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ORIGINAL ARTICLE

# To determine the frequency and severity of vitamin D insufficiency in type 2 diabetes patients

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***ABSTRACT:***

**Aim:** The study's goal is to determine the frequency and severity of vitamin D insufficiency in type 2 diabetes patients. **Methods:** In the Department of General Medicine, a case-control research was carried out. The research included a total of 100 volunteers, with 50 healthy persons serving as cases (Category A) and 50 type 2 diabetes patients serving as controls (Category B). Routine laboratory tests CBC, FBS, RBS, PP2BS, HbA1C, blood urea, serum creatinine, lipid profile, urine albumin, and Vitamin D3 levels were measured using established procedures at the Institute's central laboratory. **Results:** the prevalence of low vitamin D levels in the healthy group was just 26%, but it was 86% in the diabetic population. Among diabetic individuals with inadequate vitamin D levels, the majority (66 percent) had insufficiency, whereas just 20% had overt vitamin D deficiency. The prevalence of sufficient, insufficient, and deficient Vitamin D in patients with controlled diabetes according to HbA1C criteria was 18.18 percent, 63.64 percent, and 18.18 percent, respectively, whereas it was 10.71 percent, 67.86 percent, and 21.43 percent in patients with uncontrolled diabetes. In compared to diabetic patients with managed status, a higher proportion of uncontrolled diabetes patients (21.43 percent) had overt vitamin D insufficiency (18.18 percent). **Conclusion:** We found that diabetes state must be controlled in order to avoid vitamin D insufficiency.

**Keywords:** Vitamin D insufficiency, Type 2 diabetes mellitus, Serum vitamin D level

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## INTRODUCTION

Vitamin D is a pleiotropic hormone that, in addition to Ca and bone metabolism, is recognised to have immunomodulatory properties[1]. Its active version has been shown to have receptors on pancreatic b cells and immune cells. [2] There is evidence that vitamin D deficiency is linked to bacterial and viral illnesses. [3] Foot infection causes for 20% of diabetes patient hospitalizations each year. Immunological deficiencies, together with neuropathy and vascular abnormalities, are major contributions to the pathophysiology of diabetic foot and subsequent infections. Several studies have shown that vitamin D insufficiency causes immunological cell malfunction, b cell destruction, and decreased insulin production. [3] In addition to hyperglycemia, vitamin D insufficiency may be associated to a weakened immune system in diabetic patients, making them vulnerable to foot infection and a poor prognosis. Although the number of persons with T2DM is rising in all nations, it is mostly in emerging countries, where it is quickly becoming an epidemic. Because of the growing worldwide burden of T2DM, the pathophysiology of this illness is receiving considerable attention. The primary pathophysiologic abnormalities of T2DM are insulin resistance and -cell failure. It is mostly caused by the interaction of hereditary and environmental variables. T2DM prevalence varies by geographical location owing to changes in lifestyle and risk factors. Aside from traditional environmental risk factors including as obesity, physical inactivity, high calorie food consumption, and stress, the relevance of specific dietary variables in the pathogenesis of T2DM is still a developing idea. Evidence from multiple cross-sectional studies shows that vitamin D plays a significant role in blood glucose homeostasis, and that its shortage may lead to the development of T2DM. Vitamin D was initially characterised as a vitamin, but it is now generally understood that its active form is a hormone that is engaged not just in bone metabolism but also in a variety of non-skeletal physiological processes. Several methods have been suggested to explain vitamin D's favourable influence on insulin production and sensitivity, including a direct effect through activation of vitamin D receptors on pancreatic -cells and insulin sensitive organs and an indirect effect via modulation of calcium homeostasis. [3] The biggest epidemiological research from the NHANES population found a dose-dependent negative connection between vitamin D and type 2 diabetes, with the lowest quartiles of vitamin D having the greatest number of metabolic syndrome patients. [4] In humans, the major sources of vitamin D are sunshine, natural food, and dietary supplementation. Vitamin D from the skin and food is converted in the liver to 25-hydroxyvitamin D [25 (OH)D], which is used to assess the patient's vitamin D level. Although there is no universal agreement on what constitutes a normal level of vitamin D, most professionals classify vitamin D insufficiency as less

than 20 ng/ml. A vitamin D level of 20 to 29 ng/ml is regarded insufficient, whereas a level of 30 ng/ml or more is considered acceptable. [5,6] According to this criterion, 1 billion persons worldwide are deficient or insufficient in vitamin D. Even in the sunniest nations, such as India, vitamin D insufficiency is widespread since the majority of the body's surface is sheltered from the sun. India has a high prevalence of both T2DM and hypovitaminosis D. However, there is a scarcity of evidence on the association between the two. The study's goal was to determine the frequency and severity of vitamin D insufficiency in type 2 diabetes patients.

