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ORIGINAL RESEARCH

Relationship between vitamin D and insulin resistance in diabetic individuals with or without microvascular disease

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ABSTRACT

Background: Risk factors for both type 2 diabetes and vitamin D deficiency include ageing, obesity, low physical exercise, and American-African heritage. Additionally, there is evidence that vitamin D deficiency is connected to conditions including osteoporosis, heart disease, and issues with the metabolic syndrome. The purpose of this research was to find out how vitamin D supplementation affected insulin resistance in people with type 2 diabetes. **Material and Method:** This study was conducted at the department of medicine. 630 participants in all were split up into three groups for this study: control, T2DM without microvascular problems, and T2DM with microvascular complications. For statistical computations, SPSS software is used. **Result:** Total 630 subjects were enrolled in this study, which were divided in three groups. Group I consist 126 males and 84 females, group II consist 125 males and 85 females and group III consist 130 males and 80 females. **Conclusion:** Vitamin D supplementation is recommended as part of the therapy for type 2 diabetes since it seems to aid in the control of diabetes.

Keywords: T2DM, microvascular complications and Vitamin-D

INTRODUCTION

In recent decades, vitamin D deficiency has been associated with a number of non-skeletal conditions, such as type 2 diabetes mellitus (T2DM) [1]. Risk factors for both vitamin D deficiency and type 2 diabetes include low physical activity, ageing, obesity, and American-African heritage [2]. Additionally, there is evidence that vitamin D deficiency is associated with conditions including osteoporosis, cardiovascular disease, and issues related to the metabolic syndrome [3-5]. Vitamin D deficiency has been linked in several studies to Type 2 diabetes [6]. By affecting insulin secretion and sensitivity, vitamin D may have a functional role in glucose tolerance, according to other studies [7].

Compared to healthy controls, the circulating 25(OH)D concentrations were significantly lower in T2DM subjects [8]. Additionally, older males with vitamin D deficit release more insulin after consuming glucose, while women with type 2 diabetes are more likely to have vitamin D insufficiency [9, 10]. Studies on animals have shown that vitamin D is an essential element needed for healthy insulin synthesis [11,12]. By upregulating the insulin receptor gene and influencing the metabolism of calcium and phosphorus, vitamin D reduces insulin resistance [13]. According to one study, vitamin D supplementation increased insulin sensitivity by 54% in 5,677 individuals with low glucose tolerance [14]. Increased vitamin D intake improves insulin sensitivity, according to several studies [15, 16]. A study including 126 healthy participants discovered that vitamin D deficiency had a detrimental effect on pancreatic β-cell function and that insulin sensitivity was correlated with 25(OH)D levels [17]. Vitamin D intake was linked to a decreased incidence of type 2 diabetes, according to a follow-up examination of 4,843 people with the disease during a 20-year period [18]. Insulin resistance and β-cell dysfunction are hallmarks of type 2 diabetes [19].

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There has been contradictory research on the connection between blood vitamin-D and insulin secretion. We looked at how vitamin D supplementation affected insulin resistance in people with type 2 diabetes.

MATERIAL AND METHOD

Subjects and Study design

The institution's ethical committee gave its approval to the research. After meeting the inclusion requirements, each participant provided written informed consent in the vernacular language.

Selection of Subjects

630 subjects were planned to be enrolled in the present study.

Control group

comprising 210 staff members who were matched for age and sex and in good health. These individuals were physically active, non-diabetic, and had fasting blood glucose levels between 70 and 100 mg. Every patient was between the ages of 35 and 70. Both sexes were represented. They had no serious illnesses that would have affected the study's parameters.

Test group-1

210 people with type 2 diabetes who have had the disease for less than five years should be included. Clinically, they show no signs of any microvascular consequences from diabetes mellitus. Diabetes will be diagnosed using the same standards as established by the World Health Organisation. For example, fasting plasma glucose levels of ≥126 mg/dl combined with the typical signs and symptoms of diabetes mellitus. OR test for postprandial plasma glucose ≥200 mg/dl.

Test group-2

consists of 210 individuals with type 2 diabetes who have one or more microvascular sequelae from the disease (diabetic neuropathy, diabetic retinopathy, or diabetic nephropathy). Diabetes has been present for five years or longer.

The following techniques will be used by the physician to identify microvascular problems.

