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Assessment of Vitamin D Level in Diabetic Individuals and its Association with Glycemic Status as compared by HbA1C levels.

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Abstract

Vitamin D deficiency is a common public health problem all over the world. Vitamin D deficiency contributes significantly to the pathogenesis of the two types of diabetes by impairing insulin secretion from pancreatic beta-cells and increasing insulin resistance[1]. β-cell dysfunction and insulin resistance are also associated with low vitamin D levels.[2] It has also improved glycemic control and insulin sensitivity in people with diabetes and normal individuals.[3]

Material and Methods: This was a case control study done in department of medicine, Shri Ram Murti Smarak medical college Bareilly. We recruited randomly 50 patients of type 2 DM visiting general medicine OPD and 50 healthy subjects were taken as controls. A demographic profile were taken and after that blood was taken for Biochemical parameter after overnight fasting like fasting blood sugar, post prandial blood sugar, HbA1C and serum Vitamin D levels were measured in both cases and controls. The data was entered in Microsoft excel 2019 for analysis and tested statistically on SPSS for windows 2020 software.

Results: The mean age of the case group was 51.2±7.98 and in control group was 50.6±7.73 years. FBS in control group and in diabetic group which showed a significant difference ($p<0.001$). PPBS and HbA_1C was statistically significant between the two groups. The mean concentration of vitamin D in the case group was 17.7±9.2 ng/dl and in the control group was 26.6±11.33 ng/dl which was statistically significant ($p<0.001$). There was negative correlation between the vitamin D and FBS and PPBS level which was statistically significant ($p<0.001$) whereas vitamin D and HbA_1C shows negative correlation but was not statistically significant.

Conclusion: Vitamin D as an adjuvant to oral hypoglycemic drugs in treatment in diabetic patients, vitamin D levels being related to glycemic control in diabetes mellitus type 2. These findings may have therapeutic implications as cautious vitamin D supplementation may improve glycemic control in diabetes mellitus type 2.

Keywords: Diabetes Mellitus, HbA_1C, Vitamin D

Introduction

Diabetes mellitus is one of the largest global health challenges of this century. It is a chronic progressive metabolic disease which occurs when the body cannot effectively use the insulin it produces or pancreas does not produce enough insulin which leads to hyperglycemia. The International Diabetes Federation has estimated that globally there are 415 million people with diabetes in 2015 and is predicted to increase to 642 million by 2040.[4] It is alarming to note that more than 47% of the world's population is still undiagnosed for diabetes with the prevalence still bound to increase further. People with type 2 diabetes are increasing in every country, but more than 80% live in low and middle – income countries. Among the top 10 countries in the world, India stands second with 69.2 million people with diabetes and another 36.5 million with prediabetes which is a high-risk condition for diabetes and cardio-vascular disease.[4] A recently reported Indian Council of Medical Research - India Diabetes (ICMR-INDIAB) study conducted in four different zones of rural and urban India showed that the prevalence of diabetes and prediabetes are higher compared to previous studies. The inter-state variations in prevalence ranging from 4.3% (Bihar), 10.4% (Tamilnadu) and 13.6% (Chandigarh).[5] This increasing incidence is mainly attributed to lifestyle changes, eating habits and being physically inactive.

Approximately 30%-50% of people are recognized to have low levels of vitamin D, and insufficiency and deficiency of vitamin D are recognized as global health problems worldwide. Type 2 diabetes mellitus (T2DM) is considered as one of the non skeletal diseases related with deficiency of vitamin D. Although the presence of hypovitaminosis D increases the risk of rickets and fractures, low vitamin D levels are also associated with hypertension, cancer and cardiovascular disease. In addition, diabetes mellitus (DM) and chronic kidney disease (CKD) are also related to vitamin D levels.[6] Both T2DM and vitamin D deficiency have similar risk factors, such as obesity, aging, and sedentary lifestyle. Cardiovascular diseases (CVDs) and metabolic syndrome disorders are also associated with vitamin D deficiency. Vitamin D plays an important functional role in glucose homeostasis through its effects on insulin secretion and sensitivity.

Moreover, vitamin D seems to affect glucose homeostasis, vitamin D levels having been found to be inversely related to glycosylated hemoglobin levels in gestational diabetes mellitus.[7] However, vitamin D deficiency seems to be related with an increased risk for the development of gestational diabetes mellitus.[8] We also provided the benefits of vitamin D supplementation among patients with diabetes mellitus type 2, another chronic non-communicable disease highly prevalent. Previously reported the favourable effects of improved vitamin D status are most evident in the lipid profile of subjects, reaffirming the hypothesis that vitamin D deficiency contributes to the pathogenesis of atherogenic dyslipidemia.[9]

Early screening and intervention will aid reducing the disease burden. In view of the above facts, this study is being done to assess the vitamin D level in diabetic individuals and its association with glycemic status.

