

# The Impact of High-Dosage Vitamin D Supplementation on Insulin Resistance: A Case Report

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## Abstract

This case report investigates the therapeutic impact of high-dosage vitamin D supplementation on insulin resistance and weight reduction. In some studies and meta-analyses, we can find differing conclusions about the potential effectiveness of optimal serum blood vitamin D concentrations and their impact on insulin resistance. In this case report, we introduce the impact of high-dosage vitamin D supplementation on insulin resistance, the resolution of acanthosis nigricans, and the coinciding elevation of serum vitamin D levels into the optimal range. During 6 months of treatment patient had regular menstrual cycle, she didn't have recurrence of hidradenitis. Then we conclude improving of all secondary states, associated with insulin resistance.

**Keywords:** Insulin resistance; Vitamin D; High dose; Obesity; Treatment

## Introduction

There are increasing, largely inconsistent literatures had investigated the effect of dietary and supplementary vitamin D in association with IR/IS, glycemic indices and similar metabolic outcomes.

Vitamin D is involved in several non-skeletal health diseases, including common metabolic disorders like Metabolic Syndrome (MetS), Type 2 Diabetes (T2DM), Impaired Fasting Glucose (IFG), Non-Alcoholic Fatty Liver Disease (NAFLD) and Polycystic Ovarian Syndrome (PCOS), which are all characterized by Insulin Resistance (IR).

It has been demonstrated that there is an inverse association between vitamin D deficiency and the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR), which is used as the measure of insulin resistance and defined as an increase in insulin secretion necessary for the maintenance of glycemic homeostasis.

Studies have shown that vitamin D has direct and indirect effects on multiple mechanisms related to the pathophysiology of IR. Based on pre-clinical and animal studies, vitamin D supplementation seems to be proved improving insulin resistance and playing a regulatory role in insulin secretion and beta-cell survival [1].

Vitamin D deficiency increases the expression of pro-inflammatory cytokines, which can be the cause of insulin resistance in patients with relatively higher BMI; it has been observed that obesity is associated with hypovitaminosis D because of three reasons: Less exposure to sunlight, the low intake of vitamin D *via* nutrition and the sequestration of vitamin D in the adipose tissue.

In addition to this mechanism, it was found that high secretion of the anti-diabetic hormone leptin, whose levels are deregulated by abdominal adiposity, is associated with insulin resistance. This means that high doses of vitamin D supplements can decrease leptin levels and reduce BMI in insulin-resistant patients.

This effect would be linked to a reduced caloric intake mediated by the binding of vitamin D to its receptors in the paraventricular nucleus of the hypothalamus.

Some studies and meta-analysis showed, that the supplementation of vitamin D reduces the risk of insulin resistance and circulating levels of insulin; the inverse correlation between vitamin D and HOMA-IR becomes more robust with increasing Body Mass Index (BMI). The other studies showed, that vitamin D supplementation does not improve insulin sensitivity or secretion in vitamin D-deficient, overweight or obese adults, despite using high-dose vitamin D supplementation and robust endpoint measures. In this study the researchers didn't get the highest level of serum vitamin D-more than 50 ng/ml or 120 nmol/l.

One study showed the result of high-dosage vitamin D supplementation for 6 months, with significantly increased peripheral insulin sensitivity and  $\beta$ -cell function, suggesting that it may slow metabolic deterioration in this population. The mean 25(OH)D reached  $127.6 \pm 26.3$  nmol/L. This case report investigates the therapeutic impact of high-dosage vitamin D supplementation on insulin resistance and weight reduction in a 16-year-old female patient presenting with Acanthosis nigricans, obesity, insulin resistance related menstrual dysfunction, recurrent hidradenitis and comorbid depression [2].

Clinical trials exploring the impact of vitamin D supplementation on insulin resistance have shown promising but conflicting results. While some trials reported improvements in glycemic control and insulin sensitivity following vitamin D supplementation, others demonstrated limited or inconclusive outcomes.

