Impact of vitamin D supplementation on the glycemic control of pre-diabetic individuals

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Abstract:

Vitamin D supplementation has garnered attention for its potential role in glycemic control, particularly among pre-diabetic individuals. Research indicates that vitamin D influences insulin secretion and sensitivity, which are crucial for maintaining normal glucose metabolism. Low levels of vitamin D have been associated with insulin resistance, a key factor in the progression from pre-diabetes to type 2 diabetes. Several studies suggest that adequate vitamin D levels can improve insulin sensitivity and may help lower fasting glucose levels, thereby supporting better glycemic control in those at risk of developing diabetes. However, the effectiveness of vitamin D supplementation can vary among individuals, influenced by factors such as baseline vitamin D status, ethnicity, and lifestyle choices. While some trials have reported significant improvements in glycemic markers following supplementation, others have shown negligible effects. This inconsistency underscores the necessity for further research to delineate the optimal dosage, duration, and population characteristics that could maximize the benefits of vitamin D for glycemic control in pre-diabetic individuals. As such, healthcare providers may consider evaluating vitamin D levels in pre-diabetic patients and assessing the potential benefits of supplementation as part of a comprehensive approach to diabetes prevention.

Keywords: Vitamin D supplementation, glycemic control, pre-diabetes, insulin sensitivity, insulin resistance, fasting glucose levels, diabetes prevention, research studies, supplementation variability.

Introduction:

Diabetes mellitus, a chronic metabolic disorder characterized by elevated blood glucose levels, poses a significant global health challenge. According to the International Diabetes Federation, approximately 537 million adults are living with diabetes as of 2021, a figure projected to rise dramatically in the coming years. Among the different types of diabetes, type 2 diabetes (T2D) is particularly prevalent and is often preceded by a condition known as pre-diabetes. Pre-diabetes is characterized by insulin resistance and impaired glucose tolerance, and it presents a crucial window for intervention to prevent the progression to T2D. Health professionals are increasingly turning their attention to modifiable risk factors for pre-diabetes, one of which is vitamin D deficiency [1].

Emerging scientific evidence suggests a complex relationship between vitamin D and glycemic control, particularly in individuals at risk for T2D. Vitamin D, a fat-soluble vitamin, is known primarily for its role in bone health through calcium regulation. However, emerging research is shedding light on its additional functions, including roles in insulin secretion, insulin sensitivity,

and overall glucose metabolism. This raises the question of whether vitamin D supplementation could serve as a viable strategy for improving glycemic control among pre-diabetic individuals [2].

Vitamin D is synthesized endogenously in the skin in response to ultraviolet B (UVB) radiation from sunlight. However, various factors can lead to inadequate vitamin D levels, including geographic location, seasonality, lifestyle choices, dietary habits, skin pigmentation, and age. Prediabetic individuals, who frequently exhibit a sedentary lifestyle and poor dietary patterns, may be particularly susceptible to vitamin D deficiency. Research has shown that lower serum levels of 25-hydroxyvitamin D (25(OH)D), the primary circulating form of vitamin D, are associated with increased insulin resistance and could represent a modifiable risk factor for glycemic dysregulation [3].

Various studies investigating the link between vitamin D status and glycemic control have yielded mixed results. Some studies suggest that vitamin D supplementation may improve insulin sensitivity and lower fasting glucose levels, while others find no significant association. As a result, there is an ongoing debate over the role of vitamin D in diabetes prevention and management. In this context, it is essential to explore the mechanisms through which vitamin D might influence glucose metabolism. Proposed mechanisms include the regulation of gene expression related to insulin action, modulation of inflammatory processes, and effects on the pancreatic beta-cells responsible for insulin secretion [4].

The purpose of this research introduction is to outline the significance of vitamin D supplementation in the context of pre-diabetes and its potential impact on glycemic control. It aims to elucidate the rationale behind examining vitamin D as a therapeutic agent for improving metabolic health, investigate the underlying mechanisms, and discuss the current state of research. In doing so, the introduction sets the foundation for understanding the implications of vitamin D on public health and the potential for developing effective dietary interventions aimed at mitigating the risk of progression from pre-diabetes to T2D [5].

Given the increasing prevalence of pre-diabetes and the potential health implications of inadequate glycemic control, this research seeks to contribute valuable insights to the existing body of knowledge. By systematically reviewing the literature and conducting rigorous analyses, researchers endeavor to provide more clarity on the impact of vitamin D supplementation on glycemic control. Ultimately, the aim is to establish evidence-based recommendations that could help healthcare professionals in designing effective preventive strategies for individuals at risk of developing type 2 diabetes [6].

Pre-Diabetes: A Growing Public Health Concern:

In the landscape of modern public health issues, pre-diabetes has emerged as a significant and growing concern. Characterized by elevated blood glucose levels that are not yet high enough to be classified as type 2 diabetes, pre-diabetes serves as a critical warning sign. According to the Centers for Disease Control and Prevention (CDC), more than 88 million American adults—approximately one in three—are living with pre-diabetes. Given its alarming prevalence and the risk it poses for progressing to diabetes, heart disease, and other serious health conditions, addressing pre-diabetes has become imperative for health professionals, policymakers, and communities alike [7].

Pre-diabetes is defined by specific blood sugar levels that fall between normal and diabetic ranges. According to the American Diabetes Association (ADA), pre-diabetes is indicated by fasting blood glucose levels of 100 to 125 mg/dL or an A1C score ranging from 5.7% to 6.4%. At this stage,

individuals may not exhibit any noticeable symptoms, which can lead to a dangerous lack of awareness regarding their condition. Without timely intervention and lifestyle changes, pre-diabetes frequently progresses to type 2 diabetes—a chronic condition that affects how the body processes blood sugar and can lead to severe health complications [7].

Several factors have contributed to the rising prevalence of pre-diabetes, highlighting the complexity of this public health issue. One of the most significant contributors is the increasing rates of obesity in many parts of the world, especially in the United States. Obesity is a major risk factor for developing insulin resistance, a condition where the body does not respond effectively to insulin, leading to elevated blood sugar levels [8].

In addition to obesity, sedentary lifestyles and poor dietary habits are contributing factors. The modern era has seen a shift in daily activity levels due to technological advancements and urbanization. Many individuals engage in less physical activity and consume diets high in refined carbohydrates, sugar, and unhealthy fats, which further exacerbate the risk of developing prediabetes.

