**Vitamin D and Diabetes in Children**

**ABSTRACT**

Lack of vitamin D With many childhood diseases Including type 1 diabetes (T1DM). T1DM in children is Become more prevalent, with 23% National increase from 2001 to 2009. Similarly, it has West Virginia An increase of 8.1% in children of type I Diabetes from 2008/2009 to 2010/2011. This article highlights the Assembly Between vitamin D and sugar type 1 And discusses the potential of vitamin DRole in reduction and management Of T1DM in children1.

**INTRODUCTION**

New interest in vitamin D, that also called “sunshine vitamin,” has arisen recently as it has been associated to a lot of diseases from cancer and heart disease to diabetes.1 . Researches stay to pour into the literature that vitamin D is a fantastic if it comes to health. Although, high percent of the research is built on epidemiological, observational studies, that are significant for creating hypotheses but do not prove causes2.

The incidence of type 1 diabetes among children across the country rose by 23% between 2001 and 2009. More recently, the T1DM rate for children in West Virginia increased by 8.1% from 2008/2009 to 2010/2011. Type 1 diabetes mellitus is an autoimmune disease which lead to the destruction of beta cells of pancreas, resulting in dependence on insulin. The onset of T1DM is promoted by a lot of environmental factors and genes . An EURODIAB group do a large case study revealed that supplements of vitamin D at regular interval in childhood can help prevention of T1DM incidences ( a progressive destruction of pancreatic beta cells)3 .

Studies results submitted that vitamin D - 1, 25 hydroxyvitamin D3 – ( the biologically active form) is an immunomodulator but the mechanisms that justify this protection are not clear. Dietary Supplementation of Vitamin D Reduces the Spread of Lymphocytes and Helps to Transform Type 1 T-helper to Type 2 T Immune Cell Response. Therefore, vitamin D deficiency can induce beta cells to destroy autoimmune immunity. The deficiency of Vitamin D is common among newly and chronic diagnosed type 1 diabetics4. As the levels of vitamin D are affected by sun exposure, the fact that several studies results presented that T1DM is more frequently diagnosed in winter would prove the association. Studies have also revealed a positive relationship between latitude and T1DM diagnosis. The site increases the risk of vitamin D deficiency, for West Virginia. A little while ago if every skin production of vitamin D occurred from mid-October to mid-March. It is useful to note that staying in moderate weather does not automatically produce protection against T1DM as there is a need for adequate concentration of vitamin D for protective properties. For Compensation these geographic differences, numerous groups have recommended various vitamin D supplementation5.

**SOURCES AND PHARMACOKINITICOF VITAMIN D IN THE**

**BODY**

Vitamin D is a fat-soluble vitamin that is distributed in serum, muscle, liver and fatty tissue. Vitamin D is obtained from food sources or made in the skin when exposed to sunlight. There are two important forms of vitamin D store in the body. Vitamin D2 (ergocalciferol) and D3 (coli calciferol). Vitamin D2 is produced by UVB and is used as a dietary supplement. Vitamin D3 is produced in the skin in response to UV exposure or from food sources, dietary supplements or fortified foods. Both forms are transformed to 25 (OH) D (calcidiol) in the liver, and then transformed to 1.25 (OH) 2D (calcitriol) in the kidney that is the most active form of vitamin D. The usual amount of vitamin D can be estimated at Children through the use of different tools, which vary depending on study resources, designs and objectives6.

Dietary forms of vitamin D are absorbed in the small intestine with dietary fat and fat-soluble vitamins, while vitamin D3 enters the bloodstream after it is manufactured unmatched in the skin during exposure to ultraviolet light in sunlight. Neither vitamin D2 nor vitamin D3 has any biological function in the body until it passes through two-step metabolism. Metabolism requires different forms of vitamin D conversion in the liver and kidneys, and the active form, 1.25-dihydroxy-vitamin D (calcitriol), needs to bind to the vitamin D receptor (VDR) before biological action occurs. Thus, diabetic patients with liver or kidney problems are significantly at risk of deficiency, as are patients with gastrointestinal disorders such as gastrointestinal disease, pancreatitis, low levels of bile, or swarm7.

