VITAMIN D SUPPLEMENTATION AND HBA1C LEVELS IN TYPE 2 DIABETIC PATIENTS

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Abstract
Introduction: Type 2 diabetes mellitus (T2DM) is a major public health problem, with an estimated 65 million patients in India. Studies shown that low serum 25(OH)D concentrations are associated with an increased risk of type 2 diabetes and shown the beneficial effect of vitamin D supplementation on insulin sensitivity. Vitamin D is formed in humans by subcutaneous photosynthesis from its precursor, 7-dehydrocholesterol by exposing themselves to the sun. Older age is associated with a decrease in 7-dehydrocholesterol concentration in the human skin. This lifestyle habit and their natural diet of low vitamin D consumption may cause poor glucose control in diabetic patients. The purpose of this study was to examine the association between serum 25(OH)D and glycosylated hemoglobin (HbA1c) levels.

Material and Methods: This was a prospective observational study of T2DM patients aged 18 and above who attended the outpatient clinics of a tertiary center. The following variables were collected from the cases: age, sex, type of diabetes, HbA1c result. Baseline HbA1c and vitamin D levels were recorded prior to supplementation and after a period of 6 months of supplementation with vitamin D, HbA1c and vitamin D levels were recorded once again.

Results: A total of 169 patients were included in the study and whose follow up was completed at the end of 6 months. Mean age of the study population was 46.87 ± 15.99. There were 74(43.79%) male and 95(56.21%) female. Mean HbA1c pre-supplementation (%) was 9.58 ± 2.41 while post supplementation was 7.21 ± 1.08. There was a significant reduction of HbA1c of T2DM (P < 0.0001). Vitamin D levels pre-supplementation (nmol/L) (mean ± SD) was 38.54 ± 29.54 while, Vitamin D levels post-supplementation (nmol/L) (mean ± SD) was 38.54 ± 29.54. There was a significant increase of vitamin D levels of T2DM (P < 0.0001).

Conclusion: Significant inverse association between vitamin levels D and HbA1c in T2DM patients was observed. Also there was significant reduction in HbA1c as vitamin D levels increased. Regular screening of vitamin levels D and HbA1c in T2DM patients is advised.

Keywords: Vitamin D, diabetes, T2DM, 25-hydroxyvitamin D

Introduction
Type 2 diabetes mellitus (T2DM) is a major public health problem, with an estimated 65 million patients in India. Low serum 25-hydroxyvitamin D [25(OH)D] concentrations and dietary calcium intake have been shown to be associated with impaired insulin sensitivity or secretion in people at high risk of type 2 diabetes. Studies shown that low serum 25(OH)D concentrations are associated with an increased risk of type 2 diabetes and also shown the beneficial effect of vitamin D supplementation on insulin sensitivity.

Despite all the positive evidence showing the beneficial effect of vitamin D on many diseases and its need for optimal health status, still most of the people are vitamin D deficient and its deficiency can aggravate many diseases, commonly predisposition of diabetes and also play a role in the development of diabetes. Vitamin D is formed in humans by subcutaneous photosynthesis from its precursor, 7-dehydrocholesterol by exposing themselves to the sun. The association of low serum 25-hydroxyvitamin D [25(OH)D] concentrations with type 2 diabetes may be mediated through effects on glucose homeostasis and, in particular, a direct effect of vitamin D on the β-cell function, and thus insulin secretion. In countries at high latitude, very little pre-vitamin D is formed during the winter months. In addition, older age is associated with a decrease in 7-dehydrocholesterol concentration in the human skin. This lifestyle habit and their natural diet of low vitamin D consumption may cause poor glucose control in diabetic patients.

With this background the purpose of this study was to examine the association between serum 25(OH)D and glycosylated hemoglobin (HbA1c) levels.

Material and Methods:
This was a prospective observational study of T2DM patients aged 18 and above who attended the outpatient clinics of a tertiary center. The following variables were collected from the cases: age, sex, type of diabetes, HbA1c result. Baseline HbA1c and vitamin D levels were recorded prior to supplementation and after a period of 6 months of supplementation with vitamin D, HbA1c and vitamin D levels were recorded once again.

Results: A total of 169 patients were included in the study and whose follow up was completed at the end of 6 months. Mean age of the study population was 46.87 ± 15.99. There were 74(43.79%) male and 95(56.21%) female. Mean HbA1c pre-supplementation (%) was 9.58 ± 2.41 while post supplementation was 7.21 ± 1.08. There was a significant reduction of HbA1c of T2DM (P < 0.0001). Vitamin D levels pre-supplementation (nmol/L) (mean ± SD) was 38.54 ± 29.54 while, Vitamin D levels post-supplementation (nmol/L) (mean ± SD) was 38.54 ± 29.54. There was a significant increase of vitamin D levels of T2DM (P < 0.0001).

Conclusion: Significant inverse association between vitamin levels D and HbA1c in T2DM patients was observed. Also there was significant reduction in HbA1c as vitamin D levels increased. Regular screening of vitamin levels D and HbA1c in T2DM patients is advised.

Keywords: Vitamin D, diabetes, T2DM, 25-hydroxyvitamin D
clinics of a tertiary center. Patients were excluded if comorbid conditions like parathyroid disease is present, patients were also excluded if those currently using vitamin D or calcium and pregnancy or breastfeeding mothers. The following variables were collected from the cases: age, sex, type of diabetes, HbA1c result. Baseline HbA1c and vitamin D levels were recorded prior to supplementation and after a period of 6 months of supplementation with vitamin D, HbA1c and vitamin D levels were recorded once again.

