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Relationship between status of vitamin D and adhesive molecules biomarkers in Saudi patients with type 2 diabetes mellitus

Abstract

Background: Vitamin D (25-OHD) has an essential protective action on vascular endothelium and endothelial dysfunction is a risk valuable marker for risk of cardiovascular disorders, which are common among patients with Type 2 diabetes mellitus (T2DM).

Objective: the aim of this study was to detect the link between level of vitamin D and adhesive molecules biomarkers in Saudi patients with type 2 diabetes mellitus.

Material and methods: Two hundred Saudi patients with T2DM of both sexes (132females and 68males), their age range was 48-59years, the diabetes chronicity range was 9-11years and their body mass index (BMI) range was 31 to 37Kg/m^2. All participants received oral hypoglycemic agents e.g. metformin and/or pioglitazone and were selected from the Internal Medicine Out-patient Clinic, King Abdulaziz Teaching Hospital, Jeddah, Saudi Arabia. Participants with respiratory failure, hepatitis, renal failure, heart failure, pregnancy and smokers excluded from the study. According to vitamin D level, participants were assigned to one of three groups: vitamin D deficiency group (A):25-OHD <20ng/ml, vitamin D insufficiency group (B): 25-OHD=20–30ng/ml and normal vitamin D group(C) 25-OHD >30ng/ml.

Results: The mean values of VCAM-1, ICAM-1 and E-selectin were significantly higher in vitamin D deficiency group (A) compared to vitamin D insufficiency group (B) and normal vitamin D group(C). Moreover, vitamin D showed a strong inverse relationship with VCAM-1, ICAM-1 and E-selectin in the three groups (P<0.05).

Conclusion: There is an association between vitamin D deficiency and abnormal levels of adhesive molecules biomarkers in Saudi patients with type 2 diabetes mellitus.

Keywords: adhesive molecules, endothelial dysfunction, type 2 diabetes, vitamin D

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Introduction

Type 2 diabetes mellitus (T2DM) is a worldwide medical problem as 7-11% of world population have diabetes as reported by the International Diabetes Federation (IDF) in 2015.[1] and the number of T2DM patients is expected to reach 438 million by 2030 worldwide.[2] However, greater than 90% of this number is either overweight or obese.[3] Diabetes mellitus has a high impact on morbidity and mortality as diabetes mellitus associated with 2-4 fold risk for cardiovascular diseases and stroke in addition, diabetes is considered as a leading cause of renal disorders.[4-6]

Endothelial dysfunction is known to predict cardiovascular future events in patients with T2DM.[7,8] as endothelial dysfunction is an initial pathological change characterized by reduced vasodilation in vascular system. Moreover, endothelial dysfunction contributes in initiating and progressing of plague which plays a principle role in pathogenesis of atherosclerosis.[9] and arterial stiffness.[10] The biomarkers of endothelial cell activation molecules that commonly measured include intracellular adhesion molecule (ICAM-1), vascular cell adhesion molecule (VCAM-1) and selectins (P and E-selectin), all of which are increased with endothelial dysfunction.[11,12] However, metabolic disorders commonly associated with chronic low grade of systemic inflammation and endothelial dysfunction.[13,14] Moreover, adequate intake of vitamin D (25-OHD) plays a protective role against systemic inflammation.[15,16] in some conditions as obesity, T2DM and CVD.[17-19]

Vitamin D has an important role in function of cardiovascular system,[20,21] protective action for the vascular endothelium.[22] and important role for kidney function.[23] Recently, deficiency of vitamin D is recognized as a public medical problem as it affects about 50% of population worldwide.[24] However, vitamin D deficiency raise the risk of microvascular diabetic complications in patients with T2DM.[25,26]

As precise relationship between markers of endothelial function in T2DM subjects based on 25-OHD levels is still a matter of debate, therefore the aim of this study was to detect the link between level of vitamin D and adhesive molecules biomarkers in Saudi patients with type 2 diabetes mellitus.

