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Original Research Article

Association of vitamin D with insulin resistance in Type 2 Diabetic Mellitus patients

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Abstract

Background: Several studies have reported a correlation between vitamin D deficiency and insulin resistance however few other studies proved vitamin D supplementation not improving the glucose homeostasis. The present study was aimed to find the association of vitamin D with insulin resistance and glycemic control and duration of diabetes in type 2 diabetic patients with and without microvascular complications.

Materials and methods: total 300 subjects in the age group of 35 – 70 years were divided into 3 groups.100 healthy subjects served as control group. 100 T2DM patients without microvascular complications chosen as study group-1 and 100 T2DM patients with microvascular complications were enrolled as study group-2. 25(OH) D3 was measured by chemiluminescence immunoassay, glycosylated hemoglobin (HbA1c) was measured by latex agglutination inhibition assay .Insulin resistance was estimated by HOMA-IR method.

Results: 25(OH) D3 levels were lower in the T2DM patients with micro vascular complications compared to T2DM patients without microvascular complications and control groups, being 20.03± 6.50ng/ml , 28.92±6.66ng/ml and 35.96± 8.46ng/ml respectively ($p < 0.001$, Student's t-test).Insulin resistance was significantly higher in study groups compared to control group (9.05± 1.38 ,7.95±1.93,3.25± 0.29) respectively.

Conclusions: Vitamin D levels appeared to be lower in T2DM patients with microvascular complications compared T2DM patients without microvascular complications and control group. 25(OH) D3 levels negatively correlated to insulin resistance, duration of diabetes and glycemic control.

Keywords: Insulin resistance, Glycemic control, vitamin D, microvascular complications.

1. Introduction

Diabetes Mellitus, a state of chronic hyperglycemia due to absolute or relative deficiency of insulin, is a common metabolic disorder effecting over 420 million individuals worldwide [1]. If left untreated, T2DM can lead to a multitude of chronic microvascular and macrovascular conditions such as retinopathy, nephropathy, neuropathy and cardiovascular disease [2]. Glycemic control, age, diabetes duration, smoking, age onset of diabetes and genetic factors are the major risk factors for microvascular complications of diabetes [3]. Vitamin D has traditionally been associated with calcium and phosphorus homeostasis and bone. However, recent evidence from various lines of research suggested nontraditional roles of vitamin D in human health including cancer, autoimmune, infectious, respiratory, and cardiovascular diseases. [4-6]. Studies also showed the effects of vitamin D on glucose metabolism. In peripheral tissues, vitamin D can directly improve insulin sensitivity by receptor expression or by peroxisome proliferator-activated receptor (PPAR). Vitamin D can also affect insulin resistance indirectly through the renin-angiotensin system. It is thought that angiotensin II contributes to the development of insulin resistance by inhibiting the action of insulin in the vascular tissue and adipose tissue, contributing to worsening glucose reuptake

[7-8]. It has lead to the hypothesis that vitamin D insufficiency correlates positively with development of diabetes and insulin resistance [9].

Insulin resistance (IR) is a physiological condition in which cells fail to respond to the normal actions of the hormone insulin. The body produces insulin, but the cells in the body become resistant to insulin and are unable to use it as effectively, leading to hyperglycemia. Beta cells in the pancreas subsequently increase their production of insulin; further contributing hyperinsulinemia [10].

The present study aimed to determine the status of vitamin D and its correlation with Insulin resistance, glycemic control, onset diabetic duration and its alterations in health and type 2 diabetic patients with and without microvascular complications.

2. Materials and methods

Study was conducted in the Department of Biochemistry in collaboration with Department of General Medicine in Rama Medical College & Hospital, Kanpur, Uttar Pradesh. A total 300 subjects in the age group of 35 – 70 years were divided into 3 groups.

Group-I contains 100 healthy individuals serving as controls

Group-II consists of 100 type 2 diabetic patients without microvascular complications and suffering with diabetes less than 5 yrs.

Group-III consists of 100 type2 diabetic patients suffering at least with one of the micro vascular complications. Duration of diabetes is more than 5 yrs.

Subjects suffering with type 1Diabetes, liver, renal disease, severe congestive heart failure and those taking vitamin D or calcium supplementation were excluded from the study. The study was approved by the Ethical Committee of Institution. A written informed consent, in the vernacular language, was obtained from all the participants. The screening was done in each case to assess the associated microvascular complications, which include complete physical examination, detailed fundus examination, and other biochemical investigations includes fasting plasma glucose, HbA1c, Serum Insulin, serum vitamin D levels (25-OH vitamin D), were performed. Insulin resistance was measured by HOMA-IR method.

2.1 Statistical analyses

Statistical analyses were performed using SPSSversion19. Values are presented as mean ± SD for continuous variables or number (%) for categorical variables. *P* Values < 0.05 were considered significant. Pearson's correlations, t-tests were used to assess the relationship between continuous variables such as25-OHDlevel, age, HbA1c, and diabetes duration. Categorical data are expressed as number and percentage. Differences were analyzed by ANOVA.

