



Vitamin D Status in Patients with Type II Diabetes Mellitus: A Case Control Study

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Abstract

Introduction: Vitamin D is a product of cholesterol metabolism. One of the most important step of vitamin D production is (conversion of 7-dehydro-cholesterol to active vitamin D is dependent upon exposure to sunlight. The common causes of vitamin D deficiency include advancing age, inadequate exposure to sunlight and chronic hepatic and renal failure. The relation of vitamin D deficiency and diabetes is complex and many studies have suggested that vitamin D deficiency may be related to onset of type II diabetes and adequate vitamin D levels are necessary to reduce inflammation which is a major factor in progression to overt diabetes mellitus. We have conducted this study to know the vitamin D status of individuals with type II diabetes mellitus and compared it with healthy individuals of comparable age groups.

Materials and Methods: This was a case control study carried out in a tertiary care hospital situated in an urban area with an aim to determine the frequency of vitamin D deficiency or insufficiency in patients with type II diabetes mellitus. 50 known cases of type II diabetes were enrolled in this study as cases on the basis of a predefined inclusion and exclusion criteria. Control group comprised of 50 individuals of similar age and physical characteristic. In both these groups detailed history was taken. Investigations like Complete Blood Count, Serum Calcium and Alkaline Phosphatase was done in all the cases. The data was tabulated and analyzed using SPSS 21.0 version software.

Results: The mean weight and Body mass indexes were comparable in both the groups. The mean weight of control group was 63.28 +/- 7.42 kg while in cases group the mean weight was 69.48 +/- 8.72 kg. While mean height in control and cases group was 5.42 +/- 0.082 and 5.36 +/- 0.064 feet respectively. Serum calcium in cases and control groups was 8.24 +/- 0.22 and 8.82 +/- 0.161 while ALP was 96.30 +/- 8.12 and 106.04 +/- 6.12 respectively. 25 (OH) Vit D was found to be 94.36 +/- 7.92 in control group and 76.60 +/- 5.52 in cases group. Individuals with diabetes were found to have a statistically significantly reduced vitamin D levels as compared to individuals in control group.

Conclusion: Patients having type II DM were found to have significantly lower 25 (OH) vitamin D levels. It is essential that patients with type II DM be screened for vitamin D deficiency and if present it should be treated appropriately.

Keywords: Vitamin D, Alkaline Phosphatase, Type II Diabetes Mellitus, Insulin Resistance.

Introduction

With rapid industrialization and sedentary life styles there is a pandemic of obesity and its associated diseases such as hypertension, metabolic syndrome and type II diabetes mellitus (type II DM)¹. Diabetes is one of the common risk factors for cardiovascular morbidity and mortality. As is well known that type II DM is a clinical syndrome characterized primarily by development of insulin resistance causing diminished effect of available insulin. This resistance is initially overcome by increase secretion of insulin by beta cells of pancreas but over a period of time these islet cells can no longer meet the increase requirement for insulin needed for maintenance of optimum blood sugar levels heralding as conversion from prediabetes to overt diabetes mellitus². The insulin resistance in patients of type II DM is associated with decrease transport of glucose in the muscle cells leading to hyperglycemia. The other effects of increased insulin resistance include increase glycogenolysis and lipolysis. All these metabolic changes ultimately responsible for fluctuations in blood sugar levels causing complications such as nephropathy, neuropathy and retinopathy³.

One of the major risk factors associated with increased risk of development of insulin resistance and diabetes is obesity⁴. Various studies have conclusively proved that increased body mass index is the single most important risk factor for development of insulin resistance⁵. In addition to obesity the other risk factors which may predispose an individual for development of diabetes include increasing age, first degree relatives with diabetes, individuals with hypertension, dyslipidemia and women with a history of gestational diabetes and polycystic ovarian syndrome⁶.

Role of vitamin D in etiopathogenesis of diabetes mellitus has been the topic of great interest amongst researchers. Various authors have found that vitamin D deficiency may alter insulin synthesis and secretion consequently causing glucose intolerance, diminished insulin secretion

and diabetes mellitus⁷. The mechanism by which vitamin D deficiency may predispose an individual for development of type 2 diabetes is thought to be mediated through plasma calcium level regulation as well as through a direct effect of vitamin D on beta cells of pancreas⁸. On cellular level vitamin D deficiency cause insulin resistance by dysregulation of calcium flux through the cell membrane thereby causing disturbances in intracellular calcium which is an important factor for peripheral insulin resistance⁹. Reduced vitamin D levels may also cause secondary increase in parathyroid hormone levels and raised parathyroid level once again predisposes an individual for development of insulin resistance¹⁰. It is important to understand that vitamin D deficiency in patients with long standing diabetes may be due to diabetic nephropathy and in this situation vitamin D deficiency is the effect rather than the cause of diabetes mellitus¹¹. Irrespective of vitamin D being the cause or effect of type II DM it is important that all the patients with diabetes be screened for presence of vitamin D deficiency and if found to be deficient in vitamin D then appropriate vitamin D and calcium therapy should be instituted¹².