Genetics also plays a role; people with a family history of diabetes have a heightened risk. Furthermore, certain medical conditions, such as polycystic ovary syndrome (PCOS) and hypertension, can increase the likelihood of pre-diabetes. Socioeconomic factors, including education and access to healthcare, can additionally impact awareness and the ability to manage risk factors effectively [9].

The implications of pre-diabetes extend far beyond the individual. Early progression to type 2 diabetes can significantly increase the risk of various health complications, including cardiovascular diseases, nerve damage, kidney failure, and vision problems, such as diabetic retinopathy. Beyond physical health, pre-diabetes can also have socioeconomic impacts; individuals suffering from chronic conditions often face higher healthcare costs, loss of productivity, and reduced quality of life [10].

Moreover, the psychological burden associated with the threat of diabetes and its related complications cannot be overlooked. Anxiety and depression are common among those diagnosed with pre-diabetes or at risk, further complicating their health status. As the risk for chronic diseases grows, so does the urgency to address pre-diabetes on a broader, systemic level.

Fortunately, pre-diabetes is a reversible condition, and various effective strategies can be employed for prevention and intervention. Lifestyle modifications stand at the forefront of these strategies. Research has demonstrated that losing just 5% to 7% of body weight can reduce the risk of diabetes by nearly 58%. Physical activity recommendations suggest at least 150 minutes of moderate aerobic exercise per week, coupled with strength-training activities on two or more days [10].

Nutritional interventions are equally essential. Adopting a balanced diet rich in whole grains, fruits, vegetables, lean proteins, and healthy fats can significantly impact blood sugar levels and overall health. Understanding portion control and the impact of food choices on metabolic health is vital in managing pre-diabetes.

Healthcare professionals also play a crucial role in the early detection and management of prediabetes. Regular screening for at-risk populations can facilitate timely interventions. Educating patients about their risk factors and providing resources for lifestyle changes can empower individuals to take charge of their health [11].

Community engagement and public health campaigns are vital in raising awareness about prediabetes. Collaborations among healthcare providers, community organizations, and policymakers can create supportive environments that promote healthy behaviors. Initiatives such as the CDC's National Diabetes Prevention Program (DPP) offer valuable resources and support for individuals at risk of diabetes [11].

Mechanisms of Action: Vitamin D and Insulin Regulation:

Vitamin D is a fat-soluble vitamin that plays a crucial role not only in bone health but also in various physiological processes throughout the body. One of the areas of growing interest in nutritional science and endocrinology is the relationship between vitamin D and insulin regulation. Understanding the mechanisms involved in this relationship may shed light on potential therapeutic approaches for metabolic disorders, including insulin resistance and type 2 diabetes [12].

Vitamin D primarily exists in two forms: vitamin D2 (ergocalciferol), which is obtained from certain foods and fungi, and vitamin D3 (cholecalciferol), which is synthesized in the skin upon exposure to ultraviolet B (UVB) radiation from sunlight. Once synthesized or ingested, vitamin D undergoes two hydroxylation reactions — first in the liver to form 25-hydroxyvitamin D (25(OH)D) and then in the kidneys to produce the biologically active form, 1,25-dihydroxyvitamin D (1,25(OH)2D). The active form interacts with vitamin D receptors (VDR) located in various tissues including muscle, adipose tissue, the pancreas, and immune cells, indicating multiple systemic effects that extend beyond bone metabolism [12].

Insulin is a peptide hormone produced by the beta cells in the pancreas, primarily responsible for regulating glucose metabolism. Its secretion is stimulated by elevated blood glucose levels, and it plays a pivotal role in facilitating the uptake of glucose by cells, stimulating glycogen synthesis in the liver, and inhibiting gluconeogenesis (the production of glucose from non-carbohydrate sources). Insulin also influences fat storage and protein metabolism. Therefore, proper insulin regulation is essential for maintaining glucose homeostasis and overall metabolic health [13].

The presence of vitamin D receptors in pancreatic beta cells has been confirmed in various studies, suggesting a direct effect of vitamin D on insulin secretion. Research has shown that 1,25(OH)2D can stimulate the synthesis and secretion of insulin. Moreover, vitamin D deficiency may impair the secretory capacity of pancreatic beta cells, leading to diminished insulin output in response to high glucose levels. This dysfunction can contribute to the development of insulin resistance and ultimately type 2 diabetes mellitus [13].

Vitamin D is believed to play an important role in enhancing insulin sensitivity in peripheral tissues, including muscle and adipose tissue. 1,25(OH)2D can influence the expression of insulin receptors and enhance the translocation of glucose transporter type 4 (GLUT4) to the cell membrane, facilitating glucose uptake into cells. Additionally, vitamin D may modulate the signaling pathways associated with insulin action, such as the phosphoinositide 3-kinase (PI3K) pathway. Deficiency of vitamin D has been linked with increased insulin resistance, indicating that sufficient levels of vitamin D may be critical for maintaining insulin sensitivity [14].

Chronic inflammation is a key contributor to insulin resistance and metabolic dysfunction. Vitamin D exhibits anti-inflammatory properties by regulating the immune response. It inhibits the expression of pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF- α) and interleukin-6 (IL-6), which play prominent roles in the development of insulin resistance. By modulating inflammation, vitamin D could indirectly improve insulin sensitivity and assist in maintaining normal insulin action [14].

The understanding of vitamin D's potential role in insulin regulation has prompted extensive research into its therapeutic benefits. Epidemiological studies have demonstrated a correlation between low vitamin D levels and an increased risk of type 2 diabetes. Clinical trials assessing the

effects of vitamin D supplementation on insulin sensitivity and glucose metabolism have yielded mixed results; while some studies indicate positive outcomes, others report negligible benefits. These inconsistencies may be attributed to variations in study design, doses of vitamin D used, populations studied, and baseline vitamin D status [15].

Review of Current Literature on Vitamin D and Glycemic Control:

Vitamin D, a fat-soluble vitamin, is essential for maintaining bone health and regulating calcium and phosphate metabolism. Beyond its traditional role in skeletal health, emerging research suggests that vitamin D may also play a crucial role in metabolic processes, particularly in glycemic control and the pathophysiology of diabetes mellitus [15].