All patients were categorized in four groups according to their vitamin D level as follows: with severe Vitamin D deficiency (< 20 nmol/L), moderate Vitamin D deficiency (20 - 49.99 nmol/L), Vitamin D insufficiency (50 - 74.99 nmol/L) and Vitamin D sufficiency (≥ 75 nmol/L). An association between vitamin D levels and HbA1c was tested. All participants were receiving their regular treatment with either insulin or oral hypoglycemic agents or both.

Statistical analysis was done. Continuous variables are represented as mean ± SD and percentages. Unpaired t-test was used to analyze the difference between means. The Chi-square test was used for categorical data comparison. The data was statistically analyzed using SPSS version 21.0. P < 0.05 was considered as statistically significant.

**Results:**

A total of 169 patients were included in the study and whose follow up was completed at the end of 6 months.

**Table 1: Baseline Characteristics of the Participants**

<table>
<thead>
<tr>
<th>Age (years) (mean ± SD)</th>
<th>46.87 ± 15.99</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>74 (43.79%)</td>
</tr>
<tr>
<td>Female</td>
<td>95 (56.21%)</td>
</tr>
<tr>
<td>HbA1c pre-supplementation (%) (mean ± SD)</td>
<td>9.58 ± 2.41</td>
</tr>
<tr>
<td>HbA1c post-supplementation (%) (mean ± SD)</td>
<td>7.21 ± 1.08</td>
</tr>
<tr>
<td>Vitamin D levels pre-supplementation (nmol/L) (mean ± SD)</td>
<td>38.54 ± 29.54</td>
</tr>
<tr>
<td>Vitamin D levels post-supplementation (nmol/L) (mean ± SD)</td>
<td>84.79 ± 19.47</td>
</tr>
</tbody>
</table>

**Table 2: HbA1c pre-supplementation and post-supplementation statistics**

<table>
<thead>
<tr>
<th>HbA1c pre-supplementation and post-supplementation statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difference</td>
</tr>
<tr>
<td>Standard error</td>
</tr>
<tr>
<td>95% CI</td>
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<tr>
<td>t-statistic</td>
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<tr>
<td>DF</td>
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<tr>
<td>Significance level</td>
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</table>

**Table 3: Vitamin D pre-supplementation and post-supplementation statistics**

<table>
<thead>
<tr>
<th>Vitamin D pre-supplementation and post-supplementation statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difference</td>
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</tbody>
</table>

**Chart 1: HbA1c and Vitamin D levels**

Mean age of the study population was 46.87 ± 15.99. there were 74(43.79%) male and 95(56.21%) female. Mean HbA1c pre-supplementation (%) was 9.58 ± 2.41 while post supplementation was 7.21 ± 1.08. There was a significant reduction of HbA1c of T2DM (P < 0.0001). Vitamin D levels pre-supplementation (nmol/L) (mean ± SD) was 38.54 ± 29.54 while, Vitamin D levels post-supplementation (nmol/L) (mean ± SD) was 38.54 ± 29.54. There was a significant increase of vitamin D levels of T2DM (P < 0.0001).

**Discussion:**

Vitamin D deficiency is commonly encountered in all the population due to dietary habits and many studies reporting a deficiency in vitamin D levels among the population. Vitamin D deficiency (25(OH)D < 50 nmol/L) and insufficiency (25(OH)D = 50 -74 nmol/L) were reported in 50% and 43.8% in a study sample of pregnant women in a tertiary care center.

Several studies suggest that vitamin D is a potential risk modifier for both types of diabetes. Also it has been shown that vitamin D has a direct effect in improved insulin secretion and insulin action, and subsequently, improved glucose homeostasis through activation of the vitamin D receptor on the β-cell of the pancreas islet of Langerhans. Vitamin D also has an indirect role via regulation of calcium homeostasis on various mechanisms related to the pathophysiology of diabetes. In a meta-analysis it has been suggested that combined supplementation of vitamin D and calcium may optimize glucose metabolism. A study by Ordooei M et al they have shown that HbA1c may be reduced by
administration of vitamin D to children and adolescents with type 1 DM without changing the dose of insulin\textsuperscript{xvi}. Another study observed significant reduction in HbA1c levels from year 1 to year 2 and between year 1 and year 3 after supplementation of vitamin D in type 2 African American diabetic patients\textsuperscript{xvii}. A study by Lee C J et al showed relationship between vitamin D supplementation and change in HbA1c and fasting blood glucose among patients with T2DM found there was a modest reduction in HbA1c (-0.32% (-0.53 to -0.10), \(I^2 = 91.9\%\)) compared to placebo after vitamin D supplementation\textsuperscript{xviii}. The meta-analysis by Mirhosseini N et al\textsuperscript{xix} observed a significant reduction in HbA1c levels and following vitamin D supplementation and significant increase in serum 25(OH)D levels which was comparable with our study.

**Conclusion:**

To conclude we found that there is a significant inverse association between vitamin levels D and HbA1c in T2DM patients. Also there was significant reduction in HbA1c as vitamin D levels increased. Regular screening of vitamin levels D and HbA1c in T2DM patients is advised.

**References:**