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# Study on Association Between Vitamin D Level with or without Microvascular Complications of Type2 DM

KEYWORDS: Vitamin D, Type-2 DM and Microvascular complications.


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**ABSTRACT** *Vitamin D deficiency is an important risk factor for glucose intolerance. It mainly regulates calcium and phosphate metabolism, its deficiency may also be involved in the aetiopathogenesis of carcinomas, autoimmune diseases, infections, respiratory and cardiac diseases. Vitamin D is a known suppressor of renin biosynthesis, and vitamin D deficiency has been associated with progression of chronic kidney disease (CKD). Patients with type 2 diabetes and CKD have an exceptionally high rate of severe 25-OH vitamin D deficiency. Our aim was to investigates the vitamin D levels between Type 2 diabetic patients with and without microvascular complications. Although vitamin D deficiency is more common in patients with Type 2 diabetes mellitus than healthy subjects, no relationship between vitamin D deficiency and microvascular complications of diabetes was found.*

**Introduction:**

Although Vitamin D mainly regulates calcium and phosphate metabolism, its deficiency may also be involved in the aetiopathogenesis of carcinomas, autoimmune diseases, infections, respiratory and cardiac diseases.[1–6] Vitamin D deficiency is an important risk factor for glucose intolerance.[7] Studies have shown impaired insulin synthesis and secretion in animal models with vitamin D deficiency; diabetes onset can be delayed with 1–25-OH vitamin D intake, and some specific studies have reported that vitamin D deficiency contributes to the etiology and progression of type 2 diabetes.[8,9] 25-OH vitamin D concentrations were found to be lower in patients with type 2 diabetes with impaired glucose tolerance than in controls.[10] Vitamin D is a known suppressor of renin biosynthesis, and vitamin D deficiency has been associated with progression of chronic kidney disease (CKD). Patients with type 2 diabetes and CKD have an exceptionally high rate of severe 25-OH vitamin D deficiency. The aim of the study was to investigates the vitamin D levels between Type 2 diabetic patients with and without microvascular complications.

**Material and Methods:**

This study was conducted in the Department of Medicine, Heritage Institute of Medical Science, Varanasi, India. A total 50 patients with Type 2 diabetes mellitus was enrolled in the study, of which 25 had microvascular complications (nephropathy, retinopathy or neuropathy) and 25 did not have any microvascular complications during the period from June, 2015 to January, 2016 along with 25 healthy subjects were also enrolled as a control group. Cases comprised of persons with type-2 diabetes aged 21-65 years with or without microvascular complications who were not receiving vitamin D or calcium supplementation. The control group comprised of age, sex and socioeconomically matched normal healthy subjects. Informed consent was taken from all the samples included in the study. Exclusion criteria were as follows: Subjects with type 1 diabetes mellitus, glycosylated hemoglobin (HbA1c) ≥7.5%, vitamin D intake greater than 1000 IU/day, serum calcium <8 or >11 mg/dL, creatinine >1.5 mg/dL, white blood cell <2,000 or >15,000/mm3, urine albumin to creatinine ratio >150 were excluded. Patients having disorders that change the metabolism of vitamin D, significant cardiac, hepatic, renal and oncologic disease, use of medications known to affect serum phosphate levels, calcitonin, calcitriol, growth hormone, anticonvulsants, hormone replacement therapy, steroids, testosterone or vitamin A (>20,000 units/day) were also excluded. Those having sun exposure less than 3 h/week were also excluded. The screening was done in each case to assess the associated microvascular complications, which include complete physical examination, microfilament test, nerve conduction velocity, detailed fundus examination, ultrasonography of the abdomen and other biochemical investigations. fasting plasma glucose, 2 hrs postprandial blood sugar, HbA1c, serum vitamin D levels (25-OH vitamin D), calcium, phosphorus, urea, creatinine, liver function test and lipid profile, complete blood count, thyroid stimulating hormone, urine routine microscopy, urine microalbumin by creatinine ratio, electrocardiogram and chest X-ray were done in all subjects under study. Vitamin D deficiency was defined as levels <20 ng/ml and insufficiency 20-29 ng/ml in accordance to WHO definition.[11] Diabetic nephropathy was defined by spot urine albumin by creatinine ratio of >30. Since, vitamin D levels are affected in later stages of chronic kidney disease thus diabetics with urine albumin by creatinine ratio >150 were excluded. Vitamin D levels were done from a single laboratory using same lab assay. [15] Data were analyzed by SPSS student t-test and one way ANOVA. A P-value <0.05 was considered statistically significant.

