Original Research Article

Evaluation of vitamin-D status in premenopausal and postmenopausal type-2 diabetic women and its relation to glycemic control

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ABSTRACT

Background: Vitamin D deficiency is a public health problem around the world. In 2008, it was estimated that 1 billion persons present with vitamin D insufficiency or deficiency. Vitamin D is obtained through exposure to ultraviolet B (UVB) sunlight as well as nutritional sources. Despite the high UVB sunlight exposure in tropical countries, studies suggest Vitamin D deficiency is highly prevalent. Vitamin D is believed to help improve the body’s sensitivity to insulin, the hormone responsible for regulating blood sugar levels, thus reducing the risk of insulin resistance, which is often a precursor to Type-2 diabetes. Aim and objective of the study was to evaluate and compare the Vitamin-D levels in Premenopausal and Postmenopausal Type-2 Diabetic women and to evaluate if their Vitamin-D levels have any co-relation with their glycemic control.

Methods: The study was conducted in Government Medical College Jammu and its associated hospital on 60 Type-2 Diabetic women, 30 premenopausal and 30 postmenopausal. Vitamin-D [25(OH) Vitamin D] levels were assessed by Chemiluminescence method in the Biochemistry Lab. of Govt. Medical College Jammu. Blood sugar levels, both fasting and postprandial, were assessed by Glucose oxidase-peroxidase method in the same Lab.

HbA1C was assessed by HPLC [High Performance Liquid Chromatography] assay.

Results: Vitamin-D deficiency [Vitamin-D levels <20 ng/ml] was seen in 16.67% of premenopausal and 36.67% postmenopausal Type-2 diabetics. This was not related to the glycemic control as HbA1C was increased in both the groups.

Conclusions: Vitamin-D deficiency is more prevalent in postmenopausal Type-2 diabetics, as compared to premenopausal type-2 diabetics.

Keywords: Menopause, Type-2 diabetes mellitus, Vitamin-D

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a metabolic disease and major lifestyle disorder caused by either relative insulin deficiency or insulin resistance. It is characterized by impaired glucose tolerance, chronic hyperglycemia, and altered insulin secretion. Many studies have linked vitamin D status to insulin secretion and insulin resistance. However, the relationship between vitamin D deficiency and glycemic control remains conflicting.

Vitamin D is functionally a hormone, rather than a vitamin, and is one of the most important biological regulators of calcium metabolism, in conjunction with parathyroid hormone and calcitonin. As calciferol enters the circulation, it is metabolized to several forms, the primary one being 25-hydroxycalciferol (25-OH-D). The
first step in the metabolism of vitamin D, 25 hydroxylation, occurs mainly in the liver. In humans, only a small amount of 25-OH-D is metabolized in the kidney to other di-hydroxy metabolites. Because 25-OH-D is the predominant circulating form of vitamin D in the normal population, it is considered to be the most reliable index of people’s vitamin D status.

Vitamin D3 (cholecalciferol) is the naturally occurring form of vitamin D produced in the skin after 7-dehydrocholesterol is exposed to solar U.V. radiation. Vitamin D2 (ergocalciferol) is produced synthetically by UV irradiation of ergosterol. The two forms differ in the structures of their side chains, but they are metabolized identically and have equivalent biological activities. Both forms are used for fortification of dairy products. Because these two parent compounds provide various contributions to people’s overall vitamin D levels, it is important that both forms are measured equally. The measurement of 25-OH-D (referred to as the vitamin D assay) is becoming increasingly important in the management of patients with various disorders of calcium metabolism associated with rickets, neonatal hypocalcemia, pregnancy, nutritional and renal osteodystrophy, hypoparathyroidism, and postmenopausal osteoporosis.

Historically, vitamin D has been known for its role in the mineralization of teeth and bones through regulation of calcium and phosphorus homeostasis. More recently, there is emerging evidence of the role of vitamin D in protection against risk for malignant neoplasms, cardiovascular disease, and diabetes, along with osteoporosis and other bone disorders. This progression of skeletal and non-skeletal diseases may be influenced by circulating levels of vitamin D, based on the discovery of more than 2000 genes in the human genome that respond to vitamin D.

