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Study on Vitamin D Level and Micro Vascular Complications of Type 2 Diabetes Mellitus

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Abstracts:
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. A total of 80 cases were studied. Among the 80 patients with diabetes, 34 were female and 46 were male with a mean age of 46.9 ± 8.9 years along with 20 age and sex matched healthy controls. 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.
Key words: *25-OH Vitamin D, Type-2 DM and Microvascular complications.*

Introduction

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. Our aim to investigates the vitamin D levels between Type 2 diabetic patients with and without micro vascular complications and healthy subjects to identify any possible associations with vitamin D levels and micro vascular complications.

Material and Methods

The present study was conducted in the Department of Medicine, Hi-Tech Medical College & Hospital Bhubaneswar, Odisha, India. A total 80 patients with Type 2 diabetes mellitus was enrolled in the study, of which 40 had micro vascular complications (nephropathy, retinopathy or neuropathy) and 40 did not have any micro vascular complications during the period from November, 2012 to December, 2013 along with 20 healthy subjects were also enrolled as a control group. Cases comprised of persons with type 2

diabetes aged 20-70 years with or without micro vascular complications who were not receiving vitamin D or calcium supplementation. The control group comprised of age, sex and socioeconomically matched normal healthy volunteers. 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 80 cases were studied. Among the 80 patients with diabetes, 34 were female and 46 were male with a mean age of 46.9 ± 8.9 years. 20 age and sex matched healthy volunteers served as controls. The clinical characteristics of diabetic patients with and without microvascular complications and the healthy group are summarized in (Table-1) and the comparison of biochemical variables between the two diabetic groups in (Table-2).

Table 1: Clinical characteristics of the groups:

Parameters		Patients with microvascular complicatons (N=40)	Patients without microvascular complicatons (N=40)	Control group (N=20)
Gender	Male	22	24	10
	Female	18	16	10
Age (yrs)		47.8 ± 7.7	46.06 ± 10.16	44.06 ± 10.16
Weight (kg)		77.85 ± 6.88	78.03 ± 6.90	76.03 ± 6.90
Height (cm)		78.44 ± 8.94	79.66 ± 9.31	76.66 ± 7.31
BMI (kg/m2)		32.06 ± 2.01	31.65 ± 2.62	25.65 ± 2.62
Duration of diabetes mellitus (yrs)		5.3 ± 0.2	8.6 ± 0.1	-

Table 2: Comparison of biochemical variables between the two diabetic groups:

Parameters	Patients with micro vascular complicatons (N=40)	Patients without micro vascular complicatons (N=40)	p-value
GHb (%)	9.5±1.2	7.1±0.4	<0.0001
Microalbuminuria (mg/day)	239.6±86.2	12.5±0.1	<0.0001
Creatinine (mg/dL)	0.8±0.0	0.6±2.1	0.35
25-OH-vitamin D (ng/mL)	14.10±1.08	15.9±1.4	0.72
Total calcium (8.4–10.6 mg/dL)	10.3±0.1	9.4±1.0	0.2
Phosphorus (2.5–4.6 mg/dL)	4.1±0.3	3.6±0.02	0.15
PTH (1.6–6.9 pmol/L)	4.6±0.2	5.12±0.2	0.21

Statistically Significant (P<0.05)

In this study, we did not ascertain an association between vitamin D levels and micro vascular 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.[12,13,14] Vitamin D deficiency is a widespread disorder which is present in approximately 30% to 50% of the general population.[15,16] It is generally due to a lack of adequate sunlight exposure and/or nutritional vitamin D intake.[17] 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.[18] 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.[19] Additionally, vitamin D replacement in patients with impaired glucose tolerance has been shown to decrease insulin resistance.[20] 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 micro vascular 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.[21] Vitamin D also prevents diabetic retinopathy by regulating blood glucose levels and blood pressure.[22,23] A negative correlation between vitamin D levels and blood pressure has been shown previously.[24] Vitamin D provides a cardio protective effect by suppression of the renin-angiotensin system[25], inhibition of cardiac myocyte hypertrophy[26], reduction in the formation of vascular calcification and atherosclerosis, and has an anti-inflammatory effect.[27] Agarwal *et al* showed that vitamin D replacement therapy reduces levels of albuminuria.[28] In another study, vitamin D levels in diabetic patients were found to be lower in patients with nephropathy compared to the ones without nephropathy.[29]

Diabetic neuropathy is the most common micro vascular 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.[16] Another study demonstrated a link between hypovitaminosis D and neuropathy.[30] In contrast, in our study we did not find any differences in vitamin D levels between diabetic patients with and without micro vascular complications.

Conclusion

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 micro vascular 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. Further studies are needed to assess the role of vitamin D replacement therapy in the treatment of diabetes mellitus and prevention of micro vascular complications.

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