**METHODS AND MATERIALS**

After receiving clearance from the protocol review committee and the institutional ethics committee, a case-control research was carried out at the Department of General Medicine. Following informed permission, a comprehensive history was obtained from the patient or family. All patients were informed about the procedure's approach, risks, advantages, outcomes, and related complications. The research included a total of 100 participants, with 50 healthy persons serving as cases (category B) and 50 type 2 diabetes patients serving as controls (category A). Healthy people of the same age and gender served as controls. Patients with chronic renal disease, those who have used calcium or vitamin D supplements in the previous three months, and those who have a known chronic illness were all excluded from this research. Routine laboratory tests CBC, FBS, RBS, PP2BS, HbA1C, blood urea, serum creatinine, lipid profile, urine albumin, and Vitamin D3 levels were measured using established procedures at the Institute's central laboratory. The blood vitamin D level was further classified as adequate (30-100ng/ml), insufficient (20-29ng/ml), and deficient (less than 20ng/ml).

**RESULTS**

The mean age of category A (case) in the study population was 49.85±9.68 years, whereas category B (control) was 47.55±9.36 years. The research included 58 men and 42 females. Category A was composed of 64% men and 36% women. Category B (control) included 36% men and 64% women. When the inquiry profile of both categories A and B was evaluated, the mean values of haematological parameters such as haemoglobin, total count, and platelet count were within normal limits and similar in both categories. Surprisingly, the mean value of renal function test parameters, blood urea, and serum creatinine were all within acceptable ranges in the diabetic group, despite the fact that 10% of patients had abnormal serum creatinine levels ranging from 2.41 to 4.6 mg/dl.

The mean value of all lipid profile components was within normal limits in both categories, however 40 percent of diabetic patients exhibited dyslipidaemia, with hypertriglyceridemia being the most frequent in 32 percent of patients. The frequency distribution of participants was noticed based on the severity of their vitamin D level. In my research, the prevalence of low vitamin D levels in the healthy group was just 26%, but it was 86% in the diabetic population. Among diabetic individuals with inadequate vitamin D levels, the majority (66 percent) had insufficiency, whereas just 20% had overt vitamin D deficiency (table 1.)

The prevalence of sufficient, insufficient, and deficient Vitamin D in patients with controlled diabetes according to HbA1C criteria was 18.18 percent, 63.64 percent, and 18.18 percent, respectively, whereas it was 10.71 percent, 67.86 percent, and 21.43 percent in patients with uncontrolled diabetes. In compared to diabetic patients with managed status, a higher proportion of uncontrolled diabetes patients (21.43 percent) had overt vitamin D insufficiency (18.18 percent ). As the p value is less than 0.05, there is a significant relationship between the maintenance of euglycemia and the severity of Vitamin D level in diabetic patients (Table 2).

The Pearson correlation test revealed a negative link between HbA1C and mean vitamin D levels in the diabetic group ($r = -0.233$, p value = 0.001). It implies that when HbA1c levels rise, vitamin D levels fall, implying that the more severe the hyperglycemia and worse the diabetes management status, the greater the vitamin D insufficiency.

We also compared the mean value of vitamin D insufficiency to the length of diabetes, although there was no significant relationship (P value >0.5) between the duration of diabetes and serum vitamin D deficiency. The most prevalent microvascular consequence found in type 2 diabetes individuals was diabetic nephropathy. All three main microvascular problems - diabetic retinopathy, diabetic nephropathy, and peripheral neuropathy - were shown to have no significant link with blood Vitamin D level, as the p value for all three parameters was larger than 0.05. (Table 3). The most prevalent co-morbidity discovered in diabetics (14%) was hypertension, followed by Ischemic Heart Disease (8 percent ). All subjects had their blood vitamin D levels assessed. In group B, 86 percent of diabetics had fewer than normal vitamin D levels, whereas only 26 percent had less than normal vitamin D levels (control). The mean vitamin D value in type 2 diabetic patients was 29.83±5.97 ng/dl, whereas the mean vitamin D value in healthy persons was 38.21±3.89 ng/dl.