With the ever increasing evidence about role of vitamin D in etiopathogenesis of type II DM we undertook this study to determine the frequency of vitamin D deficiency or insufficiency in patients with type II diabetes mellitus.

Materials and Methods

This was a case control study conducted at a tertiary care medical Centre located in an urban area of India. Institutional Ethical committee duly approved the study. 50 patients who had been already diagnosed with diabetes mellitus were included in the cases group on the basis of a predefined inclusion and exclusion criteria. 50 healthy individuals (usually relatives of the patients) were included in the control group. A detailed history was taken to find out duration of diabetes, presence of complications such as

neuropathy, nephropathy and retinopathy, treatment history, dietary history and any significant past history was noted. All patients underwent a thorough general and systemic examination. Body mass index of all the patients as well as individuals in control group was determined and compared. Other anthropometric parameters such as height, weight and weight circumference were recorded in all patients and in control group. Routine investigations including blood sugar level, complete blood count and glycosylated hemoglobin was done in all the cases. The samples were collected and sent to the laboratory observing the standard protocols. Other parameters such as the Vitamin D levels, Alkaline phosphatase level and serum Calcium levels were measured by appropriate laboratory tests. Serum 25[OH] D levels were classified as vitamin D sufficiency (>75 nmol/l) vitamin D insufficiency (50–75 nmol/l) and vitamin D deficiency (< 50 nmol/l). The patients diagnosed to be having vitamin D deficiency were further subclassified into Deficiency (25-49 nmol/l) and severe deficiency (< 25nmol/l). Vitamin D deficiency in Type II DM patients (cases) as well as in any individual from control group if was treated by appropriate vitamin D and calcium supplementation. All the results obtained were documented and statistical Analysis was done on the test results. The data was analyzed using appropriate statistical methods. P value less than 0.05 was taken as statistically significant. Data analysis was done using SPSS 17.0 version

software. Microsoft excel and word were used for generating charts and graphs.

Inclusion Criteria

1. All patients between the age of 18- 45 years and who were known cases of type II DM. Healthy individuals of similar age were enrolled as controls.
2. Informed consent was given.

Exclusion Criteria

1. Pregnant Females
2. Patients having severe illnesses likely to affect calcium metabolism such as hyperparathyroidism, hyperparathyroidism or thyroid abnormalities.
3. Patients with malabsorption syndromes.
4. Patients on drugs known to cause fluctuations in Sr calcium levels like women on anticonvulsants, long term steroid therapy or antiretroviral drugs.
5. Those who refused consent
6. Patients with chronic hepatic or renal failure.

Results

A total of 50 patients with type II DM were included in the cases group whereas 50 healthy individuals were included in the control group with an aim to determine the vitamin D status of patients with type II DM and to compare it with vitamin D status of healthy individuals. In cases groups there were 36 males and 14 females whereas in control group there were 32 males and 18 females. Out of total 100 individuals there were 68 males and 32 females with a M:F ratio of 1:0.47.

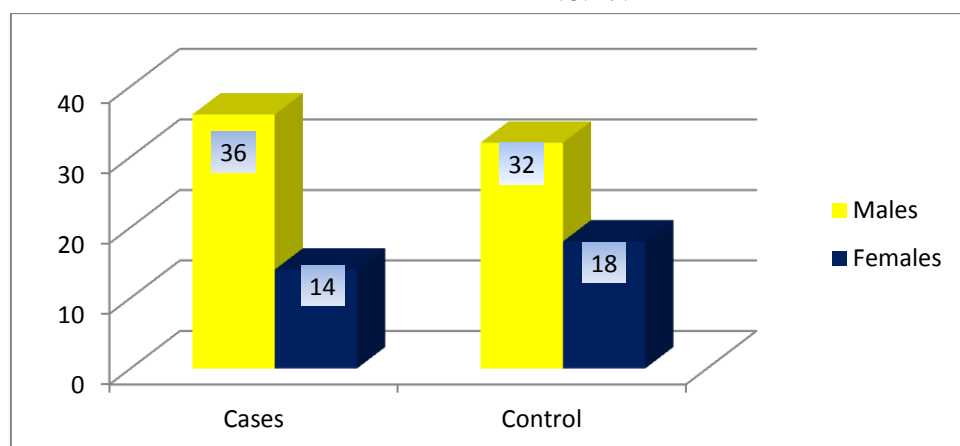


Figure 1: Gender Distribution in the studied groups

The analysis age group of the patients revealed that majority of the patients belonged to the age group of 41-50 years. The minimum age was found to be 34 years and maximum age was 68 years. The mean age in cases was found to be

