SJIF Impact Factor: 3.458

WORLD JOURNAL OF ADVANCE HEALTHCARE RESEARCH

ISSN: 2457-0400
Volume: 2.
Issue: 5.
Page N. 220-225
Year: 2018

Original Article www.wjahr.com

RELATIONSHIP BETWEEN VITAMIN D AND GLYCEMIC CONTROL IN PATIENTS WITH TYPE 2 DIABETES MELLITUS IN LATTAKIA

Dr. Abdulrahman Ahmad Zuraik*[1], Dr. Med. Samer Akel[2] and Dr. Ayman Awwama[3]

[1]Master in Microbiology Hematology and Immunology, Department of Microbiology and Biochemistry, Faculty of Pharmacy, University of Tishreen, Lattakia, Syria.
[2]Assistant Professor, Department of Oncology, Faculty of Medicine, University of Tishreen, Lattakia, Syria.
[3]Assistant Professor, Department of Microbiology and Biochemistry, Faculty of Pharmacy, University of Tishreen, Lattakia, Syria.

Received date: 12 August 2018 **Revised date:** 02 September 2018 **Accepted date:** 23 September 2018

Corresponding author: Dr. Abdulrahman Ahmad Zuraik
Master in Microbiology Hematology and Immunology, Department of Microbiology and Biochemistry, Faculty of Pharmacy, University of Tishreen, Lattakia, Syria.

ABSTRACT

This study has investigated the impact of vitamin D on glycemic control in patients with type 2 diabetes mellitus. 176 patients with type 2 diabetes mellitus were enrolled in this study between 1 June and 31 Dec 2017 (mean (S.D) age: 52.3±11 years, 32.9% were female). It was collected of patients from Diabetic Center in Lattakia. Patients were divided into two groups according to the HbA1c values: good glycemic control (HbA1c≤7%) and poor glycemic control (HbA1c>7%). It was compared 25 hydroxy vitamin 25(OH)D between the two groups. In the result that dependent on student t-test, Vitamin D was found to be significantly associated with a good glycemic control. This study indicated that vitamin D was significantly related to control blood glucose levels in type 2 diabetes mellitus.

KEYWORDS: HbA1c, vitamin D, diabetes mellitus, glycemic control.

INTRODUCTION

Vitamin D deficiency and diabetes mellitus are two common conditions in the elderly population.

Vitamin D

Vitamin D deficiency is currently a topic of intense interest, and is widely prevalent across all ages, races, geographical regions, and socioeconomic strata. Suboptimal vitamin D status contributes to many conditions, including osteomalacia, osteoporosis, falls, and fractures.[1,2] In addition, epidemiologic observations have associated low vitamin D status with an increased risk of non-musculoskeletal diseases, such as cancer,[3] multiple sclerosis,[4] type 1 diabetes mellitus,[5] type 2 diabetes mellitus[6] and cardiovascular disease.[7]

Vitamin D (calciferol) is a generic name for a group of fat steroids of which the two major forms are vitamin D2 (ergocalciferol) and vitamin D3 (colecalciferol). Both forms of vitamin D undergo identical metabolism. Vitamin D is obtained from skin irradiation and limited dietary sources. Vitamin D from the skin and diet is metabolized in the liver to 25(OH)D, which has a long life and is the major circulating metabolite and marker of vitamin D status.[8] In the kidney, 25-hydroxyvitamin D is metabolized by the enzyme 25-hydroxyvitamin D-1(alpha)-hydroxylase (CYP27B1) to its active form, 1,25(OH)2D, which exerts its effects by means of steroid hormone nuclear receptors. The characteristics of 1,25(OH)2D are those of a hormone, and consequently vitamin D is a prohormone, rather than a true vitamin.