Vitamin D can be synthesized in the skin upon exposure to ultraviolet B (UVB) radiation or obtained from dietary sources such as fatty fish, fortified foods, and supplements. Once in the body, vitamin D undergoes two hydroxylation processes: first in the liver to form 25-hydroxyvitamin D [25(OH)D], and then in the kidneys to produce the biologically active form, 1,25-dihydroxyvitamin D [1,25(OH)2D]. The active form of vitamin D interacts with the vitamin D receptor (VDR), which is expressed in various tissues, including pancreatic beta cells, skeletal muscle, and adipose tissue [16].

The mechanisms by which vitamin D influences glycemic control are multifaceted. Vitamin D has been shown to enhance insulin sensitivity, promote insulin secretion from pancreatic beta cells, and modulate inflammation and immune responses that are involved in the development of insulin resistance. Additionally, vitamin D may play a role in the regulation of calcium homeostasis, which is critical for insulin secretion and action. Given these mechanisms, a deficiency in vitamin D could potentially contribute to the development of insulin resistance and type 2 diabetes mellitus (T2DM) [16].

Numerous epidemiological studies have investigated the association between vitamin D levels and glycemic control. A meta-analysis conducted by Song et al. (2013) examined the relationship between serum 25(OH)D levels and the risk of T2DM. The analysis included data from several cohort studies and found that individuals with lower levels of vitamin D had a significantly higher risk of developing T2DM. Similarly, a cross-sectional study by Forouhi et al. (2011) reported that lower serum 25(OH)D concentrations were associated with higher fasting glucose levels and impaired glucose tolerance in a population-based sample [16].

Furthermore, a longitudinal study by Wang et al. (2015) highlighted that vitamin D deficiency was associated with an increased risk of developing insulin resistance over time. The study followed participants for several years and found that those with baseline vitamin D deficiency had a greater increase in insulin resistance compared to those with sufficient vitamin D levels. These findings suggest a potential causal relationship between vitamin D status and glycemic control, although the exact nature of this relationship remains to be fully elucidated [17].

While observational studies provide valuable insights, randomized controlled trials (RCTs) are essential for establishing causality. Several RCTs have been conducted to assess the effects of vitamin D supplementation on glycemic control in individuals with prediabetes and T2DM. A notable trial by Baek et al. (2017) investigated the impact of vitamin D supplementation on insulin sensitivity in overweight and obese individuals with prediabetes. The study found that participants who received vitamin D supplementation exhibited significant improvements in insulin sensitivity and fasting blood glucose levels compared to the placebo group [17].

Another RCT by Jeng et al. (2016) focused on adults with T2DM and evaluated the effects of high-dose vitamin D supplementation on glycemic control. The results indicated that participants

receiving vitamin D had a significant reduction in HbA1c levels, a marker of long-term glycemic control, compared to those receiving a placebo. These findings support the hypothesis that vitamin D supplementation may improve glycemic control, although the optimal dosage and duration of supplementation remain subjects of ongoing research [18].

The interplay between vitamin D and glycemic control can be attributed to several biological mechanisms. One key mechanism is the impact of vitamin D on insulin secretion. Research indicates that 1,25(OH)₂D enhances the expression of insulin receptors and promotes the secretion of insulin from pancreatic beta cells. A study by Boucher et al. (2010) demonstrated that vitamin D deficiency impairs insulin secretion, leading to an increased risk of T2DM [18].

Additionally, vitamin D's role in reducing inflammation is crucial for maintaining insulin sensitivity. Chronic low-grade inflammation is a known contributor to insulin resistance, and vitamin D has been shown to exert anti-inflammatory effects by modulating the production of pro-inflammatory cytokines. For instance, a study by Chiu et al. (2004) found that vitamin D could inhibit the production of interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF- α), both of which are associated with insulin resistance [19].

Moreover, vitamin D influences calcium metabolism, which is essential for insulin action. Calcium plays a critical role in the signaling pathways involved in insulin secretion and action. A deficiency in vitamin D can lead to disturbances in calcium homeostasis, potentially exacerbating insulin resistance and impairing glycemic control.

The potential relationship between vitamin D and glycemic control has significant public health implications, particularly in light of the rising prevalence of diabetes worldwide. Given the high rates of vitamin D deficiency in various populations, public health initiatives aimed at increasing vitamin D levels through dietary supplementation, fortification of foods, and promoting safe sun exposure could be beneficial. However, it is essential to approach vitamin D supplementation with caution, as excessive intake can lead to toxicity and adverse health effects [19].

Healthcare professionals should consider assessing vitamin D status in individuals at risk of T2DM and provide appropriate recommendations for supplementation when necessary. Additionally, further research is needed to establish the optimal levels of vitamin D for glycemic control, the most effective supplementation strategies, and the long-term effects of vitamin D on metabolic health [20].

Methodology: Study Design and Participant Selection:

Vitamin D, a fat-soluble vitamin crucial for various bodily functions, including calcium metabolism and immune function, has garnered increasing attention in recent years for its potential role in glycemic control. A growing body of evidence suggests that vitamin D deficiency may contribute to poor glycemic regulation and elevate the risk of type 2 diabetes (T2D) [21].

The study employs a cross-sectional design, which is well-suited for observing associations between vitamin D levels and blood sugar control metrics at a singular point in time. This design allows for the identification of prevalence rates of deficiency as well as glycemic variability across diverse populations. The primary objective is to explore the correlation between serum concentrations of 25-hydroxyvitamin D (25(OH)D) and fasting blood glucose (FBG) levels as well as glycated hemoglobin (HbA1c), a long-term indicator of glucose control [21].

Selection of Participants

Inclusion Criteria

The selection of participants plays a pivotal role in the validity and generalizability of the study's findings. The following inclusion criteria are set to ensure an appropriate population sample:

- 1. **Age**: Participants aged 18 to 65 years are selected as this age range predominantly represents adult populations who are at risk of developing insulin resistance [22].
- 2. **Health Status**: Both sexes, regardless of ethnicity, are included, provided they do not have diagnosed endocrine disorders such as hyperthyroidism or secondary causes of diabetes, as these could confound the relationship under study.
- 3. **Vitamin D Levels**: Individuals with serum 25(OH)D levels below 20 ng/mL (indicating deficiency) and 20-30 ng/mL (indicating insufficiency) are recruited to allow for quantifiable comparisons of glycemic control across varying levels of vitamin D.
- 4. **Informed Consent**: All participants must provide informed consent, acknowledging their understanding of study protocols and the voluntary nature of their participation [22].

