HYDROXY VITAMIN D STATUS IN TYPE 2 DIABETES MELLITUS

By

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ABSTRACT

Background: The concurrent global epidemics of type-2 DM and vitamin D deficiency raise the question whether vitamin D deficiency should be included among the risk factors for DM. Evidence is accumulating on the possible role of vitamin D in the pathogenesis of type 2 diabetes.

Objectives: assessing 25-hydroxy vit D level in type-2 diabetes mellitus and correlating it with insulin resistance and other parameters.

Patients and Methods: This study had been carried out in the diabetes clinic of Internal Medicine Department and laboratory part was done in Clinical Pathology department, Faculty of Medicine, Al-Azhar University during the period from January 2015 to October 2017.

This study included a total number of 60 adult subjects (above 18 years old), the subjects were divided into 2 groups:

Group (A): Forty diabetic patients (type 2 diabetes mellitus) and Group (B): twenty non diabetic persons.

Results: 25(OH)D level was lower in diabetic patients than in non-diabetic group with a significant difference.

Conclusion: 25(OH)D was low in diabetic patients denoting that vitamin D status has a role in maintaining glucose homeostasis.

Key words: 25(OH)D, Vitamin D deficiency, Diabetes mellitus.

INTRODUCTION

Vitamin D plays a key role in calcium and bone metabolism but emerging evidence suggests that its biological role extends beyond the skeletal system to influence a variety of systemic processes like inflammation, cell differentiation and immune regulation (D'Aurizio et al., 2015). This has led to extensive research exploring the association of vitamin D with a range of serious diseases like cancer, cardiovascular disease and type 2 diabetes. Although the plausible underlying mechanisms are not well understood, low levels of vitamin D concentrations have been associated with impaired β cell function (Alvarez and Ashraf, 2010) and insulin resistance, leading to alteration in glucose homeostasis, and, therefore type 2 diabetes. Furthermore, vitamin D receptors have also been identified in vascular endothelium, smooth muscles and cardiomyocytes thereby implicating its potential role in microvascular and macrovascular disease, leading to increased risk of cardiovascular mortality in type 2 diabetes (Zoppini et al., 2015).

It has been widely reported that vitamin D is necessary for normal islet
cell insulin secretion through direct and indirect action (Pittas et al., 2007). The direct effect is suggested by the binding of 1,25(OH)2D3 to VDR on β cells, by identification of vitamin D response element (VDRE) in the human insulin gene promoter (Maestro et al., 2003) and by the transcriptional activation of the human insulin gene caused by 1,25(OH)2D3. Several signalling pathways have been reported to play critical roles in insulin secretion and β cell growth and survival. A key regulator is ‘Akt’ located downstream in the insulin pathway which, when activated, induces phosphorylation thereby reducing the toxic effects of glucose and fatty acids on β cells. In addition, activation of Akt/JNK pathways by vitamin D can also regulate the activity of angiotensin (an active component of the renin-angiotensin system) mediated islet endothelial cell apoptosis and improve islet cell function and survival (Leung, 2015). Many studies also found that vitamin D supplementation could improve glycemic control in diabetic patients (Chunhua et al., 2017).

Vit. D deficiency may also impair insulin secretion through VDD-associated hyperparathyroidism which may actually cause a paradoxical increase in intracellular calcium level impairing the calcium signal needed for glucose-induced insulin secretion.

The aim of the present work was to assess the level of 25(OH)D in diabetes mellitus, and its correlation with insulin resistance and other parameters.

PATIENTS AND METHODS

This study had been carried out in the diabetes clinic of Internal Medicine Department, and the Laboratory part in Clinical Pathology Department, Faculty of Medicine, Al-Azhar University during the period from January 2015 to October 2017. This study included a total number of 60 adult subjects matched with age and sex, and agreed to participate in this study.

The subjects have been divided into 2 groups:

Group (A): Forty diabetic patients (type 2 diabetes mellitus).

Group (B): included 20 non diabetic persons matched with age and sex.

All subjects were subjected to:

1. Full history taking (duration of diabetes mellitus, mode of treatment and any diabetic complications).

2. General examination including: weight, height, waist circumference, Arterial blood pressure (ABP) and Body mass index (BMI) and laboratory investigations including lipid profile, kidney function test , liver function test, Complete blood count, Serum calcium (total, ionized), Serum phosphorus, fasting insulin, 25(OH)D, fasting blood sugar, post prandial blood sugar, HbA1c, urine analysis and (HOMA-IR) test.

The study used widely accepted cut-off values for 25(OH)D to create four vitamin D categories: severe deficiency, <10 ng/ml (25 nmol/l); moderate deficiency, 10-19.9 ng/ml (25-49.9 nmol/l); insufficiency, 20-29.9 ng/ml (50-74.9 nmol/l); sufficiency, ≥30 ng/ml (75 nmol/l) (Bischoff-Ferrari et al., 2006).
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**Statistical Analysis:**

Data were analyzed using Statistical Program for Social Science (SPSS) version 23. Independent-samples t-test of significance was used when comparing between two means. Mann Whitney U test was used when comparing two means of not normally distributed data. Chi-square (X2) test of significance was used in order to compare proportions between two qualitative parameters. Spearman’s correlation coefficient (r) test was used for correlating data. Spearman’s correlation coefficient (r) test was used for correlating data. P value ≤ 0.05 was considered significant.