Vitamin D is not only essential for maintaining bone health, but it also plays a role in several other biochemical mechanisms within the human body. The mechanism of action of the active form of vitamin D is similar to that of other steroid hormones and is mediated by its binding to vitamin D receptor (VDR). VDRs are found in most tissues, not just in those that participate in the classic actions of vitamin D such as bones, intestines and kidneys, and the enzyme responsible for converting 25 (OH)D to 1,25(OH)2D is also expressed in a variety of extrarenal sites, such as endothelial cells, beta cells, and immune cells.[9]

The number of subjects with type 2 diabetes mellitus is rising, due to the effect of age, the growth of the population, sedentariness and, mainly, obesity. Although changes in lifestyle, particularly weight loss and physical

activity, delay the progression of diabetes, weight loss is difficult to be achieved and maintained. The identification of easily modifiable risk factors is therefore urgently needed for primary prevention of diabetes. Certain nutritional factors, such as vitamin D are also believed to play a role, and it has been suggested that endemic low vitamin D status contributes to the increased prevalence of diabetes mellitus. There is increasing evidence that vitamin D metabolism affects the risk of diabetes. Studies in humans have shown that vitamin D supplementation in infancy reduces the risk of type 1 diabetes mellitus during early adulthood.[10] Published studies in animals identified a pancreatic receptor to the active metabolite of vitamin D. As vitamin D modulates insulin receptor gene expression and insulin secretion, it is an interesting environmental candidate for type 2 diabetes mellitus.[11]

Concept and prevalence of vitamin D insufficiency and deficiency

The concept of normal 25(OH)D concentration is a challenge. It has been suggested that vitamin D deficiency is defined as a 25(OH)D below 20 ng/mL, insufficiency as a 25(OH)D of 21 – 29 ng/mL, and sufficiency as a 25(OH)D of 30 – 100 ng/mL.[12]

A meta-analysis of high-quality primary prevention randomized control trials (RCT) of vitamin D and fracture risk consistently found that anti-fracture efficacy started at 25(OH)D levels of at least 30 ng/mL.[13]

The guideline, written by the Endocrine Society Task Force, reports that 25(OH)D levels of 30 ng/mL or higher compared with 20 ng/mL provide increase benefits.[14] In contrast, the Institute of Medicine (IOM) report, based on evidence from observational studies and recent randomized trials, suggests that a serum level of 20 ng/mL of 25(OH)D would protect 97.5% of the population against adverse skeletal outcomes.[15] Hypovitaminosis D has become endemic owing to the insufficient ingestion of vitamin D in combination with the use of sun protection clothing and sunblock. The prevalence of vitamin D deficiency has been reported with great frequency even in sunny regions of the world. Studies on the prevalence of hypovitaminosis D in Saudi Arabia, Australia, Turkey, the Arab Emirates and India have shown that 30%-50% of children and adults had 25(OH)D levels below 20 ng/ ml. In Recife (latitude 10ºS), Pernambuco, Brazil, the prevalence of vitamin D deficiency in postmenopausal women was 8% for 25(OH)D values below 15 ng/mL and 43% for those below 25 ng/mL.[16]

An observational study carried out in Italy in postmenopausal women revealed that vitamin D levels in postmenopausal women were lower in those with type 2 diabetes mellitus than in those in the control group (39% vs. 25%).[17] A Japanese study evaluating 581 diabetic patients and 51 nondiabetic ones showed a prevalence of hypovitaminosis D (< 20 ng/mL) of 75% with no differences between the type 2 diabetic patients and the control group.[18] A study carried out in the United Kingdom evaluated the prevalence of hypovitaminosis D in type 2 diabetic patients in an Asian community and its impact on the control of glycemia.[19] The results revealed that the prevalence of vitamin D (< 20 ng/mL) was > 80%, being more common in the diabetics than in the control group (83% vs. 70%; $p = 0.07$), and that the glycated hemoglobin levels were higher in the women with vitamin D deficiency.

Vitamin D and insulin resistance

The identification of 1,25(OH)2D receptors and the 1 α hydroxylase expression in pancreatic beta cells support the possibility of vitamin D role in the pathogenesis of type 2 diabetes mellitus.[20] In animals, it has been demonstrated that the secretion of pancreatic insulin is inhibited by vitamin D deficiency[21] and that in humans vitamin D deficiency is related to glucose intolerance and type 2 diabetes mellitus.[22] Hypovitaminosis D leads to a deficiency in the secretion of insulin and induces glucose intolerance,[23] while its replacement with vitamin D reestablishes these abnormalities.[24]

