk by promoting insulin sensitivity as suggested by in vitro studies and association of 25 (OH) D with insulin sensitivity.[7] Vitamin D deficiency is highly prevalent in United States, Europe and even in sunny countries. Vitamin D deficiency is common with about 30-50% of adults in Turkey, India, Lebanon, and Saudi Arabia who had Vitamin D deficiency below 20 ng/ml.[8,9] Regarding the definitions of Vitamin D, if serum level of 25 (OH) D is < 20ng/ml it is considered as deficiency, and a level between 20 and 29 are considered insufficient, and level ≥30 is considered sufficient and serum 25(OH) D levels are inversely associated with parathyroid hormones levels.[10]

The aim of this study was to assess vitamin D status, and factors associated with low serum level of vitamin D in a sample of patients attending Al-Hussein Medical Center for Diabetes (HMCD) in Salt Hospital.

Methods

This is a retrospective study which was done on subjects attending Al-Hussein Medical Center for Diabetes during the period between 1st of June 2011 and 30th of October 2012, including all subjects attending HMCD whether having type 2 DM, hypertension, dyslipidemia, and obesity and had their Vitamin D routinely assessed during the study period. No criteria were used by the attending physicians in ordering the laboratory measurement of Vitamin D for their patients, but recently, they tended to carry out the measurement in all patients with no previous measurements of Vitamin D. The investigators excluded pregnant and lactating women, patients with hepatic and renal failure, and those on corticosteroid and anticonvulsant drugs, malabsorption disorders, and type 1 DM.

A total of 590 subjects were included in the study and divided in to 2 groups: group 1 consisted of 340 subjects with type 2 DM, and group 2 consisted of 250 subjects without DM. The following data were collected, relevant socio-demographic data such as age, gender, and smoking status, current medical problem as type 2DM, hypertension, dyslipidemia, and obesity, anthropometric data as height, weight, body mass index (BMI), waist circumference, and blood pressure, and finally laboratory data as FBS, HbAIC, 25 (OH) Vitamin D level, cholesterol, low density lipoprotein-cholesterol (LDL-c), high density lipoprotein-cholesterol (HDL-c), triglyceride (TG), albumin and parathyroid hormone (PTH). Criteria for diagnosis of diabetes mellitus were symptoms (polyuria, polydipsia, and unexplained weight loss) plus causal plasma glucose concentration ≥200 mg/dL (11.1 mmol/L), FPG ≥ 126 mg/dl (7 mmol/L) and HBAIC ≥6.5. Height and weight measured while patients were wearing light clothes and after taking the shoes off. The BMI was calculated as

the ratio of weight in kilograms to the square of height in meters and was classified according to WHO criteria,[11] normal BMI if <25, overweight if BMI 25-29.9, and obese when BMI ≥30. Lipid level considered abnormal according to American Diabetic Association (ADA) criteria 2011.[12] Hypercholesterolemia was considered if total cholesterol was ≥200mg /dL, HDL was considered low if level was <40 mg/dL in males or < 50 mg/dL in females. LDL considered high if level ≥100 mg/dL and hypertriglyceridemia if TG level ≥150 mg/dl. The patient was diagnosed as dyslipidemic when one or more of the previous abnormalities exist. Hypertension is defined when average of 3 readings revealed, systolic blood pressure (SBP) ≥130 mm Hg and diastolic blood pressure (DBP) ≥80 mmHg. Patients were considered to have good glycaemic control when AIC < 7%, fair control with 7-8.5% and poor control with >8.5% according to (ADA) 2011.[13] Vitamin D level ≥30ng/mL (normal) and <30 ng/mL (low), serum 25(OH)D concentration were determined by radioimmunoassay (BIOSOURCE Europe S.A., Nivelles, Belgium).[14] Waist circumference normal < 102 cm for men and < 88 cm for women, sun exposure frequent if one or more times per day (exposed to sun at least 15 minutes 10-15 % of body exposed, and infrequent if less than one time per day, and finally milk and dairy product intake considered frequent if one cup of milk (250mL) or more per day and infrequent if less than one cup per day.

The study was approved by the HMCD ethical committee and data were used for scientific purposes only. The data were entered and analyzed using SPSS 11 (The statistical package for social science, PC version) computer soft ware. Descriptive statistics were obtained, such as mean values for continuous variables and proportions for categorical variables; chi- square analysis was performed to test for differences in proportions of categorical variables between groups. P value < 0.05 was considered as the cut – off value for significance.