**RESULTS**

Our results showed that 25(OH)D was lower in patients with type 2 diabetes mellitus and there was a significant inverse relation between 25(OH) vitamin D and type 2 diabetes mellitus (Table 1).

There was a significant difference between the two studied groups as regard fasting and post prandial blood and a significant difference between the two studied groups as regard HbA1c (Table 1).

**Table (1): Comparison between the studied groups regarding Fasting blood sugar (F.B.S), post prandial blood sugar (P.P.B.S) and glycated hemoglobin (HbA1c)**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>Controls (non-diabetics)</th>
<th>Cases (diabetics)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (%)</td>
<td></td>
<td>20 (33.3%)</td>
<td>40 (66.7%)</td>
<td></td>
</tr>
<tr>
<td>F.B.S (mg/dL)</td>
<td></td>
<td>95.5 ± 5.1</td>
<td>196.5 ± 48.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median (Range)</td>
<td></td>
<td>98 (87 - 101)</td>
<td>192.5 (110 - 299)</td>
<td></td>
</tr>
<tr>
<td>P.P.B.S (mg/dL)</td>
<td></td>
<td>113.8 ± 5.4</td>
<td>269.2 ± 50.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median (Range)</td>
<td></td>
<td>112.5 (103 - 123)</td>
<td>271 (189 - 380)</td>
<td></td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td></td>
<td>4.56 ± 0.36</td>
<td>7.7 ± 0.83</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median (Range)</td>
<td></td>
<td>4.7 (4 - 5)</td>
<td>7.6 (5.5 – 9.4)</td>
<td></td>
</tr>
</tbody>
</table>

- Mann Whitney U test.

There was no significant difference between the two studied groups as regards total calcium or ionized calcium. There was a significant difference between the two studied groups as regards serum phosphorus, and between the two studied groups as regards 25(OH)D (Mean ± SD in diabetic patients 41.4 ± 9.9 and in non-diabetics 31.0 ± 7.8) (Table 2).
Table (2): Comparison between the studied groups regarding serum calcium, phosphorus and 25(OH)D levels

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>Controls (non-diabetics)</th>
<th>Cases (diabetics)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numbers (%)</td>
<td></td>
<td>20 (33.3%)</td>
<td>40 (66.7%)</td>
<td></td>
</tr>
<tr>
<td>Total calcium (mg/dL)</td>
<td></td>
<td>9.7 ± 0.49</td>
<td>9.7 ± 0.53</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td></td>
<td>9.6 (8.8 - 10.5)</td>
<td>9.9 (8.8 – 10.5)</td>
<td></td>
</tr>
<tr>
<td>Ionized calcium (mg/dL)</td>
<td></td>
<td>5.0 ± 0.18</td>
<td>5.0 ± 0.19</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td></td>
<td>5.0 (4.8 - 5.4)</td>
<td>5.0 (4.6 - 5.3)</td>
<td></td>
</tr>
<tr>
<td>Phosphorus (mg/dL)</td>
<td></td>
<td>3.9 ± 0.35</td>
<td>3.6 ± 0.51</td>
<td>0.002</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td></td>
<td>3.9 (3 - 4.3)</td>
<td>3.6 (2.8 – 4.8)</td>
<td></td>
</tr>
<tr>
<td>25 (OH) Vit.D (ng/ml)</td>
<td></td>
<td>41.4 ± 9.9</td>
<td>31.0 ± 7.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td></td>
<td>39 (29 - 70)</td>
<td>31.5 (7 - 41)</td>
<td></td>
</tr>
<tr>
<td>Mann Whitney U test.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

There was no significant difference between the two studied groups as regards fasting insulin, and between the two groups regarding HOMA IR (Table 3).

Table (3): Comparison between the studied groups regarding fasting insulin level and HOMA IR test

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>Controls (non-diabetics)</th>
<th>Cases (diabetics)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numbers (%)</td>
<td></td>
<td>20 (33.3%)</td>
<td>40 (66.7%)</td>
<td></td>
</tr>
<tr>
<td>Fasting insulin (mIU/L)</td>
<td></td>
<td>5.66 ± 1.86</td>
<td>7.86 ± 6.23</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td></td>
<td>5.3 (3.2 - 9.2)</td>
<td>6.75 (1.0 - 19.1)</td>
<td></td>
</tr>
<tr>
<td>HOMA IR</td>
<td></td>
<td>6.06 ± 20.94</td>
<td>3.73 ± 3.18</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td></td>
<td>1.36 (0.7 - 95)</td>
<td>2.84 (0.33 – 13.3)</td>
<td></td>
</tr>
<tr>
<td>Mann Whitney U test.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

There was no significant difference between HbA1c and between HOMA-IR and 25(OH)D, and between duration of diabetes and 25(OH)D. There was a significant negative correlation between HbA1c and 25(OH)D, and between BMI and 25(OH)D (Table 4).
Table (4): Spearman’s correlation between 25(OH) D and other parameters