Material and methods

Subjects

Two hundred Saudi patients with T2DM of both sexes (132females and 68males), their age range was 48-59years, the diabetes chronicity range was 9-11years and their body mass index (BMI) range was 31 to 37Kg/m^2. All participants received oral hypoglycemic agents e.g. metformin and/or pioglitazone and were selected from the Internal Medicine Out-patient Clinic, King Abdulaziz Teaching Hospital, Jeddah, Saudi Arabia. Participants with respiratory failure, hepatitis, renal failure, heart failure, pregnancy and smokers excluded from the study. According to vitamin D level, participants were assigned to one of three groups: vitamin D deficiency group (A): 25-OHD <20ng/ml, vitamin D insufficiency group (B): 25-OHD=20–30ng/ml and

normal vitamin D group(C) 25-OHD >30ng/ml and all participants received no vitamin D supplementation. This study approved by the Ethical Committee of the Faculty of Applied Medical Sciences, King Abdulaziz University.

Measurements

An overnight fasting blood samples were drawn from all participants for measurements of the following:

Serum concentrations of 25-OH vitamin D: Measurement of 25(OH) vitamin D for all patients and controls were done by the commercial kit RIA (Elisa Kit; DiaSorin, Stillwater, MN, USA). Plasma 25(OH) vitamin D concentrations of less than 20ng/ml were defined as 25(OH) vitamin D deficiency and less than 30ng/ml as 25(OH)D deficiency and insufficiency.[27]

Measurement of adhesive molecules: Level of inter-cellular adhesion molecule (ICAM-1), vascular cell adhesion molecule (VCAM-1) and E-selectin were measured from frozen serum samples stored at −80°C using enzyme-linked immunosorbent assays (ELISAs) (R&D Systems, France).

Statistical analysis

SPSS (Chicago, IL, USA) version 23 was used for statistical analysis of data. Descriptive statistics for quantitative variables were presented as mean ±SD, while qualitative variables were presented as percentage and numbers. Analysis of variance (ANOVA) was used to compare between the three groups, P<0.05. While, Pearson's correlation coefficients (r) used to detect the degree of correlation between level of vitamin D and ICAM-1, VCAM-1 and E-selectin.

Results

Baseline characteristics of all participants who were assigned to one of three groups according to serum level of vitamin D into: vitamin D deficiency group (A): 25-OHD <20ng/ml, vitamin D insufficiency group (B): 25-OHD=20–30ng/ml and normal vitamin D group(C): 25-OHD >30ng/ml are presented in Table 1 and revealed no significant differences regarding all baseline criteria except fasting and postprandial blood sugar which were found to be significantly greater in group (A) than in group (B) and group (C) (Table 1).

The mean values of VCAM-1, ICAM-1 and E-selectin were significantly higher in vitamin D deficiency group (A) compared to vitamin D insufficiency group (B) and normal vitamin D group(C) (Table 2). Moreover, vitamin D showed a strong inverse relationship with VCAM-1, ICAM-1 and E-selectin in the three groups (Table 3) (P<0.05).

Table 1 Baseline variables of all participants

Variable	Group(A)	Group(B)	Group(C)	Significance
	25-OHD deficiency	25-OHD insufficiency	25-OHD normal	
Age(Year)	51.74±4.83	54.29±3.97	52.86±5.61	0.072
Gender(Male/Female)	42(33%):85(67)	12(36%):21(64%)	14(352%): 26(65%)	0.023
BMI(kg/m^2)	31.76±3.24	32.15±2.98	31.65±3.47	0.154
FBS(mg/dl)	184.23±26.51	151.36±22.42	138.12±18.13	0.002*
PPS(mg/dl)	267.37±35.29	214.18± 24.11	159.74±19.62	0.006*
Diabetes Duration(Year)	10.98±3.72	12.43±2.51	11.52±2.97	0.091
SBP(mm Hg)	134.21±14.13*	132.57±12.84*	131.24±12.75*	0.126
DBP(mm Hg)	87.45±6.16*	86.23±5.78*	85.38±5.91*	0.138

BMI, body mass index; FBS, fasting blood sugar; PPS, postprandial blood sugar; SBP, systolic blood pressure; DBP, diastolic blood pressure (*) indicates a Significant Difference between Groups, P<0.05.

