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# Role of Vitamin D in Prediabetes

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## Keywords

Prediabetes; Diabetes; Vitamin D

## Role of Vitamin D in Prediabetes

Prediabetes broadly refers to an intermediate stage between normal glucose levels and the clinical entity of type 2 diabetes, encompassing both Impaired Fasting Glucose (IFG) and Impaired Glucose Tolerance (IGT). Prediabetes is defined as Impaired Fasting Glucose (IFG) [Fasting plasma glucose ≥100 and ≤125 mg/dl; Impaired Glucose Tolerance (IGT) [2 hr plasma glucose ≥140 and ≤199 mg/dl] after ingesting 75 g of glucose (OGTT); or a combination of both. ADA proposes that HbA1c levels of 5.7% to 6.4% should also be considered as one of the criteria for prediabetes [1,2].

The progression from prediabetes to type 2 diabetes occurs over many years before the development of overt hyperglycemia seen in diabetes. The risk of progression to diabetes depends on the degree of insulin resistance and deficiency of Insulin secretion and other risk factors such as age, family history, overweight or obesity or history of gestational diabetes or PCOS [3,4]. Prediabetes is associated with increased risk of progressing to overt diabetes and a higher rate of cardiovascular diseases. Prediabetes is not only related to an increased risk of diabetes and its complications but there is also accumulating evidence to suggest damage on kidney and nerves already at the prediabetic stage. Identification and treatment of prediabetic individuals is therefore crucial. As per ICMR report prevalence of prediabetes in India is about 77.2 million [5]. According to an ADA expert panel, up to 70% of individuals with prediabetes will eventually develop diabetes [3].

Role of vitamin D in the regulation of calcium and bone metabolism is well known. Recent epidemiological evidence points to a potential association of vitamin D insufficiency with adverse metabolic risk and in the pathogenesis of cancer, cardiovascular diseases, type 2 diabetes and other diseases [6]. Biological mechanism that underlies the multiple effects of vitamin D on different tissues is not understood. One unifying factor is the expression of vitamin D receptors in more than 30 tissues including pancreatic islet cells [7]. Previous studies report that low serum 25(OH) D was inversely associated with metabolic syndrome risk, particularly for hyperglycemia, hypertriglyceridemia and abdominal obesity [6-8].

There is a limited available data on the relationship of vitamin D insufficiency/deficiency with glucose homeostasis among prediabetic individuals. High prevalence of hypovitaminosis D exists among prediabetics. A south Indian study has reported high prevalence of hypovitaminosis D exists among prediabetics and observed that 95% of the prediabetic cases were vitamin D deficient (*i.e.*, <30 ng/ml) compared to normoglycemics and similar results have been reported in Kashmiri and West Bengal population [9,10].

Third National Health and Nutrition Examination Survey (NHANES) have reported an inverse association between Vitamin D and metabolic syndrome risk, particularly for hyperglycemia, hypertriglyceridemia and abdominal obesity [11]. Even European Prospective Investigation into CANCER (EPIC)-Norfolk study reported an inverse association between circulating 25(OH) and type 2 diabetes [12].

Various studies indicate that vitamin D is important not only for cardiovascular health, but also for the immune response [6,13]. Several studies support that vitamin D supplementation may affect glucose homeostasis and improve insulin resistance [14,15]. A growing literature suggests that vitamin D homeostasis may play a role in the etiology of type 1 and type 2 diabetes [15,16]. Vitamin D also affects insulin resistance by stimulating the expression of insulin receptors, or indirectly by regulating calcium homeostasis. Despite proposed biological mechanisms, observational studies and clinical trials in humans did not provide consistent evidence regarding the association between vitamin D status and diabetes. In Middle East, despite ample sunshine, vitamin D deficiency is

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common due to cultural practice and dark skin color [17]. Same is the case in India where despite ample sunshine vitamin D deficiency has been reported [9,10].

Several studies have reported an impaired insulin release in association with vitamin D deficiency, and vitamin D supplementation has been shown to improve insulin release in randomized controlled trials [6,17]. Previous studies have demonstrated that vitamin D can affect both type I diabetes through its immunomodulatory effect and type II diabetes through anti-inflammatory effect [17].

There are a number of study findings that demonstrate a positive correlation between vitamin D deficiency and diabetes in humans [15]. Vitamin D has been reported to exert a direct effect on insulin synthesis and secretion because of the presence of the vitamin D response element in the human insulin gene promoter and the transcriptional activity of the human insulin gene caused by 1, 25-dihydroxyvitamin D, the active form of vitamin D [18]. A positive correlation has been demonstrated between serum vitamin D concentration and insulin sensitivity index wherein low serum vitamin D was associated with increased risk for insulin resistance [6].

The association between vitamin D deficiency and diabetes is well documented. Previous studies have established that a positive correlation exists between vitamin D deficiency and diabetes [6,18]. However, little is known about whether such an association exists with prediabetes. The effects of vitamin D supplementation on glucose tolerance and related autonomic nerve dysfunction have been a recent focus of scientific interest. Interventional studies are unpersuasive with regard to the beneficial clinical effects of vitamin D supplementation [19]. Vitamin D supplementation may prove to be an attractive therapeutic option for treating the pandemic prevalence of prediabetes and vitamin D deficiency.

Data from observational studies suggest that optimizing vitamin D status may reduce the risk of type 2 diabetes [19]. Few reports on the other hand do not support a role of vitamin D supplementation for prevention of type 2 diabetes among people with normal glucose tolerance. Future studies designed to evaluate serum 25(OH) vitamin D and vitamin D receptors levels in prediabetes would clarify this. Whether vitamin D supplementation may have a role in the prevention of diabetes in high-risk populations remains to be seen.

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