Menopause, the cessation of menstrual cycle caused by reduced secretions of estrogen and progesterone, is defined as 1 year without menses, occurring between the ages of 45-55. Oestrogen increases the activity of 1-α-hydroxylase (expressed in the kidneys) responsible for the activation of vitamin D and upregulates the vitamin D receptor (VDR). During menopausal stages, there is a gradual reduction in amount of oestrogen produced by the ovaries; this decline in oestrogen production is thought to promote vitamin D deficiency. The ensuing vitamin D challenge is related to decrease in number of vitamin D receptors. Aging in women and the subsequent drop in oestrogen levels are thus associated with decline in vitamin D levels. And a negative association exists between Vitamin-D deficiency and glycemic control.

The present study was hence conducted to evaluate the levels of 25(OH)Vitamin-D in pre- and post-menopausal Type-2 Diabetes mellitus women and to assess the association between Vitamin-D deficiency and glycemic control.

METHODS

The study was conducted in Govt. Medical College, Jammu on 60 Type-2 Diabetic women, 30 Premenopausal [age group 40 to 55 years] and 30 Postmenopausal [age group 55 to 70 years]. Period of study was between April 2019 and August 2019. Ethical clearance was obtained from the Institutional Ethical Committee.

Inclusion criteria

• Subjects chosen were those
  • With fasting blood glucose more than 130 mg/dl.
  • With duration of diabetes more than 5 years.
  • HbA1C more than 6.5%.

Exclusion criteria

• Patients with pre-existing parathyroid disease, Type-1 diabetes, metabolic bone disease and those on calcium and Vitamin-D supplementation were excluded from the study.

After obtaining proper consent from the patient, she was advised to come fasting in the morning. 2 ml of blood was withdrawn and sent to biochemistry lab for assessment of blood glucose level. Then a postprandial blood sample was also withdrawn for estimation of postprandial blood sugar level.

Glycated hemoglobin or Glycohemoglobin [HbA1C] estimation was also carried out. HbA1C evaluates glycemic control over a period of 3-4 months. In June 2009, the International Expert Committee, which represents several major diabetes groups, recommended using HbA1C to diagnose diabetes. HbA1c is considered as an important marker for the assessment of glycemic control in diabetes and DM-induced complications.

Glycosylated hemoglobin in blood was measured by HPLC assay (diagnostic value, >6.5%). Vitamin-D level was measured by Roche chemiluminescent immunoassay (CLIA), within reference values 30-70 ng/mL. (Centauro kit; competitive 1-step assay with fluorescein-marked antibody).

Statistical analysis

Statistical analysis was performed by Microsoft excel program. Comparison of results of all parameters between the premenopausal and postmenopausal group was carried out using Student’s unpaired t-test.

Correlation was assessed between Vitamin-D levels and fasting blood glucose levels by Pearson correlation coefficient. Results were expressed as mean±standard deviation. p<0.05 was considered statistically significant.
RESULTS

Of the 60 Type-2 Diabetic women, 30 were premenopausal and 30 were postmenopausal.

Vitamin-D levels ≥30 ng/ml was taken as normal; ≥20 to ≤30 were considered as insufficiency and <20 was considered as deficiency.

In case of premenopausal Type-2 diabetics 40% (12) had normal Vitamin-D levels; 43.33% (13) had Vitamin-D insufficiency and 16.67% (5) were Vitamin-D deficient. In case of postmenopausal Type-2 diabetics 16.67% (5) had normal Vitamin-D levels; 46.66% (14) had Vitamin-D insufficiency and 36.67% (11) were Vitamin-D deficient (Table 1).

Table 1: Distribution of vitamin D3 levels in premenopausal and postmenopausal diabetic females.

<table>
<thead>
<tr>
<th>Vitamin D3 level (ng/ml)</th>
<th>Premenopausal diabetics</th>
<th>Postmenopausal diabetics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>&lt;20 (deficiency)</td>
<td>5</td>
<td>16.67</td>
</tr>
<tr>
<td>≥20-&lt;30 (insufficiency)</td>
<td>13</td>
<td>43.33</td>
</tr>
<tr>
<td>≥30 (normal)</td>
<td>12</td>
<td>40</td>
</tr>
</tbody>
</table>

Age (years)

Premenopausal diabetic women were in the age group of 46.7±4.47 [Mean±SD], whereas the postmenopausal diabetic women were in the age group of 62.93±4.44 [Mean±SD]. On statistical analysis p<0.0001, which was statistically significant.

Fasting blood glucose (mg%)

In premenopausal group, the fasting blood sugar was 164.76±38.45 [Mean±SD], whereas in the postmenopausal group it was 166.96±31.03 [Mean±SD]. On statistical analysis p=0.80, which is not of significance statistically.