Vitamin D is supposed to improve the body's sensitivity to insulin and so reduces the insulin resistance risk , that often a primer to type 2 diabetes. Some scientists consider that this vitamin help Regulation of the production of insulin in the pancreas8.

Vitamin D levels should ideally be between 20-5 ng / ml (50-140 nmol / l) \*, considering anything less than 20 ng / ml. However, it is now known that raising the amount of vitamin D in the body to about 60-80 ng / ml can help keep glucose levels in the blood under control, which is vital for diabetics.the correct level of vitamin D varies from person to person. The only way to make sure that your vitamin D levels where 25-hydroxyvitamin D, or 25 (OH) D, blood test should be requested from your GP. Ideally the blood level should be 25 OH D 60ng / ml9.

**IDENTIFYING DEFICIENCY OF VITAMIN D :**

Vitamin D deficiency is predominant among children and adolescents. A study was published in 2009 in Pediatrics revealed that " 9% of the child population, was 25 (OH) D deficient, 61%, representing, 25 (OH) "According to the National Institutes of Health, 7.6 million American children and adolescents have levels of 25-hydroxy vitamin D [25] (OH) D in serum of 12 ng / ml or less, making them unable; 50.8 million have 25 (OH) D levels of 12 to 20 ng / ml, classified as insufficient or inadequate vitamin D levels for bone and overall health10.

In children and adults, symptoms of vitamin D deficiency include bone pain or tenderness, tooth abnormalities, poor growth, increased bone fractures, muscle cramps, short stature, and skeletal deformities such as rickets. "The American Academy of Pediatrics reported that the rickets were on the rise," says Temler. "Rickets are a medical condition associated with low levels of vitamin D. Low vitamin D leads to bone weakness, especially as the legs bend under the weight of the upper body"11.

Vitamin D is not ideal for healthy young children, and vitamin D status is different in infants and young children. "Skeletal abnormalities, such as bowlegs, wrists and thick ankles, are signs and symptoms of vitamin D deficiency in children," says Temler. "The curvature of the spine, the dove, the deformities of the skull, and the deformities of the pelvis are also signs of rickets in children. The bones of these children tend to be very smooth and fragile, leading to fractures. Pain, tenderness and muscle

weakness may be accompanied by bone abnormalities"

Due to the prevalence of vitamin D deficiency and inadequate children and adolescents, it is important to determine the best time to test their vitamin D levels. Experts say levels of vitamin D are checked if the condition is low or if the patient is suffering from bone deformities (rickets), poor bones, softness or fractures without real injury. "Vitamin D levels can also be used to help diagnose or monitor problems in glandular gland function where the thyroid hormone PTH is necessary to activate vitamin D," Bucksk says11,15 .

**ASSESSMENT OF STATUS AND DEFICIENCY OF VITAMIN D**

**RISK FACTORS**

Evaluation of vitamin D in clinical settings is based on serum 25 (OH) D (25 (OH) D3 plus 25 (OH) D2). The best way to evaluate an individual's vitamin D status is to standardize vitamin D (VDSP). The standard measurement of 25 (OH) D is the most accurate laboratory procedure for values obtained using the benchmarking measures measured by the National Institute of Standards and Technology (NIST) and the Gent (RMPS) measurement systems. The main steps to achieve uniformity are

(1) development of RMS. (2) the creation of a traceability series of real 25 (OH) D concentration as measured by the RMP to the research laboratory; and (iii) the creation and testing of the "end-user" testing performance to develop consistency across the various tests12.

There are potentially confusing factors affecting the condition of vitamin D, which is also known to play a role in increasing the risk of childhood metabolic syndrome. For example, increased use of television, video or computers, reduced physical activity, reduced sun exposure, reduced levels of milk consumption, and higher levels of soft drinks consumption may increase the risk of vitamin D deficiency in children aged 1-18 Year. At the age of 6-16 years, children were deficient in vitamin D in the spring and winter, and found that girls were more deficient than vitamin D compared to boys13.