Table 2 Comparison between the three groups concerning ICAM-1, VCAM-1and E-selectin

Variable	Group(A)	Group(B)	Group(C)	Significance
	25-OHD deficiency	25-OHD insufficiency	25-OHD normal	
ICAM-1(ng/ml)	93.81±11.36	89.14±9.45	85.42±8.27	0.012*
VCAM-1(ng /ml)	815.92±35.51	784.63±32.38	761.53±29.12	0.016*
E-Selectin(ng/ml)	16.11±3.24	14.25±2.71	12.16±2.46	0.025*

ICAM-1, inter-cellular adhesion molecule; VCAM-1, vascular cell adhesion molecule; (*) indicates a significant difference between groups, P<0.05.

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Table 3 Correlation coefficient (r) of vitamin D and ICAM-1, VCAM-1& E-selectin in the three groups

	Group(A)	Group(B)	Group(C)
	25-OHD deficiency	25-OHD insufficiency	25-OHD normal
ICAM-1(ng/ml)	-0.681**	-0.531*	-0.647**
VCAM-1(ng/ml)	-0.719**	-0.634**	-0.648*
E-selectin(ng/ml)	-0.547*	-0.625**	-0.512*

Spearman's correlation was used *: P<0.05**: P<0.01.

Discussion

The blood vessels endothelium is the main source of circulating adhesive molecules which are the biomarkers of endothelial function.[28,29] Alteration in levels of adhesive molecules means endothelial dysfunction, which can be considered surrogates for high cardiovascular disorders (CVD) risk.[30] However, there still contradicted data regarding the association between level of vitamin D and endothelial dysfunction in patients with T2DM. Therefore, the aim of this study was to detect the link between level of vitamin D and adhesive molecules biomarkers in Saudi patients with type 2 diabetes mellitus.

Our results revealed that the mean values of VCAM-1, ICAM-1 and E-selectin were significantly higher in vitamin D deficiency group (A) compared to vitamin D insufficiency group (B) and normal vitamin D group (C). Moreover, vitamin D showed a strong inverse relationship with VCAM-1, ICAM-1 and E-selectin in the three groups. These findings are consistent with several previous observational studies reported an associations between endothelial dysfunction and low levels of circulating vitamin D in health subjects as Tarcin et al.[31] found among 23 asymptomatic individuals, there was an association between impaired brachial artery flow mediated vasodilatation (FMD) and vitamin D deficiency which improved after vitamin D replacement. Similarly, Jablonski & Yiu et al.[32,33] found a negative relationship between inflammatory cytokines, endothelial dysfunction recorded by brachial artery FMD and level of vitamin D in adult subjects. However, Harris et al..[34] stated 16 weeks of supplemental high dose of vitamin D (60,000 IU/month) significantly improved endothelial function that measured by FMD. While, Al Mheid & Dong et al.[35,36] found improvement in vascular dysfunction in healthy subjects as evident by reduction in mean arterial pressure after supplement of vitamin D.

In the other hand, changes in level of vitamin D can influence endothelial function in pathological conditions as evident by Yiu & colleagues.[33] who stated that deficiency of vitamin D was associated with endothelial dysfunction documented by FMD in 280patients with T2DM. In addition, Sugden et al.[37] reported that brachial artery FMD of T2DM patients significantly improved after single dose of vitamin D (100,000 IU) for 2months. Moreover, Codoner-Franch et al.[35] proved that level of vitamin D was linked to systemic inflammation, oxidative stress and VCAM-1 levels in 66 obese children. There are several possible mechanisms for the link between vitamin D and endothelial function included reduction of blood pressure due to suppression of renin-angiotensin system,[39] reduction of vascular resistance,[40] modulation of inflammatory cytokines effects on blood vessels,[41] reduction of adhesive molecules, reduction of platelet aggregation.[42] and finally through reduction of oxidative stress.[43]

Conclusion

There is an association between vitamin D deficiency and abnormal levels of adhesive molecules biomarkers in Saudi patients with type 2 diabetes mellitus.

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Conflicts of interest

None.