<table>
<thead>
<tr>
<th></th>
<th>25(OH)D (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HOMA IR</td>
<td>P-value &gt; 0.05</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>P-value -.533</td>
</tr>
<tr>
<td>BMI</td>
<td>P-value -.387</td>
</tr>
<tr>
<td>Duration of diabetes</td>
<td>P-value &gt;0.05</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Some studies suggested that vit D could have a direct (via its role on the activation of pancreatic beta-cell and sensitive organs) or indirect There is a controversy about the extra skeletal effects of vitamin D. Epidemiological data together with the demonstration of the presence of vitamin D receptor in multiple organs suggest a link between vitamin D and multiple diseases, including type 2 diabetes mellitus (DM). Vitamin D deficiency is common in all populations and age groups (Calvo-Romero and Ramiro-Lozano, 2015).

In a population-based study in a sunny country like Spain, 34.7% of a sample of 1226 individuals had vitamin D deficiency, defined as a level of serum 25-hydroxy vitamin D (25(OH)D) lower than 20 ng/mL (González-Molero et al., 2013).

Our results showed that 25(OH)D was lower in patients with type 2 diabetes mellitus. These findings went with (Bayani et al., 2014) who found that vitamin D concentration was significantly lower in diabetic patients than the healthy individuals. Our results was supported by (Mauss et al., 2015) that was a cross-sectional study.

(Gagnon et al., 2011) found that the mean serum concentration of vit D in diabetic patients was lower than the non-diabetic individuals.

(Scragg et al., 2005) found an inverse association between vitamin D status and diabetes, possibly involving insulin resistance, in non-Hispanic whites and Mexican Americans.

On the other hand (Sheth et al., 2015) did not support our results as they found no effect of serum 25(OH)D deficiency on HbA1c or HOMA-IR in T2DM cases. The discrepant results obtained in the reported studies could be attributed to the inclusion of patients with different degrees of sun exposure or different types of food intake and different duration of diabetes.

(Robinson et al., 2011) did not support our results as they found that lower serum 25(OH)D levels were not associated with increased risk of developing type 2 diabetes in this racially and ethnically diverse population of postmenopausal women.

We also found no significant correlation between serum 25(OH)D levels with HOMA IR and fasting insulin. That agreed with (Sheth et al., 2015) who found no effect of serum 25(OH)D deficiency on HOMA-IR in T2DM cases. (Hjelmesth et al., 2009) also found that 25(OH)D did not differ significantly in patients with metabolic syndrome and
patients without metabolic syndrome. Our study disagreed with study of (Al-Daghri et al., 2013) and (Calvo-Romero and Ramiro-Lozano., 2015), who found an inverse correlation between serum 25(OH)D levels and insulin and HOMA-IR. The discrepant results obtained in the reported studies could be attributed to the inclusion of patients with different duration of diabetes and different degrees of insulin resistance and beta cell dysfunction.

CONCLUSION

25(OH)D level is low in diabetic patients and that support the hypothesis that Vitamin D possibly plays a role in maintaining glucose homeostasis, and 25(OH)D level has a negative correlation with type 2 diabetes mellitus.

REFERENCES


مستوى 25- هيدروكسي فيتامين د في مرض البوال السكري من النوع الثاني

محمد كمال عبد الباقى - جمال علي يبر - محمد سعيد الشوريجى - محمد قردى محمد بسيوني
قسم الأمراض الباطنية - كلية الطب - جامعة الأزهر

خلفية البحث: نسبة فيتامين د في الدم لها علاقة قريبة بما قبل السكري والذي يؤدي إلى البوال السكري. بدلاً من ذلك، تزايد الانتظار عن احتمالية وجود دور لنقص فيتامين د في تكوين مرضى السكر من النوع الثاني. التغيير في حالة فيتامين D أو فاعليته يمكن أن يؤثر على حساسية الإنسولين أو وظيفة خلايا بيتا أو الثنائية.

الهدف من البحث: تقييم مستوى 25- هيدروكسي فيتامين D في مرض البوال السكري من النوع الثاني والربط بينه وبين مقاومة الإنسولين والقياسات الأخرى.

طرق البحث: أجريت هذه الدراسة بünüادة السكر بقسم الباطنية العامة والجزء المعملي بقسم البانولوجيا الإكلينيكية بكلية الطب جامعة الأزهر في الفترة من يناير 2015 حتى أكتوبر 2016. وقد أجريت الدراسة على 60 شخصاً بالغاً جميعهم فوق 18 سنة وقد تم تقسيمهم إلى مجموعتين:

- مجموعة (ب): وتشكل من 30 فردًا غير مصابين بالبوال السكري.

النتائج: مستوى 25- هيدروكسي فيتامين D كان أقل في مرضى السكر من غير مرضى السكر وكان الفرق ذو دلالات إحصائية.

الاستنتاج: فيتامين D كان أقل في مرضى السكر من النوع الثاني مما يشير إلى أن فيتامين D له دور في تنظيم مستوى السكر بالدم.