Vitamin D affects the function of beta cells in various ways. The active form of vitamin D exerts its effects by activating the nuclear vitamin D receptor (VDR). The binding of 1,25(OH)2D to the VDR leads to the transcription of genes regulated by 1,25(OH)2D. The effect of vitamin D on insulin synthesis and secretion is evidenced by the presence of the vitamin D response element (VDRE) in the human insulin gene promoter and transcriptional activation of the human insulin gene caused by 1,25(OH)2D.[25] An indirect effect of vitamin D on beta cells may be mediated by its regulation in the extracellular concentration of calcium and the influx of calcium through the beta cells.[26]

Vitamin D may also affect insulin resistance through the renin-angiotensin-aldosterone system. It is believed that angiotensin II contributes to increased insulin resistance by inhibiting the action of insulin in the vascular tissue and skeletal muscle, leading to a decrease in glucose uptake.[27] Data support the vitamin D-VDR complex as a potential regulator of renin activity in humans and polymorphisms in the VDR gene may be associated with the pathogenesis of type 2 diabetes mellitus by influencing insulin resistance.[28]

However, whether vitamin D may influence insulin secretion and action is controversy. Although some studies found no association between serum 25(OH)D levels and parameters of insulin action,[29] others have shown positive associations. In the Canadian Prospective Metabolism and Islet cell Evaluation (PROMISE) study cohort,[30] three univariate analyses indicated a significant positive association between serum 25(OH)D and the insulin sensitivity index for the oral glucose tolerance test (IS-OGTT): $r = 0.30$, $p < 0.001$. A significant negative association was found between

serum 25(OH)D and the homeostasis model assessment (HOMA-IR): r = -0.29, p < 0.001, as well as significant positive associations between serum 25(OH)D levels and the insulinogenic index/ HOMA ratio: r = 0.14, p = 0.002. In the multivariate regression analyses, serum 25(OH)D was a significant independent predictor of insulin sensitivity and beta cell function across all models.[31]

Vitamin D and type 2 diabetes mellitus

Vitamin D deficiency appears to predispose individuals to become type 2 diabetics, and there is evidence from observational studies that suggest an association between low levels of vitamin D and a risk of type 2 diabetes mellitus.

A decrease in the concentration of vitamin D was reported in a population of Asians from Bangladesh resident in London at risk for type 2 diabetes mellitus compared with individuals with no such risk and who also presented a higher prevalence of type 2 diabetes mellitus than a British Caucasian population.[32]

An English cohort (6) comprising a total of 524 randomly selected nondiabetic men and women, aged 40-69 years at baseline, with measurements for serum 25(OH)D and IGF-1 in the population-based Ely Study, had their glycemic status (oral glucose tolerance), lipids, insulin, anthropometry, and blood pressure measured and metabolic syndrome risk (metabolic syndrome z score) derived at baseline and at 10 years of follow-up. This prospective study reports inverse associations between baseline serum 25(OH)D and future glycemia and insulin resistance. These associations are independent of risk factors and potential confounders. These findings confirm results from a Finnish cohort study showing a significant inverse association between serum 25(OH)D and risk of type 2 diabetes in a simple model. However, the association was attenuated in the multivariate analysis, adjusting for potential risk factors for type 2 diabetes.

An analysis from the Nurse Health Study demonstrated that women with a mean ingestion of vitamin D greater than 800 IU per day had a 33% lower risk of type 2 diabetes mellitus than those whose daily ingestion was less than 200 IU.[33]

To determine the association between serum 25(OH) D and diabetes risk and whether it varies according to ethnicity, an analysis of data from the Third National and Nutrition Examination Survey (1988-1994) was carried out. In this cross-sectional survey of a nationally representative sample of the U.S population, 25(OH)D was available from 6,228 people (2,766 non-Hispanic whites, 1,736 non-Hispanic blacks, and 1,726 Mexican Americans), aged ≥ 20 years with fasting and/or 2-h plasma glucose and serum insulin measurements. The results showed an inverse association between vitamin D status and diabetes, possibly involving resistance, in non-Hispanic whites and Mexican Americans, but not in non-Hispanic blacks.[34]