Results

The demographic and relevant characteristics of subjects attending HMCD are shown in Table I. The total number of study population was 590, of them 340 (57.6%) considered as group 1 with type 2 diabetes, and 250 (42.4%) were group 2 without diabetes, the majority were 40 years or older, 64.2% of them were females and 35.8%were males. Concerning vitamin D level 71.7% had low serum vitamin D (vitamin D < 30 ng/mL) whereas 18.1% had severe vitamin D deficiency (vitamin D < l0 ng/mL). Only 25.6% gave a history of frequent sun exposure, whereas 74.4% gave a history of infrequent exposure to sun light. More than half of the sample female population were wearing hijab or nigab (59.5%) and 40.5% were wearing Western dress style.

Regarding milk and dairy products intake, 86.8% gave history of frequent intake, 87.1% of the population had abnormal waist circumference, and 91.4% of them were obese. As shown in Table I, 50.9% of group one with type 2 DM were females, whereas 49.1% were males, and most of them (60.9%) were between 40-60 years, low serum vitamin D level was seen in 68.5% and 14.1% of them had severe deficiency, obesity was seen in 91.5% of group 1, 69.7% gave history of infrequent exposure to sun and another 86.5% gave history of frequent milk and dairy product intake. Regarding group 2 without DM, female constituted 82.4% whereas 17.6% of them were males, low serum vitamin D level (30 ng/mL) was seen in 76% of them and 23.6% of them had severe deficiency, obesity was nearly the same as in group one. About 81% gave history of not being exposed to sun, and 12.8% with infrequent milk and dairy product intake. Table II represents current medical and biochemical characteristics of the whole study group. Hypertension which accounts for 54.9% of the study population, 83.1% were dyslipidemic, good glycaemic control was noticed in 34.7% of group one with type 2 DM, the level of calcium, phosphorous, albumin and parathyroid hormone were normal in the majority of the study subjects population. Hypercholesterolemia was seen is 28.8%, whereas abnormal figures of low density lipoprotein and high density lipoprotein were seen in 54.6% and 61.4%, respectively.

Table III shows that, low vitamin D level in group 1 was 39.5%, while it was 32.2% in group 2. Low vitamin D level in group 1 was significant according to age, gender, smoking, body mass index, dressing style, and sun exposure.

Table I: Demographic and relevant characteristics of group1 with type 2 diabetes and group 2 subject attending HMCD (n=590)

Variables	Group 1 (No.=340) 57.6%		Group 2 (No.=250) 42.4%		Total No.	%	P-value Group 1 vs. Group 2
	No.	%	No.	%			
Age (year)							
<40	15	4.4	27	10.8	42	7.1	0.000
40-49	76	22.4	73	29.2	149	25.3	
50-59	131	38.5	102	40.8	233	39.5	
>60	118	34.7	48	19.2	166	28.1	
Means+ SD	55.25+9.54		50.96+10.31		53+10		
Gender							0.000
Male	167	49.1	44	17.6	210	35.8	
Female	173	50.9	206	82.4	380	64.2	
Smoking							0.000
Smoker	79	23.2	44	17.6	123	20.8	
Ex-Smoker	42	12.4	12	4.8	54	9.2	
Non-smokers	219	64.4	194	77.6	413	70	
Vitamin D level (ng/ml)							
<10	48	14.1	59	23.6	107	18.1	0.000
10-19	108	31.8	89	35.6	197	33.4	
20-29	77	22.6	42	16.8	119	20.2	
>30	107	31.5	60	24	167	28.3	
Vitamin D level (ng/ml)							
>30	107	31.5	60	24	167	28.3	0.004
<30	233	68.5	190	76	423	71.7	
BMI (kg/m^2)							
≥30	29	8.5	22	8.8	51	8.6	0.736
<30	311	91.5	228	91.2	539	91.4	
History of sun exposure							
Frequent	103	30.3	48	19.2	151	25.6	0.000
Infrequent	237	69.7	202	80.8	439	74.4	
*Milk & dairy product intake							
Frequent	294	86.5	218	87.2	512	86.8	0.596
Infrequent	46	13.5	32	12.8	78	13.2	

*Frequent milk intake (one cup or more per day) infrequent(less than one cup per day)

Table II: Current medical and biochemical characteristics of subjects attending HDMC (n =590)