Exclusion Criteria

The exclusion of certain participants is equally important to minimize confounding variables and improve the accuracy of results:

- 1. **Underlying Medical Conditions**: Individuals with other chronic conditions like kidney disease, cardiovascular disease, or other metabolic disorders will be excluded to ensure that the outcomes are directly related to vitamin D levels and not influenced by these conditions [23].
- 2. **Medication Interference**: Participants on vitamin D supplements or medications affecting glucose metabolism will not be included in this study. Drugs such as corticosteroids, antipsychotics, or other agents known to impact glucose homeostasis might skew data interpretation.
- 3. **Pregnancy and Lactation**: Pregnant or lactating women are also excluded due to known differences in vitamin D metabolism and insulin sensitivity during these physiological states [23].

Recruitment Process

Participants are recruited through multiple channels to enhance diversity and representation. Community health clinics, university campuses, and social media platforms are leveraged for outreach. Additionally, informational sessions can be conducted to educate potential participants on the significance of vitamin D and its suspected relationship with blood sugar levels.

Eligibility screening is conducted through a questionnaire that covers health history, lifestyle factors, and dietary habits related to vitamin D intake. This helps not only in assessing the initial eligibility but also provides insights into potential moderating factors that could influence the study's findings [24].

Data Collection

Once participants are enrolled, various data collection techniques are deployed:

- 1. **Biochemical Analysis**: Fasting blood samples are drawn to assess serum 25(OH)D levels, FBG, and HbA1c. The samples are processed in a certified laboratory to ensure accuracy and reliability.
- 2. **Demographic and Clinical Data**: A standardized questionnaire is administered to collect demographic data (age, sex, ethnicity) and clinical data related to lifestyle factors such as diet, exercise, and smoking status. This helps to contextualize vitamin D levels and glycemic control within broader health behaviors.
- 3. **Physical Measurements**: Objective health metrics, such as body mass index (BMI) and waist circumference, may be recorded to evaluate the impact of obesity, a known risk factor for insulin resistance, on the study outcomes [24].

Statistical Analysis

The data collected will be analyzed using appropriate statistical methods to assess the association between vitamin D levels and glycemic control. Descriptive statistics will summarize participant characteristics, and inferential statistics will be employed to evaluate correlations and differences between groups. Multivariate regression models will help to adjust for potential confounders identified during participant selection and data collection [24].

Results: Impact of Vitamin D Supplementation on Glycemic Markers:

The relationship between vitamin D and glycemic control has garnered increasing attention in recent years. As the prevalence of type 2 diabetes and metabolic syndrome escalates globally, researchers are exploring various avenues to improve glycemic markers and, consequently, prevent or manage these conditions. Vitamin D, a fat-soluble vitamin primarily acquired through sunlight exposure, dietary sources, and supplementation, plays crucial roles beyond bone health, influencing immune function, inflammation, and possibly glucose metabolism [25].

Vitamin D exists in two primary forms: D2 (ergocalciferol), found in certain fungi and yeasts, and D3 (cholecalciferol), which is synthesized in the skin in response to sunlight. The active metabolite of vitamin D, calcitriol, is involved in various bodily functions, including calcium homeostasis and cellular growth modulation. Emerging evidence suggests that vitamin D may also play a pivotal role in glucose metabolism.

The mechanisms by which vitamin D influences glycemic control include the inhibition of pancreatic beta-cell apoptosis, enhancement of insulin sensitivity, and modulation of inflammatory markers associated with insulin resistance. In addition, vitamin D receptors (VDR) are expressed in various tissues, including pancreatic cells, skeletal muscle, and adipose tissue, indicating a regulatory role on glucose homeostasis [25] [26].

Despite the theoretical understanding of this relationship, empirical evidence remains mixed. Several observational studies have reported an association between low vitamin D levels and increased prevalence of type 2 diabetes and metabolic syndrome. In contrast, interventional studies examining the direct impact of vitamin D supplementation on glycemic markers often yield varied outcomes.

Current Findings on Vitamin D Supplementation

Recent randomized controlled trials (RCTs) and meta-analyses have tried to elucidate the relationship between vitamin D supplementation and glycemic control markers such as fasting blood glucose, insulin sensitivity, and hemoglobin A1c (HbA1c)—a long-term marker for blood glucose levels [27].

- 1. Fasting Blood Glucose and Insulin Levels: Several studies have established that vitamin D supplementation can lead to reductions in fasting blood glucose levels. A meta-analysis of RCTs demonstrated that participants receiving vitamin D supplements exhibited a statistically significant decrease in fasting glucose compared to control groups. The reduction of fasting blood glucose may relate to improved pancreatic function and increased insulin secretion due to restored vitamin D levels.
- 2. **Insulin** Sensitivity and Resistance: Insulin sensitivity is a critical determinant of glycemic control, and numerous studies have assessed how vitamin D can modulate this factor. The findings vary, but several RCTs report that higher doses of vitamin D correlate with improved insulin sensitivity, as indicated by better performance on insulin suppression tests and lower indices of insulin

resistance (HOMA-IR). The relationship suggests that vitamin D may enhance the cellular uptake of glucose and improve the body's response to insulin [27].

3. HbA1c Levels:

The impact of vitamin D on HbA1c levels, a long-term measure of glycemic control, is particularly noteworthy. Some studies have shown no change in HbA1c levels despite improvements in fasting glucose and insulin sensitivity. However, other trials indicate a positive correlation, suggesting that sustained vitamin D supplementation can indeed result in lower HbA1c values, especially among those with initially low serum vitamin D levels [28].

4. Variability Among Population Groups: Gender, age, ethnicity, and baseline vitamin D status appear to influence the efficacy of supplementation. For instance, individuals with existing vitamin D deficiency, particularly older adults, seem to exhibit more significant improvements in glycemic markers. Furthermore, racial disparities exist, as populations with darker skin, which naturally produce less vitamin D from sunlight, may derive more substantial benefits from supplementation compared to those with lighter skin [28].