All this data suggests that hypovitaminosis D may be a major risk factor in glucose intolerance in some individuals, but not in all populations. One explanation for the lack of association could be the existence of a variable effect in the threshold between different ethnic groups. It is possible that a particular population may have a diminished sensibility to vitamin D or to the effects of the parathyroid hormone (PTH). A cross-sectional study performed on obese female adolescent Afro-Americans suggested that 25(OH)D concentrations < 15 ng/mL represent the threshold from which vitamin D deficiency produces a negative effect on insulin sensibility,[35] and adolescents in NHANES III with serum 25(OH)D levels of less than 15 ng/mL were more likely to have elevated blood glucose levels than those with the highest 25(OH)D values (> 26 ng/mL) (OR, 2.5; 95% CI, 1.0-6.4).[36]

Unlike observational studies, experimental studies lack evidence to support the hypothesis that vitamin D supplementation reduces the risk of diabetes or glucose intolerance. In a meta-analysis[37] published in 2007, none of the six studies reviewed was able to demonstrate a significant change in glucose intolerance. However, three of the studies were of short duration (≤ 3 months), and two of these employed the active form of vitamin D (1,25-dihydroxyvitamin D3). In addition, the primary outcome of these studies was not the effect of vitamin D supplementation on glucose metabolism. In the placebo-controlled Women's Health Initiative (WHI), the use of calcium supplement of 1,000 mg per day and vitamin D3 400 IU per day failed to reduce the risk of progression to diabetes over a period of seven years.[38] The null result may, however, be attributable to the use of a low dose of vitamin D in the active treatment group.

In a systematic review[39] of studies published in English using Medline up to the end of February 2011, a total of eight observational studies and 11 interventional studies were included, in order to ascertain the association between vitamin D status and the incidence of type 2 diabetes mellitus and the effect of vitamin D supplementation on blood glucose results. The daily ingestion of > 500 IU of 25(OH)D reduced the risk of diabetes by 13% against an ingestion of < 200 IU per day. Individuals with higher 25(OH)D levels (> 25 ng/mL) had a lower risk of developing type 2 diabetes than those in the group with 25(OH)D levels of < 14 ng/ml. In a post-hoc analysis of eight studies comprising individuals with normal glucose tolerance levels at baseline, and in three small studies (32-60) of patients with type 2 diabetes vitamin D supplementation had no effect on the blood glucose results.

To determine whether vitamin D supplementation, with or without calcium, improved glucose homeostasis in adults at risk for diabetes, a randomized, double-blind,

placebo-controlled study[40] was conducted, assigned in a 2-by-2 factorial-design, in which patients were given either cholecalciferol (2000 IU once daily), or calcium carbonate (400 mg twice daily) for 16 weeks. The results showed that supplementation with cholecalciferol, but not with calcium, improved beta cell function and had only a marginal effect on attenuating the rise in glycated hemoglobin. However, supplementation with cholecalciferol does not improve glycemic control in diabetic subjects with normal serum 25(OH)D levels.

METHODS AND STATISTICS

The study included 176 participants from diabetic patients enrolled at the Lattakia Diabetes Center between July 1, 2017, and December 30, 2017. Patients with type 2 diabetes were diagnosed based on the report of the Center's endocrinologist. Patients were divided into two groups according to HbA1C: The first group contains 88 patients (29 females) with poor glycemic control (HbA1c >7%) and the second group of 88 patients (29 females) with good glycemic control (HbA1c ≤ 7%).

Blood samples were taken by taking 5 ml of blood on tubes containing heparin lithium as an anticoagulant, and at 3000 rpm for 3 minutes to obtain the plasma with 25 (OH) D measured. Plasma samples were kept at +2 ° C to + 8 ° C away from light in the laboratory section until the completion of the sample collection. The 25 (OH) D rate was then measured using the ELIZA device manufactured by EUROIMMUN, Italy, located at Tishreen University Laboratory in Lattakia. Vitamin D EUROIMMUN 25-OH Vitamin D ELISA kit was used.

Design of the study statistically: cross-sectional study
Tests and statistical programs used: t student test (t-test for two independent groups): to compare two arithmetic averages.

RESULTS

In the first group "poor glycemic control" (HbA1c > 7%), the mean 25(OH)D = 25.4 ng/ml. this group is vitamin D insufficiency.