**Results and Discussion:**

A total of age, sex matched 50 cases and 25 healthy controls were studied. Among the 50 cases with type-2 diabetic, 27 were male and 23 were female with a mean age of 41.4 ± 3.06 years. The demographic characteristics of diabetic patients with and without microvascular complications and the healthy controls were summarized in (Table-1) and the comparison of biochemical parameters between the two diabetic groups in (Table-2). There were no statistically significant differences between the patients with and without microvascular complications with respect to plasma 25-OH-vitamin D ($p$ =0.82), calcium, phosphorus and PTH levels (Table-2). Fig 1 shows the contributions of male and female subjcets.

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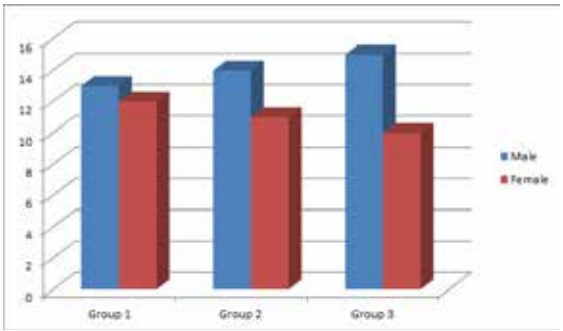


**Fig 1: Shows the contributions of male and female. Group-1(Cases with microvascular complications); Group-2(Cases without microvascular); Group-3(Healthy Control)**

**Table 1: Demographic characteristics of the groups (1, 2 & 3):**

| Parameters | Group-1 (N=25) | Group-2 (N=25) | Group-3 (N=25) |
|---|---|---|---|
| Age (Yrs) | 40.2 ± 2.01 | 42.6 ± 2.10 | 36.02 ± 4.10 |
| Weight (kg) | 61.21 ± 2.01 | 60.30 ± 2.0 | 52.03 ± 4.01 |
| BMI (kg/m$^2$) | 33.60 ± 2.03 | 34.05 ± 2.02 | 26.05 ± 2.30 |
| Duration of diabetes mellitus (Yrs) | 4.3 ± 3.01 | 9.01 ± 5.02 | - |

Statistically significant (P<0.05); Group-1(Cases with microvascular complications); Group-2(Cases without microvascular); Group-3(Healthy Control)

**Table 2: Comparison of biochemical variables between the two diabetic groups(Group 1 & 2):**

| Parameters | Group-1 (N=25) | Group-2 (N=25) | p-value |
|---|---|---|---|
| HbA1c (%) | 10.01±3.20 | 7.4±0.1 | <0.001 |
| Microalbuminuria (mg/day) | 242.6±26.1 | 12.01±0.1 | <0.001 |
| Creatinine (mg/dL) | 0.9±0.01 | 0.7±2.1 | 0.45 |
| 25-OH-vitamin D (ng/mL) | 14.02±1.06 | 15.7±3.4 | 0.82 |
| Total calcium (mg/dL) | 10.05±0.3 | 9.1±5.01 | 0.23 |
| Phosphorus mg/dL) | 4.02±0.25 | 3.9±0.00 | 0.16 |
| PTH ( pmol/L) | 4.81±0.21 | 5.22±0.2 | 0.25 |

Statistically Significant (P<0.05)

Vitamin D levels were below the normal range in both groups. When we compared the vitamin D levels among the subgroups of those with microvascular complications, we did not detect any differences ($p > 0.05$). No correlation was identified between HbA1c and vitamin D levels ($p$: 0.54, r: 0.43). There were no statistically significant differences between the diabetic and healthy groups in terms of plasma calcium, phosphorus and PTH levels. However, the healthy group had higher vitamin D levels than both diabetic groups ($p < 0.001$).