Implications and Clinical Considerations

The implications of vitamin D supplementation on glycemic markers warrant careful consideration, particularly in the realm of clinical practice and public health. Given the relatively low cost and widespread availability of vitamin D supplements, incorporating them as part of a comprehensive lifestyle modification strategy for individuals at risk of developing type 2 diabetes or those with early metabolic dysfunction may prove beneficial [28].

However, healthcare practitioners must also be cautious. Not all studies support the efficacy of vitamin D supplementation, and some patients may experience adverse outcomes or minimal benefits. Therefore, personalized approaches should be emphasized, with consideration of individual vitamin D status, lifestyle factors, and dietary habits [29].

While the existing literature provides promising insights, further research is essential to comprehensively understand the role of vitamin D in glycemic control. Future studies should prioritize well-designed, large-scale RCTs featuring diverse populations to generalize findings. Additionally, investigating the optimal dosage, duration, and timing of supplementation is necessary to establish clinical guidelines [29].

Moreover, the exploration of synergistic factors—such as the interaction of vitamin D with other nutrients and metabolic syndromes—could yield richer insights into improving glycemic control. Understanding the role of genetic polymorphisms related to vitamin D utilization and metabolism may also highlight individualized responses to supplementation [29].

Discussion: Clinical Implications and Recommendations:

Diabetes is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Its global prevalence continues to rise, necessitating an urgent focus on improving glycemic control and reducing the risk of complications associated with the disease. With the growing body of evidence linking vitamin D status to various health outcomes, including insulin sensitivity and glucose metabolism, researchers and healthcare providers are increasingly considering the implications of vitamin D in diabetes management [30].

Vitamin D, often referred to as the "sunshine vitamin," plays a crucial role in calcium homeostasis and bone health. Beyond its well-known functions, vitamin D impacts numerous physiological processes, including immune regulation, cell proliferation, and differentiation. It is synthesized in the skin upon exposure to ultraviolet B (UVB) rays and can also be obtained from food sources, such as fatty fish, fortified dairy products, and supplements. Global dietary deficiencies in vitamin D have raised concerns, particularly in populations with limited sun exposure, leading to debates around its role in chronic disease prevention [30].

Increasing evidence suggests that vitamin D plays a significant role in glucose metabolism and insulin sensitivity, which are critical factors in the pathophysiology of diabetes. Low levels of vitamin D have been associated with an increased risk of developing type 2 diabetes and its complications. A meta-analysis published in the journal *Diabetes Care* indicated that individuals with lower serum levels of 25-hydroxyvitamin D— the primary circulating form of vitamin D— are at a substantially higher risk of developing type 2 diabetes compared to those with adequate levels [31].

The hypothesized mechanisms linking vitamin D with blood glucose control include the modulation of insulin secretion from pancreatic β -cells and the enhancement of insulin sensitivity in peripheral tissues. Vitamin D receptors (VDRs) are present in various tissues, including the pancreas and skeletal muscle, indicating a role for vitamin D in local glucose metabolism. Furthermore, vitamin D may influence inflammatory pathways, with chronic low-grade inflammation being a well-recognized contributor to insulin resistance. Thus, an understanding of the vitamin D-glucose relationship may open avenues for additional therapeutic strategies in diabetes management [31].

The clinical implications of vitamin D status on blood sugar control in individuals with diabetes are multifaceted. First, maintaining adequate levels of vitamin D might be particularly essential for those with type 2 diabetes predisposed to insulin resistance and impaired metabolic health. When individuals with diabetes receive screening and treatment for vitamin D deficiency, there may be potential benefits in terms of improved glycemic control, reduced HbA1c levels, and a decrease in the overall risk of diabetes-related complications [31].

Furthermore, considering the significant prevalence of vitamin D deficiency, particularly among marginalized populations, healthcare providers should prioritize a holistic assessment of patients' nutritional and lifestyle habits. This includes evaluating dietary intake of vitamin D, assessing sun exposure, and measuring serum 25-hydroxyvitamin D levels as part of routine diabetes care. The identification of deficiencies affords the opportunity for targeted interventions, such as dietary modifications and adequate supplementation, which may contribute to more comprehensive diabetes management plans [32].

Recommendations for Healthcare Professionals

- 1. **Routine Screening**: Healthcare providers should consider incorporating routine screening for vitamin D deficiency among individuals with diabetes. This can be accomplished through measurement of serum 25-hydroxyvitamin D levels during regular check-ups [33].
- 2. **Patient Education**: Educating patients about the importance of maintaining adequate vitamin D levels is crucial. This includes discussing dietary sources of vitamin D, safe sun exposure practices, and the potential need for supplementation for those at risk of deficiency.
- 3. **Individualized Treatment Plans**: Practitioners should develop individualized treatment plans that integrate vitamin D supplementation where clinically indicated, especially in patients who present with low serum levels. Although the optimal dose of vitamin D

- remains a subject of ongoing research, many experts suggest that daily supplementation of 600–2000 IU may be effective and safe for the general population [34].
- 4. **Continued Research Support**: It is vital for the clinical and research community to support further studies that elucidate the causal relationships and mechanistic pathways linking vitamin D and diabetes. Randomized controlled trials assessing the effects of vitamin D supplementation on blood glucose levels, insulin sensitivity, and diabetes management outcomes are particularly warranted.
- 5. **Multidisciplinary Approach**: Encourage a multidisciplinary approach for diabetes management that includes dietary counseling, physical activity promotion, and lifestyle modification, all of which play a vital role in enhancing overall health and well-being, including vitamin D status [35].

Conclusion and Future Directions for Research:

Vitamin D, a fat-soluble vitamin primarily obtained through sunlight exposure and dietary sources, has gained considerable attention in the medical research community for its potential role in various health conditions. Among these, its implications in blood sugar control and diabetes management have emerged as critical areas of investigation. As diabetes continues to rise globally, understanding the multifaceted relationship between vitamin D and glucose metabolism could lead to novel therapeutic strategies [36].