In the second group "good glycemic control" (HbA1c ≤ 7%), the mean 25(OH)D = 35.1 ng/ml. this group is vitamin D sufficiency.

The statistical study showed a significant difference between the groups of study patients, i.e. there was a significant correlation between the poor glycemic control HbA1C> 7% and the deficiency or inadequacy of vitamin D (25 (OH) D <30 ng / ml) where the value t studied (t = 10.18136287) at t-value ($t_{(0.05,174)} = \pm 1.98$).

In the result with student t-test, Vitamin D was found to be significantly associated with a good glycemic control. This study indicated that vitamin D was significantly related to glycemic control in type 2 diabetes mellitus.

DISCUSSION

This cross-sectional study is the first study that observed an association between 25(OH)D levels and laboratory indicators of type 2 diabetes in Syria.

The results may be related to the lack of sports activity, where obesity is linked to the risk of type 2 diabetes, and maybe vitamin D deficiency associated with low outdoor sports activity, on the other hand, where direct sunlight is one of the most important sources of metabolism of vitamin D body, The association of vitamin D deficiency with different lifestyle factors has been studied in advance studies.[41]

Vitamin D is a fat-soluble vitamin that is more commonly found in the lipid and lipid layers, so obese patients are more prone to vitamin D deficiency because of its high concentration and difficulty in releasing it.[42] Vitamin D deficiency in women may be associated with menopause and reduced female hormones in the body.[43]

Many evidence confirms that vitamin D affects the extent to which pancreatic β cells are stimulated and cell resistance to insulin and cellular inflammations.[44]

The presence of vitamin D receptors on the cell surface has been demonstrated in many tissues including pancreatic β cells, allowing vitamin D to modify the insulin response by glucose values in the serum.[45]

In a meta-analysis study included 4996 patients, each increase in the value of 25 (OH) D by 10 ng/ml was significantly associated with a 4% reduction in the risk of type 2 diabetes.[46]

In contrast, other studies have shown no significant correlation between them.[47,48]

When evaluating the results of our study, there are things to consider such as:

1. The type of study conducted is cross-sectional and therefore it is not possible to go towards clear causal indications of the extent of association between type 2 diabetes and vitamin D deficiency.
2. The generality of the results on the society is somewhat limited. Due to the limited size of the sample, it sheds light on a fact that should be studied extensively in order to reduce the prevalence of type 2 diabetes in society.
3. Oral medications were not evaluated and their relationship to serum glucose control in the patient sample. However, we have a significant finding comparing vitamin D levels in type 2 diabetes patients with good and poor glycemic control (regardless of the cause of their serum glucose intolerance).

