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Serum vitamin D level in postmenopausal diabetic and non-diabetic women in Western Rajasthan

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Abstract

Background: During menopausal stages bone loss in women becomes rapid because of metabolic and endocrine disorder.

Aim: The study aims to evaluate vitamin D in diabetic-post menopausal women with an aim to assess the bone turnover and utility of vitamin D

Methodology: 150 post-menopausal women with type 2 diabetes mellitus were examined for serum vitamin D level by chemiluminescent immunosorbent assay method and were compared with 150 post-menopausal women without type 2 diabetes mellitus.

Results: A highly significant decrease in serum vitamin D was observed in post menopausal women with type 2 diabetes mellitus subjects as compared to post menopausal women without type 2 diabetes mellitus**.(**t=20.98, p-value<0.0001).

Conclusion: With decrease in serum vitamin D level in post menopausal age the risk of osteoporosis are higher in women with type II diabetes mellitus

Keywords: Vitamin D, Diabetes Mellitus, Estrogen Deficiency

Introduction

Menopause is a routine, non-pathologic condition involving the permanent cessation of menses for at least 12 months. Menopause occurs in all menstruating females between 45-55 years of age due to non-pathologic estrogen deficiency. It also leads to metabolic bone disorders.[1] Menopause is the most significant period for bone loss in women when rapid metabolic and endocrine changes occur. Bone loss initiates before the last menstrual period. The percent decrease in bone mineral density in the first five years of post-menopausal women can be high as 9-13%. Although menopause has a greater effect on bone loss than chronological age.[2]

Diabetes mellitus (DM) is a metabolic condition characterized by elevated blood glucose levels due to insulin resistance, deficiency, or both. Type 2 DM (T2DM), characterized by hyperglycemia, accounts for about 90% of all diabetes cases worldwide[3]. It has also been increasingly recognized that diabetes adversely affects bone health.[4] In vitro and murine studies investigated the impact of several molecules derived from osteoblasts and osteocytes on glucose metabolism. In addition, the effect of glucose on bone cells suggested a mutual cross-talk between bone and glucose homeostasis. In humans, these mechanisms are the pivotal determinant of the skeletal fragility associated with type 2 diabetes[5].

An essential and significant complication due to menopause is osteoporosis, which is the most common metabolic bone disorder that is common in postmenopausal with type 2 diabetes.[6]Type 2 Diabetes Mellitus (T2DM) and osteoporosis are both chronic conditions; the relationship between them is complex. Clinical data uniformly support that bone formation and bone micro-architectural integrity are altered in diabetic patients.[7,8] Moreover, glucose metabolism impairment has a number of detrimental effects on bone remodeling in terms of reduced bone mass[9,10] and an increased risk of fractures.[11]Microvascular complications of diabetes lead to reduced blood flow to bone contributing to bone loss and fragility[12]

Vitamin D is a steroid hormone known for its essential role in maintaining calcium homeostasis, promoting and maintaining bone health, and improving immune function. 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.[13]

Bone turnover markers (BTMs) are biochemical markers used in the evaluation as well as monitoring of treatment for osteoporosis. A study of BTMs provides an insight of the dynamics of bone turnover in many metabolic bone disorders based on the increase or decrease in the bone formation/resorption markers.[14]

Therefore, the present study is planned to evaluate vitamin D in diabetic-post menopausal women with an aim to assess the bone turnover and utility of vitamin D in detecting osteoporosis and for early diagnosis and better management of bone loss in diabetic post-menopausal women to reduce the burden of osteoporosis and its co morbidities.

Material and methods

The present study was conducted on 150 post-menopausal women with type 2 diabetes mellitus of varying age groups attending the outpatient Department of Obstetrics and Gynecology and Department of Medicine Dr. S.N. Medical College and its associated group of Hospitals, Jodhpur. All the investigation work was performed in the Department of Biochemistry, Dr. S.N. Medical College Jodhpur. The results were compared with 150 post-menopausal women without type 2 diabetes mellitus.