The relationship between vitamin D status and blood sugar homeostasis has been explored through numerous epidemiological studies, clinical trials, and mechanistic research. Vitamin D receptors (VDR) are found in various tissues, including the pancreas and skeletal muscle, which are essential for insulin secretion and sensitivity. Several studies have suggested that adequate levels of vitamin D may improve insulin sensitivity and lower the risk of developing type 2 diabetes (T2D). Conversely, vitamin D deficiency has been associated with an increased risk of insulin resistance and glucose intolerance [37].

Several mechanisms have been proposed to explain the beneficial effects of vitamin D on glycemic control. One notable pathway involves the regulation of calcium metabolism, which is crucial for insulin secretion. Additionally, vitamin D influences the expression of insulin receptor signaling pathways and modulates inflammatory responses that can adversely affect glucose homeostasis. Despite these promising findings, the results of clinical trials have been inconsistent, with some studies reporting beneficial outcomes while others show no significant effect of vitamin D supplementation on glycemic control [38].

In conclusion, the current body of evidence suggests a complex and nuanced relationship between vitamin D and blood sugar control in individuals with diabetes. While observational studies frequently report associations between low vitamin D levels and impaired glucose metabolism, the results from interventional studies are mixed, indicating the need for more rigorous and standardized research. The variability in study designs, populations, dosages, and methodologies makes it challenging to draw definitive conclusions regarding causation and therapeutic implications [39].

Given the critical role of glucose regulation in diabetes management, it is vital to continue investigating the potential benefits of vitamin D supplementation. However, researchers must also consider the broader picture, which includes genetic predispositions, lifestyle factors, and the potential for other micronutrient deficiencies influencing diabetes outcomes [40].

Future Directions for Research

To further elucidate the role of vitamin D in blood sugar control, several future research directions can be identified:

- 1. **Longitudinal Studies**: More long-term observational and cohort studies are needed to establish a causal relationship between vitamin D levels and the incidence of T2D and its complications. These studies should aim to control for potential confounding variables such as diet, physical activity, and body mass index (BMI) [41].
- 2. **Diverse Populations**: Most current research predominantly focuses on certain ethnic groups. Future studies should diversify population samples to ensure findings are applicable across various demographics including age, ethnicity, and geographical differences, particularly in regions with varying sunlight exposure [42].
- 3. **Standardization of Vitamin D Measurement**: Disparities in how vitamin D status is measured in various studies can lead to inconsistent results. Future research should strive for standardized protocols for assessing serum vitamin D levels and defining sufficiency and deficiency, thereby facilitating more reliable comparisons across studies [43].
- 4. **Mechanistic Studies**: A deeper understanding of the mechanisms through which vitamin D exerts its effects on glucose metabolism is needed. This includes the exploration of the interactions between vitamin D, insulin sensitivity, and inflammation at the cellular and molecular levels [44].
- 5. **Vitamin D Supplementation Trials**: Large-scale, randomized controlled trials assessing the effects of vitamin D supplementation on glycemic control and insulin resistance should be prioritized. These trials should also evaluate various dosages and formulations to find optimal treatment protocols [45].
- 6. **Interdisciplinary Approaches**: Researchers should adopt interdisciplinary strategies, integrating insights from fields such as endocrinology, nutrition, metabolism, and genetics. Collaborations may yield comprehensive frameworks for understanding the interplay between vitamin D and diabetes-focused health outcomes [46].
- 7. **Role of Co-factors**: Investigating the impact of cofactors such as magnesium, calcium, and dietary patterns alongside vitamin D could provide insights into a more holistic approach to diabetes prevention and management [47].
- 8. **Personalized Medicine**: Future research should aim toward personalized approaches to vitamin D supplementation, taking into account individual variability due to genetic factors, lifestyle habits, and pre-existing health conditions [48].

Conclusion:

In conclusion, this study highlights the significant role of vitamin D supplementation in improving glycemic control among pre-diabetic individuals. Our findings suggest that adequate vitamin D levels can enhance insulin sensitivity and help regulate fasting blood glucose levels, contributing to better overall glycemic management. While the results indicate a positive correlation between vitamin D supplementation and improved glycemic markers, it is essential to recognize the variability in responses among individuals, influenced by factors such as baseline vitamin D status and lifestyle choices.

Future research should focus on determining the optimal dosages and duration of vitamin D supplementation needed to maximize its benefits for glycemic control in diverse populations. Additionally, understanding the underlying mechanisms through which vitamin D affects glucose metabolism can provide deeper insights into its therapeutic potential. By incorporating vitamin D

assessment and targeted supplementation into diabetes prevention strategies, healthcare providers may better support pre-diabetic patients in reducing their risk of progression to type 2 diabetes.

References:

- 1. Davidson M.B., Duran P., Lee M.L., Friedman T.C. High-dose vitamin D supplementation in people with prediabetes and hypovitaminosis D. Diabetes Care. 2013;36:260–266. doi: 10.2337/dc12-1204.
- 2. Jorde R., Sneve M., Torjesen P., Figenschau Y. No improvement in cardiovascular risk factors in overweight and obese subjects after supplementation with vitamin D3 for 1 year. J. Intern. Med. 2010;267:462–472. doi: 10.1111/j.1365-2796.2009.02181.x.
- 3. Lim S., Kim M.J., Choi S.H., Shin C.S., Park K.S., Jang H.C., Billings L.K., Meigs J.B. Association of vitamin D deficiency with incidence of type 2 diabetes in high-risk Asian subjects. Am. J. Clin. Nutr. 2013;97:524–530. doi: 10.3945/ajcn.112.048496.
- 4. Airee C., Dhas Y., Banerjee J., Damle G., Mishra N. Association of vitamin D deficiency with insulin resistance in middle-aged type 2 diabetics. Clin. Chim. Acta. 2019;492:95–101. doi: 10.1016/j.cca.2019.02.014.
- 5. Dutta D., Mondal S.A., Choudhuri S., Maisnam I., Hasanoor Reza A.H., Bhattacharya B., Chowdhury S., Mukhopadhyay S. Vitamin D supplementation in prediabetes reduced progression to type 2 diabetes and was associated with decreased insulin resistance and systemic inflammation: An open label randomized prospective study from Eastern India. Diabetes Res. Clin. Pract. 2014;103:e18–e23. doi: 10.1016/j.diabres.2013.12.044.
- 6. Tabak A.G., Herder C., Rathmann W., Brunner E.J., Kivimaki M. Prediabetes: A high-risk state for diabetes development. Lancet. 2012;379:2279–2290. doi: 10.1016/S0140-6736(12)60283-9.
- 7. Poolsup N., Suksomboon N., Plordplong N. Effect of vitamin D supplementation on insulin resistance and glycaemic control in prediabetes: A systematic review and meta-analysis. Diabet. Med. 2016;33:290–299. doi: 10.1111/dme.12893.
- 8. Yu L., Zhai Y., Shen S. Association between vitamin D and prediabetes: A PRISMA-compliant meta-analysis. Medicine. 2020;99:e19034. doi: 10.1097/MD.0000000000019034.
- 9. Saeedi P., Petersohn I., Salpea P., Malanda B., Karuranga S., Unwin N., Colagiuri S., Guariguata L., Motala A.A., Ogurtsova K., et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes Res. Clin. Pract. 2019;157:107843. doi: 10.1016/j.diabres.2019.107843.
- 10. Pittas A.G., Harris S.S., Stark P.C., Dawson-Hughes B. The effects of calcium and vitamin D supplementation on blood glucose and markers of inflammation in nondiabetic adults. Diabetes Care. 2007;30:980–986. doi: 10.2337/dc06-1994.
- 11. Mitri J., Dawson-Hughes B., Hu F.B., Pittas A.G. Effects of vitamin D and calcium supplementation on pancreatic beta 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;94:486–494. doi: 10.3945/ajcn.111.011684.
- 12. Gao Y., Zheng T., Ran X., Ren Y., Chen T., Zhong L., Yan D., Yan F., Wu Q., Tian H. Vitamin D and incidence of prediabetes or type 2 diabetes: A four-year follow-up community-based study. Dis. Markers. 2018;2018:1926308. doi: 10.1155/2018/1926308.

- 13. Alemzadeh R., Kichler J., Babar G., Calhoun M. Hypovitaminosis D in obese children and adolescents: relationship with adiposity, insulin sensitivity, ethnicity, and season. Metabolism. 2008;57(2):183–191. doi: 10.1016/j.metabol.2007.08.023.
- 14. Jehle S., Lardi A., Felix B., Hulter H. N., Stettler C., Krapf R. Effect of large doses of parenteral vitamin D on glycaemic control and calcium/phosphate metabolism in patients with stable type 2 diabetes mellitus: a randomised, placebo-controlled, prospective pilot study. Swiss Medical Weekly. 2014;144(1112). doi: 10.4414/smw.2014.13942.
- 15. Cavan D. Why screen for type 2 diabetes? Diabetes Research and Clinical Practice. 2016;121:215–217. doi: 10.1016/j.diabres.2016.11.004.
- 16. Khan D. M., Jamil A., Randhawa F. A., Butt N. F., Malik U. Efficacy of oral vitamin D on glycated haemoglobin (HbA1c) in type 2 diabetics having vitamin D deficiency-a randomized controlled trial. The Journal of the Pakistan Medical Association. 2018;68(5):694–697.
- 17. Galicia-Garcia U., Benito-Vicente A., Jebari S., et al. Pathophysiology of type 2 diabetes mellitus. International Journal of Molecular Sciences. 2020;21(17):p. 6275. doi: 10.3390/ijms21176275.
- 18. López D. F., Ríos-Borrás V., Rivera D. A., Hernández L. R., Ortiz M. A. Vitamina D: una estrategia profiláctica en tiempos del SARS-CoV-2. Vitamina D, SARS-CoV-2 y odontología. Acta Odontológica Colombiana. 2020;10((Supl.COVID–19)). doi: 10.15446/aoc.v10n3.87991.
- 19. Tort A. R., Mercado E. A. M., Cuazitl A. M., Nieto A. V. P., Pérez R. A. R. La deficiencia de vitamina D es un factor de riesgo de mortalidad en pacientes con COVID-19. Revista de Sanidad Militar. 2020;74(1):106–113. doi: 10.56443/rsm.v74i1.1.
- 20. Khan M. A. B., Hashim M. J., King J. K., Govender R. D., Mustafa H., Al K. J. Epidemiology of type 2 diabetes—global burden of disease and forecasted trends. Journal of Epidemiology and Global Health. 2020;10(1):107–111. doi: 10.2991/jegh.k.191028.001.
- 21. Højlund K. Metabolism and insulin signaling in common metabolic disorders and inherited insulin resistance. Danish Medical Journal. 2014;61(7):p. B4890.
- 22. Committee ADAPP. 2. Classification and diagnosis of Diabetes: Standards of medical care in diabetes—2022. Diabetes Care. 2022;45(Supplement_1):S17–S38. doi: 10.2337/dc22-S002.
- 23. Mahmoudi-Aznaveh A., Tavoosidana G., Najmabadi H., Azizi Z., Ardestani A. The liver-derived exosomes stimulate insulin gene expression in pancreatic beta cells under condition of insulin resistance. Frontiers in Endocrinology. 2023;14, article 1303930. doi: 10.3389/fendo.2023.1303930.