3. Results

A total of 300 patients were enrolled for the study, which were divided into three groups. 100 healthy individuals without diabetes were serving as control group (Group-I) while 100 type2 diabetic patients without microvascular complications (Group-II) and 100 type 2 diabetic patients with micro vascular complications (Group-III) were enrolled as study groups.

Table 1: showing biochemical parameters with Mean value and S.D

Parameters	Group-I N=100	Group-II N=100	Group-III N=100	P value
FBS	83.96 ± 5.90	134.7± 24.79	185.87± 30.80	<0.0001*
Serum Insulin	15.01 ± 2.71	22.37± 4.57	25.67± 4.64	<0.0001*
Vitamin –D	35.96± 8.46	28.92±6.66	20.03± 6.50	<0.0001*
HbA1C	5.21± 0.05	7.95±1.95	8.28± 0.02	<0.0001*

Values are mean (SD) as appropriate. * To calculate p value, t-test/Levene's test used for quantitative variables and ANOVA for intergroup correlations.

The mean serum 25-OH Vitamin D levels (ng/mL) in control group was (35.96 ± 8.46) higher compared to Group-II (28.92 ± 6.66) and Group –III (20.03 ± 6.50) (Table 1). By ANOVA, Highly significant difference was found between study groups and control group (df = 297; p <0.0001). Significant difference was noticed between group-II and group III subjects (t=9.55; df = 279: P value<0.001).

The HbA1c (%) values in Group I, Group II and Group III were measured as 5.21 ± 0.05, 7.95 ± 1.95 and 8.28 + 0.028 respectively. These values were found to be significantly higher in diabetic population (group III p < 0.001 and group II p < 0.001) and negatively correlated with serum vitamin D values.

As shown in the table -1, Mean plasma insulin value of control group (15.01± 2.71) was significantly lower than group -II (22.37±4.57) and group-III (25.67±4.64) (df=198, p value <0.0001). Significant difference found between Group –II and Group-III (t=5.067; df =198; p< 0.0001).plasma insulin values are negatively correlated with serum vitamin D values.

Table 2: Effect of duration on duration of diabetes on vitamin-D and Insulin resistance

Duration	0 Yrs (n=100)A	0.1-5yrs(n=100)B	>5 yrs(n=100)C	P value
Vitamin D	35.96± 8.46	28.92±6.66	20.03± 6.50	<0.0001*
Insulin Resistance	3.25± 0.29	7.95±1.93	9.05± 1.38	<0.0001*

A group non diabetic, B group duration of diabetic less than 5 yrs Group C more than 5 years.
*Inter group comparison by t test shows significance between B versus A, C versus B.

Insulin resistance was found significantly higher in group C compared to group A and group B. when inter group comparison made between Group B & A (t=24.08, df =198; p<0.0001) and Group C and A (t=4.63, df=198; p=0.0001)(Table-2).

As seen in the table -2, mean vitamin D values were significantly declining with the duration of diabetes (p<0.0001) where as insulin resistance increasing with the duration. An inverse association found between serum vitamin D and Insulin Resistance.

4. Discussion

Recently, vitamin D has sparked widespread interest in the pathogenesis and prevention of diabetes. As the major regulator for calcium homeostasis, vitamin D directly and or indirectly improves insulin exocytosis via activating calcium-dependent endopeptidases. Vitamin D also improves glucose tolerance. [11]

The result of present study explains, Overall vitamin D deficiency was found to be more prevalent in diabetic patients with microvascular complications compared to diabetic patients without microvascular complications and healthy controls. This observation was supported by the study from Suzuki *et al* and other earlier studies. [12-17]

There are several lines of evidence supporting the role for vitamin D in pancreatic beta-cell function. Kayaniyil *et al* examined the cross-sectional association between vitamin D and beta-cell dysfunction in subjects at risk for type 2 diabetes and showed a positive association between vitamin D and beta-cell function

According to previous studies [18-21] the baseline 25(OH)D concentration was inversely associated with glycemic control, and insulin resistance. National health and nutrition examination survey III has also proposed the inverse association of 25(OH) D levels with HOMAIR [22]. Consistent with the above findings, the present study also concludes that there was inverse association of 25(OH) D withHbA1C and HOMA-IR. But the similar findings were not observed in a Study conducted by Maura - *et al* [23] this may be due several factors like small number of subjects, age of the study population and place of the study.

The present study showed a negative correlation between duration and means Vitamin D levels, that with the duration vitamin D levels decreases. Similar results were found in the studies conducted by Gagnon *et al* [24].

5. Conclusion

We conclude that 25 OH vitamin D is correlated with glycemic status and insulin resistance in type 2 DM and has a role in pathogenesis of type 2 DM and its complications.

Routine screening for vitamin D insufficiency may provide meaningful in-formation and that it could be considered for diabetic care.

Limitations of the study

This study was an observational study from a single centre; Confounders like diet, physical activity were not included.

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