The risk for diabetes and associated metabolic abnormalities increases with vitamin D deficiency.[12-14] Vitamin D status may influence the risk of developing metabolic diseases such as type 2 diabetes, metabolic syndrome, and insulin resistance.[15] In our study, we did not ascertain an association between vitamin D levels and microvascular complications of Type 2 diabetes mellitus. However, we demonstrated that vitamin D levels were below the normal range in all diabetic patients, and the healthy group had higher vitamin D levels than the diabetic groups; these findings are similar to the results of previous studies.[16,17,18]

Vitamin D deficiency is a widespread disorder which is present in approximately 30% to 50% of the general population.[19,20] It is generally due to a lack of adequate sunlight exposure and/or nutritional vitamin D intake.[21] There is no consensus on optimal serum levels of 25-OH vitamin D. According to most experts, a level of < 20 ng/mL is defined as a certain deficiency, a level between 20 and 30 ng/mL is insufficiency, and a level of ≥ 30 ng/mL is normal.[22] Our healthy group also had low vitamin D levels which may be associated with the high prevalence of vitamin D deficiency in the Indian population.

Several studies suggesting the role of vitamin D in the pathogenesis of diabetes mellitus have been published. A study by Gedik and Akalin revealed that vitamin D supplementation increased insulin secretion from the pancreas.[23] Additionally, vitamin D replacement in patients with impaired glucose tolerance has been shown to decrease insulin resistance.[24] In our study, we did not detect any association between HbA1c and vitamin D levels in Type 2 diabetic patients. However, diabetic patients had lower vitamin D levels than the healthy group.

A link between hypovitaminosis D and microvascular complications in Type 2 diabetic patients has been proposed. Albert *et al* demonstrated that calcitriol, the active metabolite of vitamin D, inhibits retinal revascularization and plays a protective role in the development of retinopathy.[25] Vitamin D also prevents diabetic retinopathy by regulating blood glucose levels and blood pressure.[26,27] A negative correlation between vitamin D levels and blood pressure has been shown previously.[28] Vitamin D provides a cardioprotective effect by suppression of the renin-angiotensin system[29], inhibition of cardiac myocyte hypertrophy[30], reduction in the formation of vascular calcification and atherosclerosis, and has an anti-inflammatory effect.[31] Agarwal *et al* showed that vitamin D replacement therapy reduces levels of albuminuria.[32] In another study, vitamin D levels in diabetic patients were found to be lower in patients with nephropathy compared to the ones without nephropathy.[33]

Diabetic neuropathy is the most common microvascular complication of diabetes mellitus. In the study carried out by Lee *et al*, an association was detected between hypovitaminosis D and diabetic neuropathy. Researchers indicated that neuropathic pain decreased after vitamin D replacement therapy.[20] Another study demonstrated a link between hypovitaminosis D and neuropathy.[34] In contrast, in our study we did not find any differences in vitamin D levels between diabetic patients with and without microvascular complications. The results obtained in our study compare well with those obtained in above studies.

**Conclusion:**

These findings suggest that the vitamin D deficiency is more common in patients with Type 2 diabetes mellitus than healthy subjects. Previous reports have shown that a low concentration of serum 25-OH vitamin D increases the risk of developing diabetes later in life and is also associated with an increased risk of diabetic microvascular complications. The vitamin D status of patients with diabetes should be considered during their regular follow-up, and supplementation should be provided to those at risk of deficiency.

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