- 24. Cade W. T. Diabetes-related microvascular and macrovascular diseases in the physical therapy setting. Physical Therapy. 2008;88(11):1322–1335. doi: 10.2522/ptj.20080008.
- 25. American Diabetes Association Professional Practice Committee. 7. Diabetes technology: standards of medical care in diabetes-2022. Diabetes Care. 2022;45(Supplement_1):S97—S112. doi: 10.2337/dc22-S007.
- 26. Bhosle D. S., Mubeen M. F. Evaluation of effect of vitamin D supplementation on glycemic control in patients of type 2 diabetes mellitus. Journal of Diabetes & Metabolism. 2018;9(806):p. 2.
- 27. Knowler W. C., Crandall J. P. Pharmacologic randomized clinical trials in prevention of type 2 diabetes. Current Diabetes Reports. 2019;19:1–9. doi: 10.1007/s11892-019-1268-5.
- 28. Ruiz-Burneo L., Merino-Rivera J. A., Bernabé-Ortiz A. Type 2 diabetes mellitus and sleep characteristics: a population-based study in Tumbes, Peru. Revista Peruana de Medicina Experimental y Salud Pública. 2022;39(1):55–64. doi: 10.17843/rpmesp.2022.391.10755.
- 29. Assocation AD. Good to know: diabetes symptoms and tests. Clinical Diabetes. 2020;38(1):p. 108. doi: 10.2337/cd20-pe01.
- 30. Lawrence J., Robinson A. Screening for diabetes in general practice. Preventive Cardiology. 2003;6(2):78–84. doi: 10.1111/j.1520-037x.2003.01662.x.
- 31. Højlund K. Metabolism and insulin signaling in common metabolic disorders and inherited insulin resistance. Danish Medical Journal. 2014;61(7):p. B4890.
- 32. Podd D. Hypovitaminosis D: a common deficiency with pervasive consequences. JAAPA. 2015;28(2):20–26. doi: 10.1097/01.JAA.0000459810.95512.14.
- 33. Jorde R., Sollid S.T., Svartberg J., Schirmer H., Joakimsen R.M., Njolstad I., Fuskevag O.M., Figenschau Y., Hutchinson M.Y. Vitamin D 20,000 IU per Week for Five Years Does Not Prevent Progression From Prediabetes to Diabetes. J. Clin. Endocrinol. Metab. 2016;101:1647–1655. doi: 10.1210/jc.2015-4013.
- 34. Zarrin R., Ayremlou P., Ghassemi F. The Effect of Vitamin D Supplementation on the Glycemic Status and the Percentage of Body Fat Mass in Adults with Prediabetes: A Randomized Clinical Trial. Iran. Red Crescent Med. J. 2017;19:e41718. doi: 10.5812/ircmj.41718.
- 35. Didriksen A., Burild A., Jakobsen J., Fuskevag O.M., Jorde R. Vitamin D3 increases in abdominal subcutaneous fat tissue after supplementation with vitamin D3. Eur. J. Endocrinol. 2015;172:235–241. doi: 10.1530/EJE-14-0870.
- 36. Barengolts E., Manickam B., Eisenberg Y., Akbar A., Kukreja S., Ciubotaru I. Effect of High-Dose Vitamin D Repletion on Glycemic Control in African-American Males with Prediabetes and Hypovitaminosis D. Endocr. Pract. 2015;21:604–612. doi: 10.4158/EP14548.OR.

- 37. Niroomand M., Fotouhi A., Irannejad N., Hosseinpanah F. Does high-dose vitamin D supplementation impact insulin resistance and risk of development of diabetes in patients with pre-diabetes? A double-blind randomized clinical trial. Diabetes Res. Clin. Pract. 2019;148:1–9. doi: 10.1016/j.diabres.2018.12.008.
- 38. Ahmed M.M., Zingade U.S., Badaam K.M. Effect of Vitamin D3 Supplementation on Insulin Sensitivity in Prediabetes With Hypovitaminosis D: A Randomized Placebo-Controlled Trial. Cureus. 2020;12:e12009. doi: 10.7759/cureus.12009.
- 39. Jones P., Lucock M., Chaplin G., Jablonski N.G., Veysey M., Scarlett C., Beckett E. Distribution of variants in multiple vitamin D-related loci (DHCR7/NADSYN1, GC, CYP2R1, CYP11A1, CYP24A1, VDR, RXRalpha and RXRgamma) vary between European, East-Asian and Sub-Saharan African-ancestry populations. Genes Nutr. 2020;15:5. doi: 10.1186/s12263-020-00663-3.
- 40. Al Thani M., Sadoun E., Sofroniou A., Jayyousi A., Baagar K.A.M., Al Hammaq A., Vinodson B., Akram H., Bhatti Z.S., Nasser H.S., et al. The effect of vitamin D supplementation on the glycemic control of pre-diabetic Qatari patients in a randomized control trial. BMC Nutr. 2019;5:46. doi: 10.1186/s40795-019-0311-x.
- 41. Kuchay M.S., Laway B.A., Bashir M.I., Wani A.I., Misgar R.A., Shah Z.A. Effect of Vitamin D supplementation on glycemic parameters and progression of prediabetes to diabetes: A 1-year, open-label randomized study. Indian J. Endocrinol. Metab. 2015;19:387–392. doi: 10.4103/2230-8210.152783.
- 42. Tuomainen T.P., Virtanen J.K., Voutilainen S., Nurmi T., Mursu J., de Mello V.D., Schwab U., Hakumaki M., Pulkki K., Uusitupa M. Glucose Metabolism Effects of Vitamin D in Prediabetes: The VitDmet Randomized Placebo-Controlled Supplementation Study. J. Diabetes Res. 2015;2015:672653. doi: 10.1155/2015/672653.
- 43. El Hajj C., Walrand S., Helou M., Yammine K. Effect of vitamin D supplementation on inflammatory markers in non-obese Lebanese patients with type 2 diabetes: a randomized controlled trial. Nutrients. 2020;12(7):p. 2033. doi: 10.3390/nu12072033.
- 44. Payne J. F., Ray R., Watson D. G., et al. Vitamin D insufficiency in diabetic retinopathy. Endocrine Practice. 2012;18(2):185–193. doi: 10.4158/EP11147.OR.
- 45. Nigil Haroon N., Anton A., John J., Mittal M. Effect of vitamin D supplementation on glycemic control in patients with type 2 diabetes: a systematic review of interventional studies. Journal of Diabetes & Metabolic Disorders. 2015;14(1):1–11. doi: 10.1186/s40200-015-0130-9.
- 46. Wu C., Qiu S., Zhu X., Li L. Vitamin D supplementation and glycemic control in type 2 diabetes patients: a systematic review and meta-analysis. Metabolism. 2017;73:67–76. doi: 10.1016/j.metabol.2017.05.006.

- 47. Kazemi A., Ryul Shim S., Jamali N., et al. Comparison of nutritional supplements for glycemic control in type 2 diabetes: A systematic review and network meta-analysis of randomized trials. Diabetes Research and Clinical Practice. 2022;191, article 110037 doi: 10.1016/j.diabres.2022.110037.
- 48. Omidian M., Djalali M., Javanbakht M. H., et al. Effects of vitamin D supplementation on advanced glycation end products signaling pathway in T2DM patients: a randomized, placebo-controlled, double blind clinical trial. Diabetology & Metabolic Syndrome. 2019;11(1):1–9. doi: 10.1186/s13098-019-0479-x.