What do studies say about the link between diabetes and vitamin D levels?

Proposing that vitamin D is a panacea that could prevent, or even cure, a range of diseases is a sure way to start a fight in some circles. The role of vitamin D in diabetes has been investigated for years without yielding clear conclusions. So what do the studies actually say?

Does vitamin D play a role in diabetes? Image credit: Joan Slatkin/Education Images/Universal Images Group via Getty Images.

Diabetes, both types 1 and 2, are potentially life threatening and certainly life changing conditions that affect people worldwide. Case numbers increased nearly fourfold between 1980 and 2014 according to the World Health Organization (WHO), with associated increases in mortality and disability caused by the disease.

The majority of those cases are <u>type 2 diabetes</u>, caused by excess visceral fat, though the <u>interaction</u> between genetic susceptibility, environment, obesity, and sedentary lifestyle is complex. It is <u>not uncommon</u> for people to have a moderate <u>body mass index (BMI)</u> and type 2 diabetes, though they still respond to weight loss.

Case numbers of <u>type 1 diabetes</u> are also growing. The reasons for this are not well understood, but some have compared the increase in type 1 diabetes cases to those of other autoimmune diseases such as <u>multiple sclerosis</u>. Both are more common in the northern hemisphere, as is <u>vitamin D deficiency</u>.

In fact, estimates suggest that as many as $\underline{40\%}$ of Europeans are vitamin D deficient, and 13% may be severely so — and the situation is worse still for individuals with dark skin. It is also difficult to ascertain how many people are deficient, as debate rages over the definition of deficiency.

<u>Dr. Victoria Salem</u>, a consultant endocrinologist and clinical scientist based at Imperial College London, told *Medical News Today* in an interview: "We know that type 1 diabetes is much more prevalent in the northern hemisphere and that's usually put down to the fact that we get less sunlight and therefore have less vitamin D levels. That's true also for multiple sclerosis. But it's essential that that's an association."

While it is just an association, the links do not stop there. "[There is] quite good data showing that vitamin D deficiency, frank deficiencies — so children who've got <u>rickets</u> — are much more likely later in life to develop type 1 diabetes. But equally, people who are given a high dose of vitamin D [...] are also less likely to get type 1 later on," she explained.

Of course, suggesting vitamin D, or lack of it, is responsible for disease or susceptibility to it, is rife with controversy. Particularly with the <u>heavily racialised</u> discussion over the role of vitamin D deficiency in susceptibility to COVID-19.

The controversy over the role of vitamin D in diabetes is most likely due to poorly designed trials that have failed to adequately measure the impact of vitamin D supplementation on groups that can be generalized, a recent update in the <u>European Journal of Clinical Nutrition</u> argued.

Vitamin D and the pancreas

Type 2 diabetes is typically diagnosed when high blood glucose levels are detected. This is ultimately caused by low <u>insulin</u> sensitivity in the tissues which makes it hard for the body to take glucose out of the blood.

To compensate for this lack of sensitivity, the body creates a larger amount of insulin until eventually the beta cells in the pancreas give up, and the affected individual cannot produce enough insulin to transport glucose into their cells, resulting in high blood sugar. It is often at this point that people receive the diagnosis of type 2 diabetes.

<u>Dr. James Brown</u> from Aston Research Centre for Healthy Ageing, Aston University in Birmingham, United Kingdom, studies type 2 diabetes and metabolism and explained the theory to *MNT* in an interview:

"If you look at the basic biology of vitamin D and what happens in diabetes, there is evidence that vitamin D improves what we call insulin sensitivity, which is a key part of

type 2 diabetes. And also evidence that vitamin D increases insulin secretion, and those two things are what effectively go wrong in type 2 diabetes as you become insulin resistant and your insulin doesn't work as well [...] So there is, if you like, a theoretical basis for these studies being done."

Dr. James Brown

Early intervention could be the key

This theory has led to studies that hoped to determine if vitamin D could prevent or even treat type 2 diabetes. The largest of those studies in recent years was the <u>D2D study</u>. This National Institutes of Health-funded study was the first large-scale randomized control trial of its kind and sought to determine if vitamin D supplementation would help reduce the risk of type 2 diabetes among people with <u>prediabetes</u>, a condition where blood glucose is already slightly elevated.

Researchers followed 2,423 participants for 2.5 years, with half assigned to take 4,000 IU — 100 micrograms (mcg) — of vitamin D supplementation a day, while half took no supplement.

At the end of the trial, results in the <u>New England Journal of Medicine</u> showed that those who had taken vitamin D supplementation had a higher level of vitamin D in their blood. Though they were 12% less likely to develop type 2 diabetes during the study, this was not found to be significantly different to the group who received no supplementation.