Diagnosis of menopause by a gynaecologist according to STRAW study criteria and post-menopausal period for up to 5 years [Harlow SD et al, 2012] Diabetes was defined as self-report of diabetes diagnosed by a physician previously, in accordance with the American Diabetes Association criteria. [Fasting plasma glucose ≥126 mg/dl (7.0 mmol/l) and 2-h plasma glucose ≥ 200 mg/dl (11.1 mmol/l) during OGTT and HbA1c ≥6.5 (48 mmol/mol), and Random plasma glucose ≥200mg/dl (11.1 mmol/l)].[15]

The subjects with parathyroid disease, thyroid disease, bone diseases, chronic kidney disease, liver disease, hysterectomy, steroids and history of hormone replacement therapy, calcium or vitamin D supplementation, and usage of medicines able to affect BMD in the last one year were excluded from the study.

Physical examination and blood sample collection for biochemical parameters was done after apprising the nature and objective of the study.

Study Design: Analytical cross-sectional.

Sample size- Sample size was calculated by following formula-

$$n = \frac{4P(1-P)}{L^2}$$

Collection of samples

After overnight fast of 10-12 hours 5ml of venous blood sample was collected from all the subjects from antecubital vein by using aseptic technique and blood was transferred to plain vial for the estimation of serum vitamin D, after that the blood sample was allowed to clot and serum was separated immediately.

Serum Vitamin –D: Chemiluminescent Immunosorbentassay Method [Holick MF et al 1995][16]

Principle

The Access 25 (OH) Vitamin D Total assay is a two-step competitive binding immune enzymatic assay. In the initial incubation, samples added to a reaction vessel with a vitamin D binding protein (DBP) releasing agent and paramagnetic particles coated with sheep monoclonal anti-25 (OH) vitamin D antibody. 25 (OH) vitamin D is released from DBP and binds to the immobilized monocleonal anti-25 (OH) vitamin D on the solid phase. Subsequently, a 25(OH) vitamin D analogue-alkaline phosphatase conjugate is added which competes for binding to the immobilized monoclonal ant 25(OH)vitamin D. After a second incubation, material bound to the solid phase were held in a magnetic field while unbound materials were washed away.

Then, the chemiluminescent substrate Lumi-Phos* 530 was added to the vessel and light generated by the reaction was measured with a luminometer. The light production is inversely proportional to the concentration of 25(OH) vitamin D in the sample. The amount of analyte in the sample was determined from a stored, multi-point calibration curve.

Reagents

1. R1 ACCESS 25(OH) Vitamin D Total Reagent Packs

- R1a: Paramagnetic particles coated with sheep monoclonal anti-25(OH)vitamin D antibody suspended in a TRIS buffered saline, goat IgG, bovine serum albumin (BSA), <0.1% sodium azide, and 0.1% ProClin 300.
- R1b: Formic Acid, Poly (vinyl alcohol) and 0.1% ProClin 300.
- R1c: Formic Acid, Poly (vinyl alcohol) and 0.1% ProClin 300.
- R1d: Vitamin D analog-alkaline phosphatase conjugate, ACES, <0.1% sodium azide, and 0.1% ProClin 300.

2. Access 25 (OH) Vitamin D Total Calibrators

3. Quality Control material

4. Access Substrate

5. Access Wash Buffer II

6. Vortex mixer with a continuous ‘On’ mode and a maximum speed between 2500 and 3200 rpm.

Assay procedure

- Reagent pack was mixed using a vortex mixer immediately before loading the reagent pack on the instrument for the first time, to ensure that the

paramagnetic particles in the reagent pack are fully suspended.

- Use 30 µL of sample for each determination in addition to the sample container and system dead volumes (150µL).
- The assay was initiated as directed in the user's manual.

Calculation

System performs all calculations internally to produce the final reported result. Test results were determined automatically by the system software. The amount of analyte in the sample was determined from the measured light production by means of the stored calibration data**.**

Reference range

Vitamin D status	25 (OH) Vitamin D Concentration Range	25 (OH) Vitamin D Concentration Range
	(ng/mL)	(nmol/L)
Deficient	<20	<50
Insufficient	20 to <30	50 to <75
Sufficient	30-100	75-250
Upper safety limit	>100	>250

Results

Table 1: Mean Serum vitamin D3 level (ng/ml) level of the subjects studied

Sn.	Studied Group (n=150)	Mean±SD (Range)
1	Post-menopausal women without type 2 diabetes mellitus	27.77±2.77 (15.15-31.55)
2	Post-menopausal women with type 2 diabetes mellitus	20.10±3.51 (11.11-25.52)