**TREATMENT OF DEFICIENCY AND DOSING IN CHILDEREN**

Two forms of vitamin D supplements are D2 (ergocalciferol) and D3 (cholecalciferol). Both increase the vitamin D in the blood. Vitamin D supplements are readily available, inexpensive, easy to administer, and safe. When taking high doses, vitamin D2 may be less potent than vitamin D3. The maximum safe vitamin D is 1000-1500 IU per day for infants, 2500 to 3,000 IU / day for children aged 1 to 8 years, and 4000 IU / day for children 9 9 years of age14.

Some experts have found that between 2000 and 4000 IU / day of vitamin D3 is necessary to reduce the risk of cancer and autoimmune diseases and therefore recommends these high doses for patients with these specific conditions. Experts also recommend the completion of infants and children of at least 400 IU / day of vitamin D3, especially infants breastfed15.

The disparity in clinical recommendations and practices has the potential to confuse patients with healthcare providers, but it suggests that there may be a wide range of dose recommendations for vitamin D depending on the state of a particular disease situation and the level of deficiency. It is reassuring to know that vitamin D supplementation is relatively safe and that toxicity is rare and has been observed only when taking 40,000 IU / day16.

**Vitamin D and Diabetes**

There is evidence that vitamin D deficiency can be a major factor in type 1 diabetes and type 2 diabetes. Basically, the insulin-producing pancreas contains VDRs in addition to the 1 alpha hydroxylase enzyme. Evidence suggests that vitamin D therapy improves glucose tolerance and insulin resistance. Vitamin D deficiency leads to decreased insulin secretion. Vitamin D supplementation has been shown to restore insulin secretion in animals. The researchers also found indirect effects on insulin secretion, and may have a calcium effect on the secretion of insulin17. Vitamin D contributes to the normalization of extracellular calcium, which ensures the flow of natural calcium through cell membranes. Therefore, vitamin D deficiency may reduce the ability of calcium to affect the secretion of insulin. Other potential mechanisms associated with vitamin D and diabetes include improving insulin function by stimulating the expression of insulin receptor, enhancing the insulin response to glucose transfer, and indirectly affecting the possible insulin action by the effect of calcium on secretion of insulin, and enhancing systemic inflammation through the direct effect on cytokines 18.

**VITAMIN D AND TYPE 1 DIABETES IN CHILDREN**

Low vitamin D may be associated with an increased risk of type 1 diabetes. For example, there is a greater proportion of type 1 diabetes related to geographic diversity, with sites in higher latitudes that have more type 1 diabetes. This may be due to less sunlight and therefore lower levels of vitamin D19.

Because the destruction of cells usually starts in childhood or early childhood and continues until the diagnosis of type 1 diabetes, such studies are interesting in terms of vitamin D benefit in people with type 1 diabetes. It is wished that taking a vitamin D supplement rapidly after birth will be a good and protective strategy against the incidence of type 1 diabetes20.

Pregnant women and lactating mothers should take dietary supplements to ensure that vitamin D serum levels are optimal. Because vitamin D is a powerful organ of the immune system and helps to regulate and differentiate cell proliferation, it seems clear that vitamin D can play a role in the prevention of type 1 diabetes. Their research showed that the development of adequate vitamin D in mothers had an effect on reducing the development of type 1 diabetes in their children21.

Studies are also suppose that lacking to support that vitamin D would improve the treatment of Type 1 diabetes after diagnosis. Only a few intervention studies examined the effect of vitamin D supplements on type 1 diabetes, and were not successful22,26.

**Vitamin D and insulin secretion.**

Vitamin D can promote pancreatic beta cell function in several ways. The active form of vitamin D (1,25(OH)2D), enters the beta cell from the circulation and interacts with the vitamin D receptor-retinoic acid x-receptor complex (VDRRXR), which binds to the vitamin D response element (VDRE) found in the human insulin gene promoter, to enhance the transcriptional activation of the insulin gene and increase the synthesis of insulin. Vitamin D may promote beta cell survival by modulating the generation (through inactivation of NF-kB) and effects of cytokines. The antiapoptotic effect of vitamin D may also be mediated by downregulating the Fas-related pathways (Fas/Fas-L). Activation of vitamin D also occurs intracellularly by 1-alpha hydroxylase, which is expressed in pancreatic beta cells. Vitamin D also regulates calbindin, a cytosolic calcium-binding protein found in beta cells, which acts as a modulator of depolarization-stimulated insulin release via regulation of intracellular calcium. Calbindin may also protect against apoptotic cell death via its ability to buffer intracellular calcium. The effects of vitamin D may be mediated indirectly via its important and well-recognized role in regulating extracellular calcium (Ca21), calcium flux through the beta cell and intracellular calcium ([Ca21]i). Alterations in calcium flux can directly influence insulin secretion, which is a calcium-dependent process. insulin target tissues may contribute to peripheral insulin resistance (27,28).via an impaired insulin signal transduction,(29, 30) leading to decreased glucose transporter activity (31).