Dr. Salem said she thought the study was "underpowered", but did show an important trend. She explained:

"When they did sub-analyses, they showed that the people who weren't vitamin D deficient, who were made replete, or the people who were very good at taking their vitamin D, were significantly less likely to convert to type 2 diabetes. So that was really the best study that was prospective. And showed that if you replace vitamin D early on in the progression that you can reduce the risk of developing it."

- Dr. Victoria Salem

A couple of months later, results from a smaller randomized <u>placebo</u> control trial were published in the <u>European Journal of Endocrinology</u>, showing the impact of a supplement of 5,000 IU (125 mcg) of vitamin D on 48 patients at risk of type 2 diabetes compared to a group of 48 patients who took a placebo.

Researchers looked at insulin sensitivity and secretion and found that vitamin D supplementation <u>improved</u> both sensitivity and beta cell function.

These results lead to the question: What is behind the link between vitamin D and diabetes?

Dr. Salem explained: "There are lots of studies of in vitro data that suggests that vitamin D is good for beta cells and that vitamin D is also good generally in terms of modulating inflammation. And we know that type 2 diabetes is associated with metabolic syndrome, and that's generally a sort of hyper-inflammatory state. The mechanism remains unclear and is likely to be multifactorial."

Dr. Brown concurred that the disease is multifactorial and stated that it is unlikely that vitamin D alone will prevent it.

"If you're a typical, overweight, or obese, middle-aged male, taking a vitamin D tablet is unlikely to have a significant or marked impact on your risk of getting type two diabetes. But it's possible that if it's taken alongside a healthy diet, or if you have a diet that's rich in vitamin D naturally, that might alongside a healthy lifestyle, have an impact."

- Dr. James Brown

Identifying at-risk children for interventions

Whether or not vitamin D could be used to prevent or delay the onset of type 1 diabetes is yet another question. This is one of the questions behind the ongoing <u>TEDDY Study</u>, a longitudinal, global study into the environmental causes of type 1 diabetes.

Type 1 diabetes differs from type 2 diabetes in that it is an autoimmune disease. Beta cells in the pancreas are destroyed, meaning no insulin is produced and has to be replaced with insulin injections. It tends to be diagnosed in children aged between 4–14 years.

One paper to come out of the TEDDY study was published in the journal <u>Diabetes</u> in 2018. It outlined research undertaken as part of the study, which looked at 8,676 children born with genetic risk factors for type 1 diabetes.

The authors undertook a nested case-control study within this cohort, which means that they specifically searched for children who had persistent evidence of <u>islet autoimmunity</u> (376 cases) and compared them to 1,041 controls from the same cohort who had no signs of islet autoimmunity.

In children with islet autoimmunity, the body reacts against specific antigens, including insulin.

The observational study looked at vitamin D levels in the blood from early infancy and through childhood. It showed that having high enough levels of vitamin D in infancy was associated with a 41% lower risk of islet autoimmunity, a sign of type 1 diabetes, compared with those that were insufficient.

In childhood, the lower risk was 32%. It also found the protective effect of vitamin D increased for children with certain genetic makeup.

This paper showed vitamin D was important, said Dr. Salem, "but it's not a panacea." She added: "There will still have been plenty of people who received vitamin D, who still went on to develop type 1 diabetes. And they also may well have developed it later, which is still a good thing because delaying the onset is a good thing."

Dr. Victoria Salem told us the story of a friend who was concerned her younger daughter was about to develop type 1 diabetes, like her older sister: "She was checking her second daughter's blood sugars and noticed that they were getting higher, but she wasn't quite yet at the diagnostic level of type 1, and she said, 'I'm absolutely convinced that my daughter's about to get diabetes because it's not normal to have slightly high blood sugars'."

"She was sort of on tenterhooks for 6 months waiting for her to become diagnosed with type 1 diabetes. And of course, during that critical window, who knows whether the introduction of things like immune modulators and vitamin D is going to have a significant effect on reducing that girl's risk of developing type 1 diabetes?"

- Dr. Victoria Salem

This was an absolutely critical question, said Dr. Salem, but as she pointed out, there have been no large, prospective studies looking at whether giving vitamin D as a supplement can delay or prevent the onset of type 1 diabetes in children.

Diabetes and vitamin D: What we know

This poses "a really important question," she said, that "if you've got a young person who's at high risk of type 1 diabetes, should we be giving these patients very high doses of vitamin D to try and slow down or reduce their risk of progression to overt type 1?"

While the jury is out over the evidence for such interventions, the question becomes an ethical one. Do we sit on the knowledge that vitamin D could help, or do we potentially give false hope to individuals either at risk of type 1 or type 2 by suggesting they could reduce their risk by supplementing with vitamin D?

Hopefully, as our understanding of the genetic determinants of diabetes grows we may be able to offer more personalised advice to individuals, which could help answer that question.

Written by Hannah Flynn on January 21, 2022 — Fact checked by Hilary Guite, FFPH, MRCGP

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