Group 1 type 2 DM	340	57.6%
Group 2 without Type 2 DM	250	42.4%
Hypertension		
Yes	324	54.9%
No	266	45.1%
Dyslipidemia		
Yes	490	83.1%
No	100	16.9%
HbA1c for group 1 with type 2 DM		
<7 % Control	118	34.7%
7-8.5 % Fair control	133	39.1%
>8..5 % Poor control	89	26.2%
Calcium mg/dl		
Normal (8.5-10,5mg/dl)	551	93.4%
Low (<8.5mg/dl)	17	2,9%
High (>10mg/dl)	22	3.7%
Phosphorous mg/dl		
Normal (2.6-4.5mg/dl)	522	88.5%
Low (<2.6mg/dl)	28	4.7%
High (>4.6mg/dl)	40	6.8%
Parathyroid hormone pg/ml		
Normal (9-55pg/ml)	354	60%
High (>55pg/ml)	236	40%
Cholesterol mg/dl		
Normal (<200mg/dl)	420	71.2%
Abnormal (>200mg/dl)	170	28.8%
Low density lipoprotein mg/dl		
Normal (<100 mg/dl)	268	45.4%
Abnormal (>100mg/dl)	322	54.6%
High density lipoprotein mg/dl		
Normal (M>40mg/dl,F>50mg/dl)	228	38.6%
Abnormal (M<40mg/dl,F<50mg/dl)	362	61.4%
Triglycerides mg/dl		
Normal (<150mg/dl)	337	57.1%
Abnormal (>150mg/dl)	253	42.9%
Albumin mg/dl		
Normal (34-48mg/dl)	531	90%
Low (<34mg/dl)	18	3.1%
High (>48mg/dl)	41	6.9 %

However, low vitamin D level in group 2 was significant according to the following variables studied, age, gender, smoking, sun exposure, and milk and dairy product intake.

Discussion

Analysis was conducted using data from the United States National Health and Nutrition Examination survey (2001-2006) on samples that included 15,431 adults aged ≥20yrs, results showed that the average serum Vitamin D concentration decreased steadily across the range of fasting serum glucose: normoglycemia (FSG<100mg /dL) Pre DM (FSG100-125mg /dL) and undiagnosed diabetes (FSG ≥126mg/dL) with mean concentration of 66.2, 66.3 and 54.2nmol/L respectively. Mean Vitamin D concentration was significantly lower in adults

Table III: The frequency and percentage of low serum vitamin D level (<30 ng/ml) among group 1 and group 2 according to socio- demographic and clinical characteristics.(n =590)

Variables	Low Vitamin D Level (<30ng/ml) in group 1 N =233			Low Vitamin D Level (<30ng/ml) in group 2 N =190		
	Number	**%**	**P-value**	**Number**	**%**	**P-value**
Age(year)						
<40	9	3.9		24	12.6	
40-49	56	24.0	0.00	61	32.1	.002
50-59	90	38.6		71	37.4	
≥60	78	33.5		34	17.9	
Gender						
Male	96	41.2	0.00	28	14.7	.000
Female	137	58.8		162	85.3	
Smoking						
Smoker	49	21.0		33	17.4	
Ex-Smoker	27	11.6	0.041	5	2.6	.001
Non-smoker	157	67.4		152	80	
Waist Circumference						
Normal (M<102cm, F<88cm)	16	6.9		33	14.7	
Abnormal (M≥102cm, F≥88cm)	217	93.1	0.002	157	82.6	.683
BMI(kg/m2)						
<30	12	5.2		14	7.4	
≥30	221	94.8	0.000	176	92.6	.938
Dress style						
Western	102	43.8		35	18.4	
Hijab and/or Niqab	131	56.2	0.000	155	81.6	.000
Hypertension						
Yes	144	61.8		79	41.6	
No	89	38.2	0.044	111	58.4	.589
Dyslipidemia						
Yes	199	85.4		148	77.9	
No	34	14.6	0.726	42	22.1	.091
History of sun exposure						
Frequent	46	19.7	0.000	23	12.1	0.000
In frequent	187	80.3		167	87.9	
Milk & dairy product intake						
Frequent	199	85.4	0.209	161	84.7	0.001
Infrequent	34	14.6		29	15.3	
Calcium mg/dl						
Normal	218	93.5		178	93.7	
Low	6	2.6	0.629	7	3.7	0.107
High	9	3.9		5	2.6	
Phosphorus mg/dl						
Normal	203	87.1		168	88.5	
Low	13	5.6	.613	13	6.8	0.710
High	17	7.3		9	4.7	
Parathyroid hormone g/ml						
Normal (9-55pg/ml)	132	56.7	.006	89	46.8	.010
High (>55pg/ml)	101	43.3		101	53.2	

with pre DM and undiagnosed diabetes compared with those with normoglycemia (p=0.004 and p=0.0002, respectively).[9,10]