Diabetic Retinopathy

To check for retinal vascular microaneurysms, blot and cotton wool spots (non-proliferative diabetic retinopathy), and the onset of neovascularisation (proliferative diabetic retinopathy), a comprehensive fundus examination was performed.

Diabetic Neuropathy

To check for polyneuropathy, radiculopathy, or mononeuropathy, a thorough motor and sensory examination was performed. Diabetic Nephropathy: Serum creatinine and urinary microprotein estimation will be performed. Fasting Blood glucose and HbA1C, Serum insulin, Insulin Resistance, Serum 25Hydroxy vitamin D were evaluated.

Exclusion criteria

- Patients with type I Diabetes Mellitus.
- Pregnant and lactating females.
- Patients taking diuretics, lipid-lowering, and multivitamins drugs.
- Patients with disease unrelated to diabetes which may alter chosen parameters i.e. AIDS, thyroid disease, tuberculosis, and cancer patients.

Statistical Analysis

Data were collected and entered in MS Excel worksheets and results were analysed with appropriate statistical tools like student t-test, tests of significance, logistic regression analysis.

Estimation of Serum 25-Hydroxyvitamin D [20, 21]

Method: Electrochemiluminescence binding assay (ECLIA) by Cobas.

Principle: Competitive protein binding assay.

Specimen: Serum or plasma (heparin or citrate plasma) can be used in this assay.

RESULTS

Total 630 subjects were enrolled in this study, which were divided in three groups. Group I consist 126 males and 84 females, group II consist 125 males and 85 females and group III consist 130 males and 80 females.

Table 1: Comparison of fasting blood glucose (mg/dl), HbA1C, Insulin and HOMA-IR levels between the groups

Groups	Description of group	Fasting blood glucose (mg/dl) (MEAN±SD)	HbA1C (MEAN±SD)	Insulin (MEAN±SD)	HOMA-IR (MEAN±SD)
Groups-I	Control	87.16±8.34	6.22±0.50	6.71±0.97	2.32±0.18
Groups-II	T2DM without microvascular complications	141±31.74*	7.86±0.76*	10.97±8.4*	4.88±3.1*
Groups-III	T2DM with microvascular complications	173.56±53.8*#	8.95±2.82*#	12.4±9.54*	6.17±3.5*

(*p<0.05 significant compared Group-I with other groups, #p<0.05 significant compared Group-II with other Groups).

Table1 indicates the average fasting blood glucose (mg/dl), HbA1C, Insulin and HOMA-IR readings in three groups. Fasting blood glucose (mg/dl), HbA1C, Insulin and HOMA-IR levels increased significantly in both

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diabetes groups as compared to the control group. Group II exhibited a substantial difference from Group III. Group-III had the greatest rise in fasting blood glucose (mg/dl), HbA1C, Insulin and HOMA-IR compared to Groups II and I.

Table 2: Comparison of Vitamin-D3 levels between the groups

Groups	Description of group	Vitamin-D3 (Mean ± SD)
Group-I	Control	22.38±12.04
Group-II	T2DM without microvascular complications	20.18±9.20*
Group-III	T2DM with microvascular complications	16.51±8.37*,#

(*p<0.05 significant compared Group-I with other groups, #p<0.05 significant compared Group-II with other Groups)

Table-2 shows the mean Vitamin D levels in all study groups. Mean Vitamin-D level was more in control group compared other groups. The difference between Group-II and III, Iwas statistically significant. Low Vitamin-D3 was observed in Group-III.

Table 3: Comparison of mean HbA1C, HOMA-IR, vitamin-D3, MDA within the Group-II and III based on the duration of diabetes

Observation	Less than 1 year (Mean ± SD)	1-3 years (Mean ± SD)	Above 3 years (Mean ± SD)
HbA1C	7.18±0.88	8.89±2.33*	9.86±0.96*,#
HOMA-IR	2.56±0.35	4.48±0.44*	5.10±0.46*
Vitamin-D3	21.29±10.43	19.18±9.22*	17.89±8.26*,#
MDA	2.19±0.31	3.01±0.74	3.48±0.97*

(*p<0.05 significant compared less than 1 year with other time periods, #p<0.05 significant compared 1-3 years with other time periods)

HbA1C, HOMA-IR, MDA, values shown a significant increase with the duration of onset of diabetes. Highest values of HbA1C, HOMA-IR and MDA were, noticed in above 3 years duration. While Vitamin D3 significantly declines with the duration of diabetes.