**Table.1 Severity grading of vitamin d deficiency in Category A and Category B**

| | Category A =50 | % | Category B =50 | % |
|---|---|---|---|---|
| **Deficiency** | 10 | 20 | - | |
| **Insufficient** | 33 | 66 | 13 | 26 |
| **Sufficient** | 7 | 14 | 37 | 74 |

**Table 2: The association of severity of vitamin D level with the category of diabetes control**

| Diabetes control | Vitamin D Level | | | Chi Sq (p value) |
|---|---|---|---|---|
| | Sufficient | Insufficient | Deficiency | |
| Controlled Diabetic (N = 22) | 4(18.18%) | 14 (63.64%) | 4(18.18%) | 2.88 |
| Uncontrolled Diabetic (N= 28) | 3(10.71%) | 19 (67.86%) | 6 (21.43%) | (0.001) |

**Table 3: Comparison of mean vitamin D level with duration and micro vascular complication of diabetes mellitus**

| | Parameters | | Mean value of vitamin D (ng/dl) | p value |
|---|---|---|---|---|
| | 0-5 years | | 28.21±5.73 | |
| Duration of diabetes | 5-10 years | | 30±4.77 | 0.17 |
| | >10 years | | 27.94±2.87 | |
| Micro-vascular complication | Diabetic | Present | 25.93±4.231 | |
| | retinopathy | Absent | 29.07±4.84 | 0.066 |
| | Diabetic | Present | 31.23±4.73 | |
| | nephropathy | Absent | 28.76±5.79 | 0.063 |
| | Peripheral | Present | 27.29±3.97 | |
| | neuropathy | Absent | 30.36±4.89 | 0.11 |

**Table 4: Subcategory analysis- means vitamin D level in diabetes patients in relation with age, gender and associated co-morbidities**

| Parameters (Number of patients) | | Mean value of vitamin D | p value |
|---|---|---|---|
| Age category | Below 35 (40) | 28.32±4.75 | |
| | Above 35 (10) | 28.02±2.59 | 0.25 |
| Gender | Male (32) | 31.15±4.36 | |
| | Female (18) | 28.12±3.48 | 0.032 |
| HTN | Yes (7) | 24.36±3.82 | |
| | No (43) | 28.38±5.61 | 0.041 |
| IHD | Yes (4) | 31.23±5.52 | |
| | No (46) | 29.27±4.62 | 0.14 |

## DISCUSSION

The research on the effect of 25(OH) vitamin D in vascular calcification is conflicting. Higher levels of 25(OH) vitamin D have been related with enhanced vascular calcification in experiments, although lower levels of 25(OH) vitamin D seem to have similar impact in vivo. This implies that 25 (OH) vitamin D may have a biphasic relationship with risk of Vascular Calcification in both excess and deficiency.[7] However, vitamin D insufficiency affects 50-90 percent of the average healthy population in India.[8] In our research, the prevalence of vitamin D insufficiency in the normal population was 26%, which is comparable to the global prevalence but much lower than the prevalence observed in Indian studies. Other Indian research contradicted this low frequency in a healthy population. Another ongoing investigation on vitamin D levels in a comparable location found a 16% incidence of vitamin D insufficiency in the healthy population. Vitamin D influences calcium metabolism and hence the skeletal system; however, it also has extra-skeletal effects on the cardiovascular system, endocrine problems, and autoimmune illnesses. Several studies have shown that vitamin D has an active role in the functional control of the endocrine pancreas, notably the beta-cells.

India has previously been designated as the "Diabetes Capital of the World." Diabetes mellitus is recognised as a serious developing pandemic in India, with 41 million diabetes people now and a projected increase to 70 million by 2025. Because vitamin D has been shown to have an influence on the pathophysiology of diabetes and there is a very high prevalence of vitamin D insufficiency, we decided to conduct this research to explore how these two high prevalence illnesses interact.