46.94+/- 9.58years whereas the mean age of control group was found to be 42.1 +/- 9.72 years. The difference was found to be statistically significant (P=0.01)

Table 1: Age Group of the studied cases

Age group	Cases		Control	
	Number Of cases	Percentage	Number Of Cases	Percentage
< 30 years	2	4 %	5	10 %
31-40 years	5	10 %	12	24 %
41-50 years	24	48 %	23	46 %
51-60 years	16	32 %	8	16 %
61-70 years	3	6 %	2	4 %
Total	50	100 %	50	100 %
	Mean Age= 46.94+/- 9.58		Mean Age= 42.1 +/- 9.72	
P= 0.01 (Significant)				

Overweight and obesity was found to be one of the common features of the studied cases. In cases group 34 (68%) patients were either overweight or obese. Remaining 16 (32%) patients had a normal BMI. The analysis of BMI of the individuals in

control group showed that 8 patients were obese (BMI => 30) and 12 patients were overweight (BMI=> 25 but < 30). Rest of the patients had BMI less than 25.

Table 2: Body Mass Index of the studied cases

Body Mass Index	Cases		Control	
	Number Of cases	Percentage	Number Of Cases	Percentage
Normal BMI (< 25)	16	32 %	30	60 %
Overweight (BMI=> 25 but < 30)	20	40 %	12	24 %
Obese (BMI => 30)	14	28 %	8	16 %
Total	50	100 %	50	100 %
Mean BMI	27.18 +/- 3.88		25.24 +/- 3.73	
P= 0.01 (Significant)				

Comparison of signs and symptoms which could be attributed to deficiency of vitamin D was analyzed in cases as well as control group. It was found that symptoms such as tiredness, bone pain,

weakness, hair loss, depressed mood and back pain were more common in patients with type II DM as compared to individuals in control group.

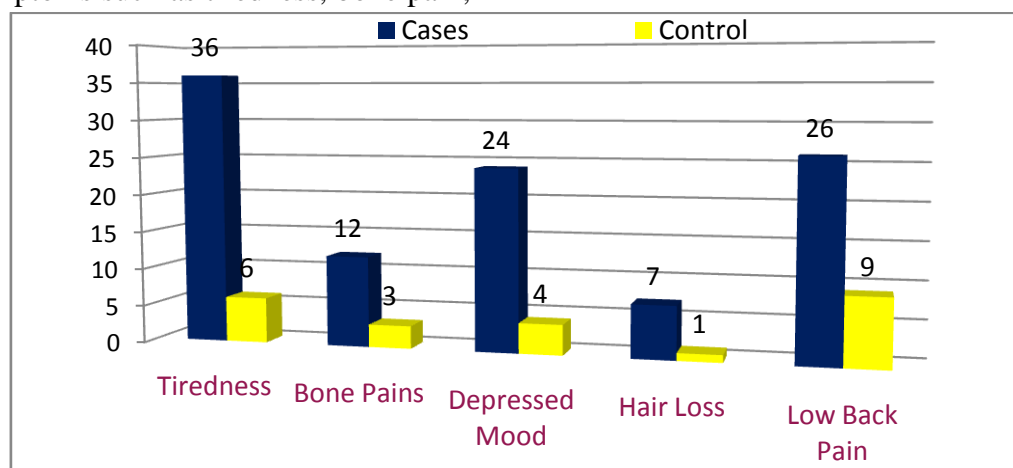


Figure 2: Signs and symptoms in the studied cases

The vitamin D status of the patients and individuals in control group was determined by estimation of 25 (OH) vitamin D levels. In patients with Type II DM only 12 (24%) were found to have sufficient vitamin D levels and remaining 38 (76%) patients were either having insufficiency (50-74 nmol/Lit), deficiency (25-49 nmol/Lit) or severe deficiency (< 25 nmol/Lit) of