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## Case Presentation

The patient, diagnosed with overweight-BMI 26.7, SDS+1,34 exhibited Acanthosis nigricans, menstrual dysfunction, recurrent hidradenitis and depressive symptoms. The patient's medical history revealed insulin resistance. She was prescribed metformin with no improvement of body weight and Acanthosis nigricans during 12 months. Laboratory findings revealed increased fasting insulin level and vitamin D deficiency. Given the concurrent diagnosis of vitamin D insufficiency (serum levels below 15 ng/mL), a high-dosage-weekly 100000 IU vitamin D3 supplementation regimen was initiated. Throughout the intervention, the patient's fasting insulin level, glucose level, HOMA-IR and serum vitamin D concentrations were monitored during six months of treatment.

The outcomes showed notable improvements in multiple domains. The levels of serum vitamin D increased to 70 ng/ml. The patient exhibited gradual weight reduction -5 kg, BMI-24.7, alongside improvements in insulin sensitivity, evidenced by reduced fasting insulin levels and HOMA-IR scores. (Figure 2). Simultaneously, the resolution of Acanthosis nigricans was observed, coinciding with the elevation of serum vitamin D levels into the optimal range. During 6 months of treatment patient had regular menstrual cycle, she did not have recurrence of hidradenitis. Nevertheless, the patient's depressive symptoms showed considerable amelioration during the intervention. The patient reported no adverse effects or complications associated with the high-dosage vitamin D supplementation during the course of follow-up. The patient didn't keep some diets or do exercises, can affected on weight loss (Figure 1).



Figure 1: The resolution of Acanthosis nigricans.

## Results and Discussion

Molecular mechanisms underlying the pathophysiological hypothesis of the possible association between hypo-vitaminosis D and insulin resistance are mainly associated with the expression of insulin receptors and the production of inflammatory cytokines and polymorphism of VDR expressed in the  $\beta$ -cells of the pancreas [5]. In particular, vitamin D acts upon gene transcription *via* genomic and non-genomic mechanisms. Based on the above, hypovitaminosis D and insulin resistance are genetically interrelated. In detail, it was shown that vitamin D works as an epigenetic factor, affecting the transcription level of many genes involved in insulin sensitivity, like Insulin Receptor Substrate (IRS), which is increased by 2.4-fold in high-fat mice models treated with vitamin D. As a result, insulin sensitivity improves in the target tissues because IRS protein increases insulin

sensitivity. In addition, vitamin D improves the sensitivity of insulin receptors to insulin and glucose transport and promotes the conversion of proinsulin to insulin [6]. Some data suggest that VDR gene polymorphism in combination of genotypes is associated with the risk of T2DM and thus requires further studies as a probable genetic risk marker for T2DM (Figure 2).

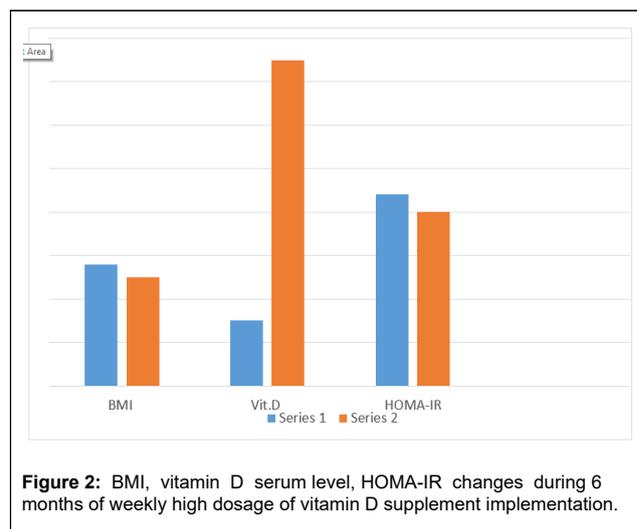


Figure 2: BMI, vitamin D serum level, HOMA-IR changes during 6 months of weekly high dosage of vitamin D supplement implementation.

It would be informative to conduct studies to determine the relationship between VDR gene polymorphism and the development of insulin resistance, as well as to determine the relationship between achieving high levels of vitamin D in the blood and the manifestation of clinical effects [7].

## Conclusion

This case report underscores the potential multifaceted benefits of high-dosage vitamin D supplementation in attenuating insulin resistance, aiding weight reduction and potentially influencing dermatological manifestations, such as Acanthosis nigricans, in adolescent individuals with obesity-related complications. However, larger-scale studies and investigations are warranted to elucidate the precise mechanisms and confirm the efficacy and safety of high-dosage vitamin D supplementation in such clinical contexts.

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