**Type 1 Diabetic Children Should get Vitamin D Testing and More**

**Studies Needed**

"To our knowledge, this is the first study that has been sufficiently activated to examine the association between 25-hydroxy-vitamin D and HbA1c (a measure of diabetes control) in children," Dr. Terry Lippman, lead author of the study, told a news briefing. Adolescents with type 1 diabetes, "These data point to the need to monitor vitamin D in all young people with this disorder," he said22.

The researchers call for follow-up studies in this area because the resulting data are not statistically significant. In the summary of this experiment, the authors noted that "the association between 25 hydroxy vitamin D and HbA1c was not positive, calling for longitudinal studies to confirm these results.21,22,"

Vitamin D deficiency is a widespread issue in the United States. The CDC approved that "in 2001-2006, two-thirds of the population had adequate vitamin D, defined by the Institute of Medicine as a 25-hydroxyvitamin D (25OHD) serum value of 50-125 nmol / l, about a quarter of whom were at risk of hypoproteinemia Vitamin D (serum 25OHD 30-49 nmol / L), and 8% were at risk of vitamin D deficiency (serum 25OHD less than 30 nmol / L)23.

**SUMMARY AND CONCLUSION**

However the role of vitamin D in regulating blood glucose is remain poorly understood, status of vitamin D plays a role in the incidence and treatment of diabetes24. Optimal vitamin D levels in the serum may be different for people at risk of diabetes, diabetes, and diabetes. According to Danesco et al., "Both animal and human studies revealed that adequate vitamin D supplementation may decrease type 1 diabetes and possibly type 2 diabetes and enhance metabolic control in the case of diabetes." Mechanisms are unclear and need more investigation "He said25.

**REFERENCES**

1. Mayer-Davis et. al. Increase in prevalence of type 1 diabetes from the SEARCH for Diabetes in Youth Study:2001-2009, in American Diabetes Association 72nd Scientific Sessions 2012: Philidelphia, PA.
2. Rewers, M. Epidemiology of type 1 Diabetes Mellitus. Adv Exp Med Biol, 2004. 552: p. 219-46.
3. Vitamin D supplement in early childhood and risk for Type I (insulin-dependent) diabetes mellitus. The EURODIAB Substudy 2 Study Group. Diabetologia, 1999. 42(1): p. 51-4.
4. DeLuca. Vitamin D and autoimmune diabetes. J Cell Biochem, 2003. 88(2): p. 216-22.
5. Pozzilli, P. Low levels of 25-hydroxyvitamin D3 and 1,25-dihydroxyvitamin D3 in patients with newly diagnosed type 1 diabetes. Horm Metab Res, 2005. 37(11): p. 680-
6. L. Adorini, The coming of age of 1,25-dihydroxyvitamin D(3) analogs as immunomodulatory agents. Trends Mol Med, 2002. 8(4): p. 174-9.
7. Cantorna., 1,25-dihydroxyvitamin D3 is a positive regulator for the two anti-encephalitogenic cytokines TGF-beta 1 and IL-4. J Immunol, 1998. 160(11): p. 5314-9.
8. Et al., High prevalence of vitamin D deficiency in children and adolescents with type 1 diabetes. Swiss Med Wkly, 2010. 140: p. w13091.
9. https://www.health.harvard.edu/blog/vitamin-d-whats-right-level-2016121910893

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10. Alemzadeh. , Hypovitaminosis D in obese children and adolescents: relationship with adiposity, insulin sensitivity, ethnicity, and season. Metabolism, 2008. 57(2): p. 183-91.