Table 3: 25 (OH) vitamin D levels in studied cases

25 (OH) vitamin D levels	Cases		Control	
	Number Of cases	Percentage	Number Of Cases	Percentage
Sufficiency (> 75 nmol/Lit)	12	24%	24	48%
Insufficiency (50-74 nmol/Lit)	20	40%	12	24%
Deficiency (25-49 nmol/Lit)	10	20%	8	16%
Severe Deficiency (< 25 nmol/Lit)	8	16%	6	12%
Total	50	100%	50	100%
Mean 25 (OH) Vitamin D	49.64+/- 21.05		62.66+/- 23.11	
P= 0.004 (Highly significant)				

The estimation of calcium and alkaline phosphatase was also done in cases as well as controls. The mean calcium level in cases was found to be 9.72+/- 0.62 mg/dl where as in control group mean calcium level was 9.54 +/- 0.58 mg/dl. The difference was not found to be

Table 4: Serum calcium and alkaline phosphatase in studied cases

	Cases		Control		Significance
	Mean	Std Deviation	Mean	Std Deviation	
Serum Calcium	9.72	0.62	84.32	28.12	P=0.13 Not Significant
Serum Alkaline Phosphatase	9.54	0.58	62.72	22.32	P<0.0001 Significant

Discussion

There is a rapid increase in incidence of type II diabetes mellitus due to changes in life style of the population. There is a direct link between obesity and diabetes mellitus. There are many studies which have suggested that there is a link between vitamin D deficiency and incidence of type II DM. Moreover there are studies which have suggested that adequate vitamin D levels may postpone onset of overt diabetes¹³.

In our study the most common age group to be affected by type II DM was found to be between 41-50 years followed by 51-60 years. Mean age of the patients affected by diabetes was found to be 46.94 +/- 9.58 years. Nguyen QM et al conducted

vitamin D. In control group 24 (48%) individuals had vitamin D sufficiency. The mean 25 (OH) vitamin D levels in cases and control group was found to be 49.64+/- 21.05 and 62.66+/- 23.11 respectively. The individuals with type II DM were found to have a statistically significant low levels of 25 (OH) vitamin D (P=0.004).

statistically significant (P=0.13). The mean alkaline phosphatase levels in cases and control groups was found to be 84.32 +/- 28.12 and 62.72 +/- 22.32. The difference was found to be statistically highly significant (P<0.0001).

a prospective study of 144 individuals who were followed for 16 years¹⁴. The authors found the incidence of diabetes to be highest between the age group of 30-39 years. In our study the most common affected age group was between 41-50 years but the many patients had the history of type II DM since many years hence it can be said that the age of onset of type II diabetes as reported by Nguyen QM et al and our study was similar. There are other authors who have reported that there is a decrease in age at onset for type II DM. Koopman RJ et al reported that there is decrease in mean age at onset of type II DM from 52.0 to 46.0 years¹⁵.

Being overweight is one of the most important predisposing factors for development of overt diabetes. Obesity is associated with increased insulin resistance which is one of the cardinal pathophysiologic mechanism by which type II DM develops. In our study the patients with Type II DM was having high BMI as compared to individuals in control group. The difference was found to be statistically significant ($P=0.01$). The link between increased BMI and prediabetes and diabetes had been reported by innumerable studies including those by Golay et al¹⁶ and Al-Goblan AS et al¹⁷.

In our study individuals with type II DM were found to have a statistically significant low level of 25 (OH) vitamin D. The mean 25 (OH) vitamin D levels in cases and control group was found to be 49.64 +/- 21.05 and 62.66 +/- 23.11 respectively. The individuals with type II DM were found to have a statistically significant low levels of 25 (OH) vitamin D ($P=0.004$). Many studies have postulated that vitamin D deficiency plays a crucial role in etiopathogenesis of type II DM. Ayhan R et al conducted a study to evaluate vitamin D levels and metabolic parameters in patients with prediabetes, compared to healthy controls¹⁸. The authors found that Pre DM patients' mean plasma 25[OH] D level (25.7 ± 14.9 nmol/l) was statistically lower than the control group (31.4 ± 17.8 nmol/l). On the basis of this finding the authors concluded that low 25 (OH) levels may play an important role in the development of type 2 diabetes. Similar low vitamin D levels in Type II DM patients were reported by Abbasi et al¹⁹ and Lim S et al²⁰.

Conclusion

There is convincing evidence about the role of vitamin D in the pathogenesis of type II of diabetes. In our study vitamin D levels were found to be lower in patients with Type II DM as compared to healthy individuals and the difference was found to be statistically significant. Whether vitamin D supplementation lowers type 2

diabetes risk needs to be proved by appropriate randomized controlled trials.

Conflict of Interest: None.

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