In Arab countries, a hospital – based study in Saudi Arabia of 100 healthy male employees aged 25-35 yrs and 100 healthy male visitors aged 6-50 yrs reported low Vitamin D level i.e. 20ng/ml (28% of first group and 37% of the second group.[15] In Jordan, a study was conducted by Mishal [16] in which a total of 131 women and 23 men were enrolled in the Islamic hospital in Amman, with same clothing manner over 6-12 month, the study concluded that Vitamin D deficiency as a whole was 62.3%, with no significant differences between women, with different clothing styles. Women with clothing covering the whole body have adverse effects on 25- OHD level.[16] Another study to assess Vitamin D status among Jordanians was conducted at the national level, assessed in a sample of 5,640 subjects ≥25 yrs, the result showed that the prevalence of low Vitamin D status (25 (OH) D <30 ng/ml) was 37.3% in females compared to 5.1% in males.[17] Dress style in females was independently related to low Vitamin D status, women wearing hijab (OR = 1.7, p= 0.004) or nigab (OR = 1.5, p= 0.061) were at high risk for low Vitamin D status.[17]

Inconsistencies between studies may be due to different characteristics of study population. A study had shown independent association between 25 - (OH) D and risk of diabetes in non - Hispanic white and Mexican – Americans.[18] In our study, low serum vitamin D was highly prevalent in group 1 with type 2 DM subject (68.5%) with 14.1% of them with severe deficiency (< l0 ng /mL) and this is consistent with the study of Anoop *et al.*[19] which showed high prevalence of vitamin D deficiency (91.1%) in type 2 DM subjects with (35.5%) having serum deficiency (< l0 ng/mL). In our study, low serum vitamin D level was higher in females of both groups (58.8%, 85.3% respectively) vs. (41.2 %, 14.7%) males in both groups (p=0.000). and this result coincides with the study of Batieha *et al.* [17] in which prevalence of low vitamin D status (25 (OH) D < 30 ng /mL) was 37.3% in females compared to 5.1% in males. Prevalence of low serum vitamin D was higher among females wearing hijab compared with females wearing Western style dress (56.2% vs. 43.8% in group1 and 81.6% and 18.4% in group 2 without DM (p value < 0.000) and this result is similar to that of Batieha *et al.*[17] and Mishal.[16] Both studies showed that hypovitaminosis was more common in groups wearing hijab or nigab.

There was a significant association between body mass index and serum 25 - (OH) D, in group I with type 2 DM, but not in group 2 without DM (p=0.000 and p=0.938 respectively) and this also consistent with a study conducted by Worsman *et al.*[20] Waist circumference also showed a significant association with serum vitamin D in group I with type 2 DM but not in group 2 without DM (p=0.002 and p=0.683 respectively), and this was consistent with a study conducted by McGill *et al.*[21] Lack of sun exposure showed significant association with vitamin D level in both groups (p=0.000) respectively and this is similar to the study reported by Thomas *et al.*[22] Infrequent milk and dairy product intake showed significant association with low vitamin D level in group 2 without DM but not in group I with type 2 DM (p=0.001, p=0.209 respectively), and this is consistent with a study conducted by Pittas *et al.*[6] HbA1C showed a significant association with vitamin D level and it is also similar to the study reported by McGill *et al.*[21] (p=0.045). High parathyroid hormone level showed significant association with low vitamin D level in both study groups with significant association (p=0.006 and p=0.010 respectively) which is also consistent with the results of Souberbielle *et al.*[23]

Limitations of the Study

Patients with manifestation of vitamin D deficiency were more likely to have vitamin D level checked and this may overestimate rate of vitamin D deficiency in our study. The different gender composition between group 1 and group 2 may be interpreted as selection bias. Selection of the study group (group 1 and group 2) was not random, but all patients attending HMCD during the study period were included in the study.

Conclusion

Prevalence of vitamin D deficiency in both study groups is high and main risk factors associated with vitamin D deficiency are female gender, lack of sun exposure, dress style and

milk and dairy product consumption. A high percentage of Jordanian women have less than optimal vitamin D level, these result underscore the need for optimization of vitamin D status in all Jordanian population by fortification of food supplement with adequate amount of vitamin D and also provide better education about importance of sun exposure and milk and dairy product consumption. A national plan for education, screening and control of risk factors associated with vitamin D deficiency is highly recommended.

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