Aims and Objective

Assessment of vitamin D level in diabetic individuals and its association with glycemic status as compared by HbA_1C levels.

Material and Method

Study was done after obtaining the approval from the institutional ethical committee. Total of 50 diabetic patients who were on oral hypoglycemic drugs were selected from the diabetic OPD of medicine department

and 50 non diabetic healthy controls were selected from the people who came for executive cardiac health check up from September 2019 to March 2020 with age group of 30-60 years irrespective of duration of diabetes. Demographic profile and blood pressure was recorded and blood sample was taken in overnight fasting state for fasting blood sugar, vitamin D, HbA_1C and PPBS sample was taken 2 hours after meals.

Inclusion Criteria

Known case of type 2 DM between the age of 30 – 60 years irrespective of duration of diabetes, without any diabetic complications and on oral hypoglycemic drugs with HBA1c level in between 7-9 % were included in this study .

Exclusion Criteria

Patients were excluded if diagnosed as Type 1 DM, age less than 30 years as well as more than 60 years, on insulin, vitamin D supplementation for last 12 weeks, any acute or long term co morbidity and pregnant or lactating women, gestational diabetes, diabetes with any endocrinopathies.

Statistical Analysis

The data was entered in Microsoft excel sheet for analysis and tested statistically on SPSS for windows version 20 software. Quantitative variable were described in descriptive statistical analysis was done for continuous variables, frequency distribution, mean ± SD and their percentages for categorical variables were calculated. T-test was used for normal distributed data. P value < 0.05 is considered significant. Correlation between vitamin D and blood sugar and HbA_1C was done using Pearson correlation.

Result

After taking clearance from the ethical committee, total 100 subjects were enrolled in this study which was divided into diabetics and non diabetics each having 50 subjects.

Table 1: Demographic profile of the study population

Demographic Profile			
Variables	Diabetics (n=50)	Non - Diabetics (n=50)	P- value
	Mean ± SD	Mean ± SD	
Age (Years)	51.23 ± 6.84	50.11 ± 6.58	0.1
Duration of Diabetes (Years)	5.54 ± 2.93	-	-
BMI (Kg/m^2)	24.71 ± 1.03	24.52 ± 0.88	0.1
Waist Circumference (cm)	98.24 ± 16.84	89.55 ± 12.92	0.004
Hip Circumference (cm)	96.19 ± 14.34	92.96 ± 9.62	0.18
Waist Hip Ratio (WHR)	1.03 ± 0.13	0.96 ± 0.07	0.001

Table 1 shows- The mean age of patients was 50.11 ± 6.58 years in control group and 51.23 ± 6.84 years in study group. 25 males and females were selected in each group. BMI in diabetic group was 24.71 ± 1.03 and in control group was 24.52 ± 0.88 and were not significant but they were under overweight category according to BMI for Asian population. Waist Hip Ratio was 1.03 ± 0.13 in diabetic groups whereas in control group it was 0.96 ± 0.07 and is statistically significant ($p<0.001$). This shows that central obesity is more in diabetic group.

Table 2: Co-relation of blood sugar levels and Vit D levels in the study population

Blood Sugar & Vitamin D_3			
Variables	Diabetics (n=50)	Non - Diabetics (n=50)	P- value
	Mean ± SD	Mean ± SD	
Blood Sugar (Fasting) (mg/dl)	151.13 ± 35.46	87.89 ± 5.05	<0.0001
Blood Sugar (PP) (mg/dl)	183.78 ± 58.49	114.74 ± 9.07	<0.0001
HbA_1C (%)	7.97 ± 1.05	5.61 ± 0.13	<0.0001
Serum Vitamin D_3 (ng/dl)	17.7 ± 9.2	26.6 ± 11.33	<0.0001

Table 2 shows the comparison of mean HbA_1C (glycated hemoglobin), FBS and PPBS and serum Vitamin D3 level which shows a significant difference between the two groups.

Table 3: Comparison of Vit D deficiency in the study population

Vitamin D levels	Diabetic	Non Diabetic	p - value
Deficient (0-20 ng/dl)	N=25 9.97 ± 1.05	N=15 15.81 ± 2.05	<0.001
Insufficient (21-29 ng/dl)	N=23 (23.22±0.81)	N=30 (28.16±0.97)	<0.001
Sufficient (30-100 ng/dl)	N=2 38.59±1.22	N=5 49.27±1.01	<0.001

Table 3 shows Vitamin D_3 level was deficient in 25, insufficient in 23 whereas only 2 individuals have sufficient levels. In case of non diabetic, 15 have insufficient, 30 have insufficient where as 5 had significant level of vitamin D3. The differences between the groups were statistically significant.

Table 4: Statistical analysis of the result

Serum Vitamin D	r - Value	p - Value
FBS	-0.527	<0.001
PPBS	-0.311	<0.001
HbA1C	-0.149	0.57

Table 4 shows Vitamin D_3 level was negatively correlated with FBS, PPBS and was significant. Vitamin D_3 was negatively correlated with Glycosylated hemoglobin, but was not statistically significant.