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References

1. International Diabetes Federation. *IDF diabetes atlas*. 7th ed. Brussels: Inter–national Diabetes Federation. 2015.
2. Zhang N, Yang X, Zhu X, et al. Type 2 diabetes mellitus unawareness, prevalence, trends and risk factors: National Health and Nutrition Examination Survey (NHANES) 1999–2010. *J Int Med Res*. 2017;45(2):594–609.
3. Centers for Disease Control and Prevention. National diabetes fact sheet: national estimates and general information on diabetes and prediabetes in the United States, 2011. *Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, USA*. 2011.
4. American Diabetes Association. *The cost of diabetes*. 2013.
5. International Diabetes Federation (IDF). *Diabetes atlas global burden, epidemiology and morbidity*. Diabetes and impaired glucose tolerance. 2011.
6. Krul–Poel YHM, Westra S, Wijland HJJV, et al. Vitamin D status and health–related quality of life in patients with Type 2 diabetes. *Diabet Med*. 2016;33(3):300–306.
7. Yiu YF, Chan YH, Yiu KH, et al. Vitamin D deficiency is associated with depletion of circulating endothelial progenitor cells and endothelial dysfunction in patients with T2DM. *J Clin Endocrinal Metab*. 2011;96(5):E830–E835.
8. Kim JA, Montagnani M, Koh KK, et al. Reciprocal relationship between insulin resistance and endothelial dysfunction: Molecular and pathophysiological mechanisms. *Circulation*. 2006;113(15):1888–1904.
9. Nadar S, Blann AD, Lip GY. Endothelial dysfunction: Methods of assessment and application to hypertension. *Curr Pharm Des*. 2004; 10(29):3591–3605.
10. Endemann DH, Schiffrin EL. Endothelial dysfunction. *J Am Soc Nephrol*. 2004;15(8):1983–1992.
11. Bellia A, Garcovich C, D'Adamo M, et al. Serum 25–hydroxyvitamin D levels are inversely associated with systemic inflammation in severe obese subjects. *Intern Emerg Med*. 2013;8(1):33–40.
12. Alyami A, Soares MJ, Sherriff JL, et al. Vitamin D & endothelial function. *Indian J Med Res*. 2014;140(4):483.
13. Hotamisligil GS. Inflammation and metabolic disorders. *Nature*. 2006;444(7121):860–867.
14. Szmitko PE, Wang CH, Weisel RD, et al. New markers of inflammation and endothelial cell activation part I. *Circulation*. 2003;108(16):1917–1923.

15. Lai YH, Fang TC. The pleiotropic effect of Vitamin D. *ISRN Nephrol*. 2013;2013:898125.

16. Calton E, Keane K, Soares M. The potential regulatory role of vitamin D in the bioenergetics of inflammation. *Cur Opin Clin Nutr Metab Care*. 2015;18(4):367–73.

17. Hossein–nezhad A, Holick MF. Vitamin D for health: a global perspective. *Mayo Clin Proc*. 2013;88(7):720–755.

18. Mitri J, Muraru MD, Pittas AG. Vitamin D and type 2 diabetes: a systematic review. *Eur J Clin Nutr*. 2011;65(9):1005–1015.

19. Soares MJ, Pathak K, Calton EK. Calcium and vitamin d in the regulation of energy balance: where do we stand? *Int J Mol Sci*. 2014;15(3):4938–4945.

20. McGreevy C, Williams D. New insights about vitamin D and cardiovascular disease: A narrative review. *Ann Intern Med*. 2011;155(12):820–826.

21. Sanchez–Niño MD, Bozic M, Córdoba–Lanús E, et al. Beyond proteinuria: VDR activation reduces renal inflammation in experimental diabetic nephropathy. *Am J Physiol Renal Physiol*. 2012;302(6):F647–F657.

22. Molinari C, Uberti F, Grossini E, et al. 1α,25–dihydroxycholecalciferol induces nitric oxide production in cultured endothelial cells. *Cell Physiol Biochem*. 2011;27(6):661–668.

23. Liu Z, Woo J, Wu S, et al. The Role of Vitamin D in Blood Pressure, Endothelial and Renal Function in Postmenopausal Women. *Nutrients*. 2013;5(7):2590–2610.

24. Mahajan M, Sharma R. Current understanding of role of vitamin D in type 2 diabetes mellitus. *International Journal of Recent Scientific Research*. 2015;6(2):2602–2607.