REFERENCE

1. Holick MF. Vitamin D: importance in the prevention of cancers, type 1 diabetes, heart disease, and osteoporosis. Am J Clin Nutr, 2004; 79(3): 362-71.
2. 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): 1999-2006.
3. Garland CF, Garland FC, Gorham ED, Lipkin M, Newmark H, Mohr SB, et al. The role of vitamin D in cancer prevention. Am J Public Health, 2006; 96(2): 252-61.
4. Munger KL, Levin LI, Hollis BW, Howard NS, Ascherio A. Serum 25-hydroxyvitamin D levels and risk of multiple sclerosis. JAMA, 2006; 296(23): 2832-8.
5. Mathieu C, Badenhoop K. Vitamin D, and type 1 diabetes: state of the art. Trends Endocrinol Metab, 2005; 16(6): 261-6.
6. Forouhi NG, Luan J, Cooper A, Boucher BJ, Wareham NJ. Baseline serum 25-hydroxyvitamin D is predictive of future glycemic status and insulin resistance: the Medical Research Council Ely Prospective Study, 1990-2000. Diabetes, 2008; 57(10): 2619-25.
7. Wang TJ, Pencina MJ, Booth SL, Jacques PF, Ingelsson E, Lanier K, et al. Vitamin D deficiency and risk of cardiovascular disease. Circulation, 2008; 117(4): 503-11.
8. DeLuca HF. Overview of general physiologic features and functions of vitamin D. Am J Clin Nutr, 2004; 80(6): 1689S-96S.
9. Bikle D. Nonclassic actions of vitamin D. J Clin Endocrinol Metab, 2009; 94(1): 26-34.
10. Hyppönen E, Läärä E, Reunanen A, Järvelin MR, Virtanen SM. Intake of vitamin D and risk of type 1 diabetes: a birth-cohort study. Lancet, 2001; 358(9292): 1500-3.
11. Ortlepp JR, Metrikat J, Albrecht M, Von Korff A, Hanrath P, Hoffmann R. The vitamin D receptor gene variant and physical activity predict fasting glucose levels in healthy young men. Diabet Med, 2003; 20(5): 451-4.
12. Holick MF. Vitamin D deficiency. N Engl J Med, 2007; 357(3): 266-81.
13. Bischoff-Ferrari HA, Willett WC, Wong JB, Giovannucci E, Dietrich T, Dawson-Hughes B. Fracture prevention with vitamin D supplementation: a meta-analysis of randomized controlled trials. JAMA, 2005; 293(18): 2257-64.
14. 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.
15. IOM (Institute of Medicine). Dietary reference intakes for calcium and vitamin D. Washington, DC: The National Academies Press, 2011; 260-2.
16. Bandeira F, Bandeira C, Freese E. Occult vitamin D deficiency and its relationship with bone mineral density among postmenopausal women in Recife, Brazil. J Bone Miner Res., 2003; 18(Supl 2): S407-9.
17. Isaia G, Giorgino R, Adami S. High prevalence of hypovitaminosis D in female type 2 diabetic population. Diabetes Care, 2001; 24(8): 1496.
18. Suzuki A, Kotare 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(4): 503-10.
19. 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.
20. Bland R, Markovic D, Hills CE, Hughes SV, Chan SL, Squires PE, et al. Expression of 25-hydroxyvitamin D3-1alpha-hydroxylase in pancreatic islets. J Steroid Biochem Mol Biol., 2004; 89-90(1-5): 121-5.
21. Norman AW, Frankel JB, Heldt AM, Grodsky GM. Vitamin D deficiency inhibits pancreatic secretion of insulin. Science, 1980; 209(4): 823-5.
22. Chiu KC, Chu A, Go VL, Saad MF. Hypovitaminosis D is associated with insulin resistance and beta cell dysfunction. Am J Clin Nutr., 2004; 79(5): 820-5.
23. Cade C, Norman AW. Vitamin D3 improves impaired glucose tolerance and insulin secretion in the vitamin D-deficient rat in vivo. Endocrinology, 1986; 119(1): 84-90.
24. Tanaka Y, Seino Y, Ishida M, Yamaoka K, Yabuuchi H, Ishida H, et al. Effect of vitamin D3 on the pancreatic secretion of insulin and somatostatin. Acta Endocrinol (Copenh), 1984; 105(4): 528-33.
25. Maestro B, Dávila N, Carranza MC, Calle C. Identification of a vitamin D response element in the human insulin receptor gene promoter. J Steroid Biochem Mol Biol., 2003; 84(2-3): 223-30.
26. Sergeev IN, Rhoten WB. 1,25-dihydroxivitamin D3 evokes oscillations of intracellular calcium in a pancreatic beta-cell line. Endocrinology, 1995; 136(7): 2852-61.
27. Sowers JR. Insulin resistance and hypertension. Am J Physiol Heart Circ Physiol, 2004; 286(5): H1597-602.
28. Chiu KC, Chuang LM, Yoon C. The vitamin D receptor polymorphisms in the translation initiation codon is a risk factor for insulin resistance in glucose tolerant Caucasians. BMC Med Genet, 2001; 2: 2.
29. Gulseth HL, Gjelstad IM, Tierney AC, Lovegrove JA, Defoort C, Blaak EE, et al. Serum vitamin D concentration does not predict insulin action or secretion in European subjects with the metabolic syndrome. Diabetes Care, 2010; 33(4): 923-5.