11. http://www.bprcem.com/article/S1521-690X(11)00073-X/fulltext

1. M.F., Vitamin D deficiency. N Engl J Med, 2007. 357(3): p. 266-
	1. 14. Borkar, V.V., et al., Low levels of vitamin D in North Indian children with newly diagnosed type 1 diabetes. Pediatr Diabetes, 2010. 11(5): p. 345-50.
2. Bener, High prevalence of vitamin D deficiency in type 1 diabetes mellitus and healthy children. Acta Diabetol, 2009. 46(3): p. 183-9.
3. Saad MF. Hypovitaminosis D is associated with insulin resistance

and beta cell dysfunction. Am J Clin Nutr. 2004;79(5):820–5. 15. Kovacheva R. The effect of vitamin D3 on insulin secretion and

peripheral insulin sensitivity in type 2 diabetic patients. Int J Clin Pract. 2003;57(4):258–61. Kromhout D. Vitamin D, glucose tolerance and insulinaemia in elderly men. Diabetologia. 1997;40(3):344–7.

16. Roesler S, et al. Low serum 25-hydroxyvitamin D concentrations are associated with insulin resistance and obesity in women with polycystic ovary syndrome. Exp Clin Endocrinol Diabetes. 2006;114(10):577–83.

17. Yeh J. A randomized controlled trial of vitamin D3 supplementation in African American women. Arch Intern Med. 2005;165(14):1618–23.

18. Gmyr V, et al. 1,25-Dihydroxyvitamin D3 protects human pancreatic islets against cytokine-induced apoptosis via down-regulation of the Fas receptor. Apoptosis. 2006;11(2):151–9.

19. Grodsky GM. Vitamin D deficiency inhibits pancreatic secretion of insulin. Science. 1980;209(4458):823–5.

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20. https://www.diabetes.co.uk/food/vitamin-d.html

21. Walton V, et al. Efficacy and metabolic effects of metformin and troglitazone in type II diabetes mellitus. N Engl J Med. 1998;338(13):867–72.

22. Dawson-Hughes B. The effects of calcium and vitamin D supplementation on blood glucose and markers of inflammation in nondiabetic adults. Diabetes Care. 2007;30(4):980–6. Epub 2007 Feb 2.

23. Wise PH. Vitamin D replacement in Asians with diabetes may increase insulin resistance. Postgrad Med J. 1998;74(872):365–6.

24. Bell NH. Vitamin D metabolism is altered in Asian Indians in the southern United States: a clinical research center study. J Clin Endocrinol Metab. 1998;83(1):169–73.

25. Noonan K, et al. Vitamin D receptor (VDR) mRNA and VDR protein levels in relation to vitamin D status, insulin secretory capacity, and VDR genotype in Bangladeshi Asians. Diabetes. 2002;51(7):2294–300.

26. Scragg R, Sowers M, Bell C. Serum 25-hydroxyvitamin D, diabetes, and ethnicity in the Third National Health and Nutrition Examination Survey. Diabetes Care. 2004;27(12):2813–8.

27. Draznin B, Sussman KE, Kao M, et al. Relationship between cytosolic free calcium concentration and 2-deoxyglucose uptake in adipocytes isolated from 2- and 12-month-old rats. Endocrinology 1988;122:2578–83.

28. Ohno Y, Suzuki H, Yamakawa H, et al. Impaired insulin sensitivity in young, lean

normotensive offspring of essential hypertensives: possible role of disturbed calcium metabolism. J Hypertens 1993;11:421–

29. Zemel MB. Nutritional and endocrine modulation of intracellular calcium: implications in obesity, insulin resistance and hypertension. Mol Cell Biochem

1998;188:129–36.

30. Williams PF, Caterson ID, Cooney GJ, et al. High affinity insulin binding and

insulin receptor-effector coupling: modulation by Ca21. Cell Calcium 1990;11:

547–56.

31.Reusch JE, Begum N, Sussman KE, et al. Regulation of GLUT-4 phosphorylation by intracellular calcium in adipocytes. Endocrinology 1991;129:3269–73.