Postprandial blood glucose (mg%)

In premenopausal group 237.86±61.89 [Mean±SD], whereas in the postmenopausal group it was 248.03±57.29 [Mean±SD]. On statistical analysis p=0.51, which is not statistically significant.

Vitamin D3 (ng/ml)

In premenopausal group the Vitamin-D3 level was 28.35±11.59 [Mean±SD], whereas in the postmenopausal group it was 22.56±9.51 [Mean±SD]. On statistical analysis p=0.03, which is statistically significant.

HbA1C [%]

In premenopausal group HbA1C was 7.95±2.02 [Mean±SD], whereas in the postmenopausal group it was 7.22±0.95 [Mean±SD]. On statistical analysis p=0.07, which is of no significance statistically (Table 2).

Table 2: Comparison of variables between premenopausal and postmenopausal diabetic females.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Premenopausal diabetics (n=30)</th>
<th>Postmenopausal diabetics (n=30)</th>
<th>Statistical inference (unpaired t test)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean±sd</td>
<td>Mean±sd</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>46.7±4.47</td>
<td>62.93±4.44</td>
<td>T=14.1; p&lt;0.0001*</td>
</tr>
<tr>
<td>Blood sugar fasting (mg%)</td>
<td>164.76±38.45</td>
<td>166.96±31.03</td>
<td>T=0.24; p=0.80*</td>
</tr>
<tr>
<td>Blood sugar postprandial (mg%)</td>
<td>237.86±61.89</td>
<td>248.03±57.29</td>
<td>T=0.66; p=0.51</td>
</tr>
<tr>
<td>Vitamin D3 (ng/ml)</td>
<td>28.35±11.59</td>
<td>22.56±9.51</td>
<td>T=2.11; p=0.03</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>7.95±2.02</td>
<td>7.22±0.95</td>
<td>T=1.79; p=0.07</td>
</tr>
</tbody>
</table>

*Significant; **Not significant

DISCUSSION

Vitamin D is a steroid hormone known for its essential role in maintaining calcium homeostasis, promoting and maintaining bone health, and improving immune function. Although its role in skeletal health has long been recognized, now it has been seen that this vitamin plays a ubiquitous role in the function of essentially all major organ systems. Also, the clinical manifestations of a vitamin-D-deficiency state may vary across the lifespan, as does the vulnerability to the deficiency state. This is particularly apparent for women. In premenopausal women, the primary manifestations of vitamin D deficiency are osteoporosis and an increased risk of breast and colon cancer. In postmenopausal women a further increase occurs in the expression of these malignancies and in bone loss.

Vitamin D deficiency is increasingly recognized as a major health issue. Despite the high UVB sunlight...
exposure in tropical countries, studies suggest vitamin D deficiency is prevalent and is further influenced by age and gender.28,29 Low serum vitamin D level has been proven to be correlated with type 2 diabetes mellitus. It is known that normal insulin secretion in pancreatic B-cell depends on vitamin D. A reduction in vitamin D level can result in an increase in insulin resistance and reduction in insulin secretion.30 Abnormal vitamin D level and glucose homeostasis are two most chronic medical conditions leading to cardiovascular disease following menopause transition in females.31

Vitamin-D plays an important role in women’s health because menopause affects the metabolism of Vitamin-D. The “prohormone” Vitamin D exists in two forms, the plant source (ergocalciferol [Vitamin D2]) and the animal source (cholecalciferol [Vitamin D3]). Vitamins D2 and D3 are ingested from the diet; however, the major source of Vitamin D is Vitamin D3 synthesized in the skin upon exposure to ultraviolet-B (UVB) light. Vitamin D is then hydroxylated in the liver to 25-hydroxyvitamin D (25(OH)D). This metabolite is further hydroxylated to 1,25-dihydroxyvitamin D (1,25(OH)2D), the biologically active form of the vitamin, by the enzyme 1-hydroxylase, found in the kidney. 1,25(OH)2D binds to a nuclear receptor protein, the Vitamin D Receptor (VDR), to exert most of the biologic actions of the hormone.27

Menopause represents an important transition in vitamin D requirements because of the dependence of the VDR on estrogen. The increased requirement for calcium across the menopausal transition is a reflection of the loss of VDRs and an increased requirement for vitamin D.32 Vitamin D was found to be negatively correlated with increased age and HbA1C in postmenopausal women. The finding of a higher vitamin D deficiency in the postmenopausal women may be related to advanced age. Aging is directly related to decreasing vitamin D levels. The diminishing levels of 25(OH)D with age is due to impaired intestinal absorption of vitamin D as well as a decline in the concentration of vitamin D precursors normally stored in the skin coupled with reduced capacity to synthesize vitamin D in the skin when exposed to UVB radiation.33,34 Additionally, decline in oestrogen associated with postmenopausal women decreases the activity of 1-alpha hydroxylase vitamin D responsible for activating Vitamin D and its Receptors (VDRs).