Various studies conducted in various geographical regions and cultural backgrounds have shown a wide range of prevalence of vitamin D insufficiency in the diabetic population, ranging from 67 percent to 98.8 percent.[8-11] Our research, along with studies by Bashir et al and Ifigenia-Kostoglou A et al, found a greater incidence of vitamin D insufficiency in diabetes

mellitus patients than in healthy persons, although two other investigations found no difference in prevalence between diabetic and healthy populations. [8-11] As a result, we compared the mean blood vitamin D level in diabetes patients and healthy people from diverse studies. Several research, including ours, found that diabetes individuals had lower mean vitamin D levels than the general population. [8,11,12]

The prevalence of sufficient, insufficient, and deficient Vitamin D in patients with controlled diabetes according to HbA1C criteria was 18.18 percent, 63.64 percent, and 18.18 percent, respectively, whereas it was 10.71 percent, 67.86 percent, and 21.43 percent in patients with uncontrolled diabetes. In compared to diabetic patients with managed status, a higher proportion of uncontrolled diabetes patients (21.43 percent) had overt vitamin D insufficiency (18.18 percent ). The p value is less than 0.05, indicating a significant relationship between the preservation of euglycemia and the severity of Vitamin D level in diabetic patients. Mukherjee B et al. had similar findings. Uncontrolled diabetes patients had a lower mean vitamin D level (19.47±4.76) than managed diabetic patients (23.63±3.71). [12] Modi KD et colleagues discovered that vitamin D levels were 22.41±8.6 in individuals with managed diabetes and 19.91±8.3 in uncontrolled diabetic patients, which was statistically significant. Overall insufficiency is more frequent in diabetic patients regardless of diabetic management level, but severe vitamin D deficiency is more likely in individuals with uncontrolled diabetes than in patients with managed diabetes (21.43 percent and 18.18 percent respectively). The research found a negative association between HbA1C levels and blood vitamin D levels using Pearson correlation. It suggests that when HbA1C levels rise, serum vitamin D levels fall. When the patient and control categories were analysed jointly, Ifigenia-Kostoglou A et al discovered that 25(OH) D3 levels were negatively linked with HbA1c (p = 0.008, r2 = 0.058, linear regression analysis). [11] According to Mukherjee B et al, there is a clear negative association between Vitamin D levels and diabetes (r= -0.94 and -0.97), and poorly managed diabetics have even lower Vitamin D levels. [12] Akshaykumar SV et colleagues found a statistically insignificant negative negligible co-relation between vitamin D levels and HbA1C (r = 0.017, p value 0.741). [10] The unfavourable connection between vitamin D level and glycemic control shown in this research suggests that vitamin D plays an active role in the aetiology of type 2 diabetes mellitus.

Diabetes duration and the prevalence of microvascular complications had little influence on blood vitamin D levels. There was no influence of increasing age on vitamin D level in diabetes patients, and no similar link was seen in other trials. Female diabetes patients had lower vitamin D levels than male counterparts; this might be owing to reduced exposure to sunlight due to home activities. In our investigation, the most prevalent comorbidity detected in diabetes individuals (14%) was hypertension. According to a study conducted by Shalini P et al, vitamin D insufficiency is more common (80.4 percent) in hypertension patients than in healthy (67.7 percent) people. In my research, hypertension diabetes patients had lower vitamin D levels than non-hypertensive diabetic patients, which was statistically significant (p value = 0.041). Another comorbidity associated with diabetes was ischemic heart disease, however there was no significant difference in mean Vitamin D levels between diabetic patients with and without ischemic heart disease.

## CONCLUSION

The current investigation supports the hypothesis that vitamin D deficiency is more prevalent in diabetic foot infection. Diabetics have reduced wound healing, but vitamin D is required for a healthy immune system. The most active vitamin D metabolite, 1,25-dihydroxyvitamin D3, stimulates the synthesis of antimicrobial peptides in keratinocytes from diabetic foot ulcers. This research raises the topic of vitamin D insufficiency as a potential risk factor for diabetic foot infections and proposes the necessity for vitamin D supplementation in such individuals to avoid or adjuvant antibiotic treatment for infection management. Our findings further suggest that 25(OH)D might be used as an additional approach for detecting the risk of foot problems in diabetics.

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