25. Huang Y, Li X, Wang M, et al. Lipoprotein lipase links vitamin D, insulin resistance, and type 2 diabetes: a cross sectional epidemiological study. *Cardiovasc Diabetol*. 2013;12:17.

26. Bajaj S, Singh RP, Dwivedi NC, et al. Vitamin D levels and microvascular complications in type 2 diabetes. *Ind J Endocrinol and Metab*. 2014;18(4):537–541.

27. Holick MF. Vitamin D deficiency. *N Engl J Med*. 2007;357(3):266–281.

28. Scalia R. The microcirculation in adipose tissue inflammation. *Rev Endocr Metab Disord*. 2013;14(1):69–76.

29. Pontiroli AE, Pizzocri P, Koprivec D, et al. Body weight and glucose metabolism have a different effect on circulating levels of ICAM–1, E–selectin, and endothelin–1 in humans. *Eur J Endocrinol*. 2004;150(2):195–200.

30. Ertek S, Akgül E, Cicero AF, et al. 25–Hydroxy vitamin D levels and endothelial vasodilator function in normotensive women. *Arch Med Sci*. 2012;8(1):47–52.

31. Tarcin O, Yavuz DG, Ozben B, et al. Effect of vitamin D deficiency and replacement on endothelial function in asymptomatic subjects. *J Clin Endocrinol Metab*. 2009;94(10):4023–4030.

32. Jablonski KL, Chonchol M, Pierce GL, et al. 25–hydroxyvitamin D deficiency is associated with inflammation–linked vascular endothelial dysfunction in middle–aged and older adults. *Hypertension*. 2011;57(1):63–69.

33. Yiu YF, Chan YH, Yiu KH, et al. Vitamin D deficiency is associated with depletion of circulating endothelial progenitor cells and endothelial dysfunction in patients with type 2 diabetes. *J Clin Endocrinol Metab*. 2011;96(5):E830–E835.

34. Harris RA, Pedersen–White J, Guo DH, et al. Vitamin D3 supplementation for 16 weeks improves flow–mediated dilation in overweight african–american adults. *Am J Hypertens*. 2011;24(5):557–562.

35. Al Mheid I, Patel R, Murrow J, et al. Vitamin D status is associated with arterial stiffness and vascular dysfunction in healthy humans. *J Am Coll Cardiol*. 2011;58(2):186–192.

36. Dong Y, Stallmann–Jorgensen IS, Pollock NK, et al. A 16–week randomized clinical trial of 2000 international units daily vitamin D3 supplementation in black youth: 25–Hydroxyvitamin D, adiposity, and arterial stiffness. *J Clin Endocrinol Metab*. 2010;95(10):4584–4591.

37. Sugden JA, Davies JI, Witham MD, et al. Vitamin D improves endothelial function in patients with type 2 diabetes mellitus and low vitamin D levels. *Diabet Med*. 2008;25(3):320–325.

38. Codoñer–Franch P, Tavárez–Alonso S, Simó–Jordá R, et al. Vitamin D status is linked to biomarkers of oxidative stress, inflammation, and endothelial activation in obese children. *J Pediatr*. 2012;161(5):848–854.

39. Li YC, Kong J, Wei M, et al. 1,25–Dihydroxyvitamin D3 is a negative endocrine regulator of the renin–angiotensin system. *J Clin Investig*. 2002;110(2):229–238.

40. Norman PE, Powell JT. Vitamin D, shedding light on the development of disease in peripheral arteries. *Arterioscler Thromb Vasc Biol*. 2005;25(1):39–46.

41. Zehnder D, Bland R, Chana RS, et al. Synthesis of 1,25–dihydroxyvitamin D3 by human endothelial cells is regulated by inflammatory cytokines: A novel autocrine determinant of vascular cell adhesion. *J Am Soc Nephrol*. 2002;13(3):621–629.

42. Aihara K, Azuma H, Akaike M, et al. Disruption of nuclear vitamin D receptor gene causes enhanced thrombogenicity in mice. *J Biol Chem*. 2004;279(34):35798–35802.

43. Ureña–Torres P, Metzger M, Haymann JP, et al. Association of kidney function, vitamin D deficiency, and circulating markers of mineral and bone disorders in CKD. *Am J Kidney Dis*. 2011;58(4):544–553.