30. Kayaniyil S, Retnakaran R, Harris S, Vieth R, Knight JA, Gerstein HC, et al. Prospective associations of vitamin D with β-cell function and glycemia: the PROspective Metabolism and ISlet cell Evaluation (PROMISE) cohort study. Diabetes, 2011; 60(11): 2947-53.
31. Kayaniyil S, Vieth R, Retnakaran R, Knight JA, Qi Y, Gerstein HC, et al. Association of vitamin D with insulin resistance and beta-cell dysfunction in subjects at risk for type 2 diabetes. Diabetes Care, 2010; 33(6): 1379-81.
32. Boucher BJ, Mannan N, Noonan K, Hales C, Evans JW. Glucose intolerance and impairment of insulin secretion in relation to vitamin D deficiency in East London Asians. Diabetologia, 1995; 38(10): 1239-45.
33. Pittas AG, Dawson-Hughes B, Li T, Van Dam RM, Willett WC, Manson JE, et al. Vitamin D and calcium intake in relation to type 2 diabetes in women. Diabetes Care, 2006; 29(3): 650-6.
34. Scragg R, Sowers MF, Bell C. Serum 25-hydroxivitamin D, diabetes, and ethnicity in the Third National Health and Nutrition Examination Survey. Diabetes Care, 2004; 27(12): 2813-8.
35. Ashraf A, Alvarez J, Saenz K, Gower B, McCormick K, Franklin F. Threshold for effects of vitamin D deficiency on glucose metabolism in obese female African-American adolescents. J Clin Endocrinol Metab, 2009; 94(9): 3200-6.
36. Reis JP, von Mühlen ED, Miller ER, Michos ED, Appel LJ. Vitamin D status and cardiometabolic risk factors in the United States adolescent population. Pediatrics, 2009; 124(3): e371-9.
37. Pittas AG, Lau J, Hu FB, Dawson-Hughes B. The role of vitamin D and calcium in type 2 diabetes. A systematic review and meta-analysis. J Clin Endocrinol Metab., 2007; 92(6): 2017-29.
38. de Boer IH, Tinker LF, Connely S, Curb J, Howard BV, Kestenbaum B, et al. Calcium plus vitamin D supplementation and the risk of incident diabetes in the women's health initiative. Diabetes Care, 2008; 31(4): 701-7.
39. Mitri J, Muraru MD, Pittas AG. Vitamin D and type 2 diabetes: a systematic review. Eur J Clin Nutr., 2011; 65(9): 1005-15.
40. Mitri J, Dawson-Hughes B, Hu FB, Pittas AG. Effects of vitamin D and calcium supplementation on pancreatic β cell function, insulin sensitivity, and glycemia in adults at high risk of diabetes: the Calcium and Vitamin D for Diabetes Mellitus (CaDDM) randomized controlled trial. Am J Clin Nutr, 2011; 94(2): 486-94.
41. Thuesen B, Husemoen L, Fenger M, Jakobsen J, Schwarz P, Toft U, et al. Determinants of vitamin D status in a general population of Danish adults. Bone, 2012; 50: 605–10.
42. Narula R. Vitamin D Deficiency Among Postmenopausal Women with Osteoporosis. JCDR, 2013; 7: 336–38.
43. Pittas AG, Lau J, Hu FB, Dawson-Hughes B. The role of vitamin D and calcium in type 2 diabetes. A systematic review and meta-analysis. J. Clin. Endocrinol. Metab, 2007; 92: 2017–29.
44. Anagnostis P, Athyros VG, Adamidou F, Florentin M, Karagiannis A. Vitamin D and cardiovascular disease: a novel agent for reducing cardiovascular risk? Curr Vasc Pharmacol, 2010; 8: 720–30.
45. Song Y, Wang L, Pittas AG, Del Gobbo LC, Zhang C, Manson JE, et al. Blood 25-hydroxy vitamin D levels and incident type 2 diabetes: a meta-analysis of prospective studies. Diabetes Care, 2013; 36: 1422–28.
46. Buijsse B, Boeing H, Hirche F, Weikert C, Schulze MB, Gottschald M, et al. Plasma 25-hydroxyvitamin D and its genetic determinants in relation to incident type 2 diabetes: a prospective case-cohort study. Eur J Epidemiol, 2013; 28: 743–52.
47. Schafer AL, Napoli N, Lui L, Schwartz AV, Black DM. Serum 25-hydroxyvitamin D concentration does not independently predict incident diabetes in older women. Diabet Med., 2014; 31: 564–69.