Table 4: Comparison of mean fasting blood glucose, HbA1C, HOMA-IR, within the Group-III based on the complication

Observation	Retinopathy(n=81 (Mean ± SD)	Nephropathy (n=63) (Mean ± SD)	Neuropathy (n=30) (Mean ± SD)	Multiple complications (n=56)
FBS	152.59±45.86	188.79±53.50*	181.39±52.22*	195.41±56.03*#
HbA1C	9.15±4.77	9.39±4.22*	9.66±5.15*	10.19+6.11*#
HOMA-IR	5.38±3.93#	4.88±2.23	5.89±2.87*	5.19±2.40*#

(*p<0.05 significant compared retinopathy with others, #p<0.05 significant compared nephropathy with others)

Table-4 displaying a comparison of variables such as FBS, HbA1C and HOMA-IR within Diabetic patients, where they were further divided into Retinopathy, Nephropathy, neuropathy and multiple complications. FBS and HbA1C were significantly higher in multiple complications while HOMA-IR was significantly higher in neuropathy.

Table 5: Comparison of mean vitamin-D3, MDA, creatinine, albumin, ACR within the Group-III based on the complications

Observation	tinopathy (n=81) (Mean ± SD)	hropathy (n=63) (Mean ± SD)	uropathy (n=30) (Mean ± SD)	e complications (n=56)
Vitamin-D3	18.19±7.87	15.89±4.54	14.69±5.21	14.59±8.31
MDA	4.01±0.94	3.84±0.95	4.02±0.85	4.44±0.89

(*p<0.05 significant compared retinopathy with others, #p<0.05 significant compared nephropathy with others)

Table 5 shows the mean Vitamin D and MDA levels in group-III, which were further, divided into retinopathy, nephropathy, neuropathy and multiple complications. There was a significant increase in MDA levels in multiple complication group.

DISCUSSION

This study's main objective was to investigate how vitamin D supplementation affects glucose homeostasis. The results showed that giving T2DM patients vitamin D dramatically decreased their blood levels of FBG, insulin, and HOMA-IR.

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Although vitamin D and calcium metabolism have long been linked, there has been a lot of attention in the aetiology and prevention of diabetes in recent years. A number of explanations have been put out to explain why type 2 diabetes is more common in those who are vitamin D deficient. Adipose, pancreatic, and potentially muscle cells express vitamin D receptors (VDRs) [22, 23]. Given that the insulin promoter genes include VDR motifs, vitamin D seems to directly regulate insulin manufacturing in the pancreas via the nuclear VDR [24]. Additionally, vitamin D may decrease apoptosis, enhance the morphology of pancreatic islet cells, and have nongenomic effects via the messenger VDR [25].

In the present study, we found that vitamin D deficiency was more common in diabetic patients with microvascular problems than in diabetic patients without microvascular problems or healthy controls. The analysis by Suzuki et al. and a number of other investigations [26–28] supported this finding.

Both case groups' mean 25(OH) vitamin D levels were significantly below those of the controls. This suggests that 25(OH) vitamin D may have a role in the development of type 2 diabetes and its aftereffects. This discovery aligns with the findings of Yu et al. (2012) [29] and Subramanian et al. (2011) [26].

When we attempted to link 25(OH) vitamin D levels with FBS and HbA1C in our research, we discovered a statistically significant negative association between FBS HbA1C and 25(OH) vitamin D levels.

These findings align with those reported by Havilah et al. (2013) [31] and Vijetha et al. (2014) [30]. Hypovitaminosis D may be linked to the long-term, abnormal glucose metabolism of type 2 diabetes and insulin resistance, as shown by the negative correlation seen between vitamin D, FBS, and HbA1c. According to our present knowledge of the aetiology of type 2 diabetes, cytokine-induced apoptosis may affect a-cell function, whereas inflammation is believed to be a key factor in insulin resistance. By regulating their expression, vitamin D may shield cells against cytokine-induced apoptosis.

However, other studies showed the opposite findings, which might be due to a number of variables, including the study's location, age of the population, and the small sample size.

The present research discovered a negative correlation between mean vitamin D levels and the duration of T2DM onset, suggesting that vitamin D levels decrease as diabetes worsens. Gagnon et al. found similar results in 2011 [32].

CONCLUSION

Vitamin D supplementation is recommended as part of the therapy for type 2 diabetes since it seems to aid in the control of diabetes.

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