The aim of the present study was to evaluate the status of vitamin D in pre- and postmenopausal diabetic women and assess the relationship between vitamin D deficiency and markers of glycemic control. Levels of fasting and postprandial blood glucose, HbA1C and vitamin D were measured in pre and postmenopausal T2DM women.

This study observed that 60% premenopausal Type-2 Diabetic women were Vitamin-D deficient, whereas the incidence was higher in postmenopausal Type-2 Diabetic women, with about 83% being deficient in Vitamin-D.

This findings are similar to those of Mori and colleagues, who observed that 91.8% of postmenopausal diabetic women are deficient of vitamin D.35 In another cross-sectional study in India, Kanwar and coworkers reported a higher prevalence of vitamin D deficiency among postmenopausal T2DM women compared to premenopausal T2DM women (80% versus 60%).19 Another cross-sectional study in Indonesia by Hidayat et al, observed a prevalence of 78.2% vitamin D deficiency among elderly T2DM women.36 Likewise, studies by Sarmidi et al.37 and Setiati and Sutrisna observed a prevalence of 61.9% and 35.1%, respectively.38

This study showed high fasting blood glucose in both the premenopausal and postmenopausal Type-2 Diabetic women and the glycemic control in both groups was poor, with HbA1C more than 7% in both the premenopausal and postmenopausal Type-2 Diabetic women. So, there was significant negative association between vitamin D sufficiency and FBG and Hba1c in both pre- and postmenopausal Type-2 Diabetic women.

Need et al, as well as Ford et al,’s study reported an inverse relationship between FBG and serum 25(OH) D levels.39,40 A cross-sectional study by Doddamani et al. on newly detected type 2 diabetics also reported an inverse association between vitamin D and FBG. They also reported higher HbA1c levels in patients with severe vitamin D deficiency compared to subjects with mild to moderate deficiency.31 Similarly, Dalgård et al, and Shanthi et al.42,43 observed an inverse association between vitamin D and HbA1c. Chiu and colleagues in a cross-sectional study also observed a negative correlation between serum 25(OH) D3 and postprandial glucose concentration and a positive association between vitamin D and insulin.44 The observed association between vitamin D, FBG, and HbA1c is suggestive of the fact that good control of blood sugar is essential for optimal vitamin D levels among diabetic women. Pannu et al, in a population-based study in Australia have reported on a protective effect of higher 25(OH)D on FBG and HbA1c.45 It is unclear whether vitamin D deficiency and poor glycemic control are causally related or represent two independent features of T2DM. Previous studies have reported inconclusive results regarding the association between vitamin D status and HbA1c.46,47

CONCLUSION

Menopause not only marks an end of a woman’s reproductive life, but it also embraces various other changes like increased risk of cardiovascular diseases, mood swings, osteoporosis and many other negative health outcomes which have to be taken care of well in time. This crucial period also marks an important transition in vitamin D requirement as ageing skin is unable to effectively absorb sunlight and synthesize the required amount of vitamin D. Vitamin D deficiency is high in
both pre- and postmenopausal T2DM especially among postmenopausal T2DM women.

In this study, both premenopausal and postmenopausal Type-2 Diabetic women were found to be Vitamin D deficient, but this deficiency was more prevalent in postmenopausal diabetic women as compared to premenopausal diabetic women. This greater decline in Vitamin D levels in post-menopausal females is due to the effect of decreased levels of estrogen.

Also, Vitamin D deficiency in both premenopausal and postmenopausal Diabetic women is associated with poor glucose control, with HbA1C >6.5% in both groups.

Adequate vitamin D may play a role in long term glucose control. Vitamin D screening and supplementation should be incorporated into management plan for all T2DM women to serve as an early tool for prevention of vitamin D deficiency.

Current recommendation by National Institute of Health is to maintain vitamin D levels above 50 nmol/l, and postmenopausal females should take 600-800 IU/day.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee of GMC, Jammu, India

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