Discussion

Diabetes mellitus is a complex, progressive disease, accompanied by multiple complications. Hyperglycemia has been accepted as being essential for the development of diabetic complications. The DCCT showed that improvement of glycemic control, as measured by reduction in glycosylated hemoglobin levels, significantly reduced the risk of development or progression of all diabetic complications and also reduced the mortality and morbidity due to cardiovascular diseases in diabetes mellitus patients.

India is a tropical country and is sunny all around the year. Vitamin D_3 deficiency is found to be an epidemic inspite of plenty of sunlight.[10] There are many risk factors for

vitamin D insufficiency or deficiency, including lack of sun exposure, inadequate dietary intake, darker skin colour, age, obesity, and use of various medications. There is evidence that vitamin D is important in the prevention of islet cell death and might be useful to improve the survival of islet cell grafts.[11] Vitamin D is required for and improves the production of insulin, and also improves insulin sensitivity.[8]

Vitamin D deficiency occurs when individuals do not have a proper dietary intake or are exposed to ultraviolet B (UVB, 290–320 nm).[12] Vitamin D and its metabolites may be important in preventing type 2 DM by increasing insulin production and secretion and improving overall β-cell function.[13] In vitro and in vivo studies have proved that 1,25 (OH)2D3 is crucial for insulin secretion and glucose homeostasis.[14]

Moreover, one of the hallmarks of T2DM is low-grade inflammation, which can result from a rise in circulating cytokines. High amounts of circulating inflammatory cytokines such as tumor necrosis factor-alpha (TNF–α) and interleukin 6 (IL-6) contribute significantly to insulin resistance in muscle and adipose tissues.[15] It has been suggested that vitamin D3 metabolites such as 1,25 (OH)2D3 cause an increase in insulin sensitivity by increasing insulin receptor gene expression and reducing inflammatory cytokines.[16] Furthermore, 1,25 (OH)2D3 is believed to be vital for insulin exocytosis by increasing the expression of calbindin-D28K in β-cells. Moreover, calbindin-D28K plays a protective role by decreasing inflammatory cytokine-induced ß-cell apoptosis.[17]

Insufficiency of vitamin D in two groups also had higher prevalence. When we compare the vitamin D levels among the three categories between the two groups it also shows a significant difference between the two groups. Need et al showed that the patients who had higher levels of vitamin D concentration had lower FBS in comparison with the other groups. These results were similar to our findings.[18] Lee et al found that 89% of their study individuals suffered from deficiency of this vitamin and just 9 out of 300 persons had sufficient vitamin D concentration. They also found that the mean concentration of vitamin D in their patients was 26.11 ± 13.6 this is higher than our findings in the diabetic patients.[19] Gagnon et al found that the mean serum concentration of vitamin D in diabetic patients was lower than the non-diabetic individuals.[20] Taheri showed that mean serum concentration of vitamin D in diabetic patients was 20.6 ± 11.4 and in non-diabetic individuals was 22.22 ± 16.03.[21] These results were almost similar to the findings of our study.

The objective of this study was to examine the relationships between vitamin D status and FBS, PPBS, HbA_1C in patients with Type 2 DM. In the present study, lower vitamin D levels were observed in a type 2 diabetes mellitus patient group than in a control group and an inverse relationship was observed between glycosylated hemoglobin levels and vitamin D levels in the patient group, implying that vitamin D levels may affect glucose control in type 2 diabetes mellitus.

It appears that vitamin D may be related to glucose control in type 2 diabetes mellitus. Vitamin D receptors have been found in pancreatic beta cells, which additionally have been found to express the enzyme 1- α -hydroxylase, an enzyme that is usually present in kidney activating vitamin D leading to the production of its biologically active form. Vitamin D facilitates the secretion of insulin from pancreatic beta cells, thus appearing to regulate insulin secretion.[22]

Therefore, vitamin D deficiency may be related to impaired insulin secretion in type 2 diabetes mellitus. In addition, as vitamin D stimulates the expression of the

insulin receptor, vitamin D deficiency may be related with insulin resistance.

In conclusion, our findings demonstrated that vitamin D concentration in diabetic patients was significantly lower in comparison to non-diabetic individuals. According to the high prevalence of vitamin D deficiency in this group, treating with vitamin D supplements maybe useful and seems to be necessary.

Conclusion

Emerging evidence is accumulating on the important role of vitamin D in the pathogenesis of diabetes. Many prospective studies have shown associations between vitamin D status and diabetes. However, there are contradictory findings regarding whether restitution of normal vitamin D levels modifies the occurrence or clinical course of these diseases. Although there is a concern that vitamin D may be a surrogate marker for poor health status, further well-designed clinical trials are needed in this area. So, advising patients to get tested for lower vitamin D values and correct any deficiency if found may result in better blood glucose control and benefit the patient's overall health.

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