Graph 1

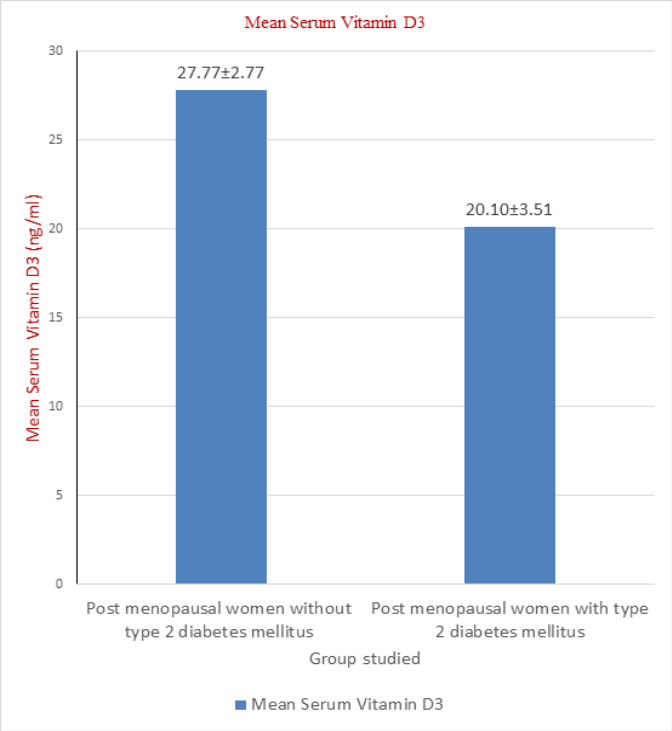

Table 2: Statistical analysis of serum vitamin D ((ng/ml) among the group studied:

Sn.	Studied Group (n=150)	t value	p value
1	Post-menopausal women without type 2 diabetes mellitus Vs Post-menopausal women with type 2 diabetes mellitus	20.98	<0.0001(HS)

Students t test applied, HS= highly significant Serum Vitamin D3

The mean serum vitamin D3 level was observed in post-menopausal women without type 2 diabetes mellitus and with type 2 diabetes mellitus groups was 27.77±2.77 varied from 15.15-31.55 and 20.10±3.51 varied from 11.11-25.52 respectively **[Table: 1, Graph: 1].**

Similarly, statistical analysis between post-menopausal women without type 2 diabetes mellitus and with type 2 diabetes mellitus groups(t-value = 20.98, p-value =<0.0001) was also statistically highly significant. **[Table: 2]**

Summary

A highly significant decrease in serum vitamin D was observed in post-menopausal women with type 2 diabetes mellitus subjects as compared to post-menopausal women without type 2 diabetes mellitus**.(**t=20.98, p-value<0.0001)

Discussion

Menopause is defined as the point of time when **menstrual cycles permanently cease** due to the natural depletion of ovarian oocytes from aging. It marks the permanent end of fertility and which is characterized by low production of estrogen that impacts the body mass index and alters the adipose tissue distribution consequently incomplete energy expenditure along with insulin secretion, insulin sensitivity that can predispose to the development of T2DM.[17]

Various facets of the bone and its metabolism including the structure, density, skeletal integrity, and biochemical markers of bone turnover may be affected by diabetes. The fact remains that bone disease is frequently overlooked as a complication of diabetes.

These findings were in accordance with those of Enrique López Gavilanez et al[18] in year 2018 , who found serum vitamin D levels were significantly lower (p<0.034) in the T2DM group and in another study conducted by Linda Ahenkorah Fondjo et al[19] (2018**)** showed the prevalence of vitamin D inadequacy was 92.2%. Hypovitaminosis D was more prevalent among the postmenopausal T2DM women (63.8% versus 58.2%)(p<0.001). Hence, a high prevalence of vitamin D insufficiency in the Ecuadorian postmenopausal women with type 2 diabetes mellitus was observed. Hanan Al Kadai et al[20] studied Vitamin D Status in Saudi women with Type 2 diabetes mellitus and reported that non-significant and marginally lower 25(OH) vitamin D levels among diabetic postmenopausal women as compared to their age and BMI matched control group.

Our results are contrary to the results of Nada M Alselami et al[21] in the year 2015they had estimated a significant elevation in Ca, and Pi levels in diabetic postmenopausal patients group compared to the healthy group.

Conclusion

The study concludes that post-menopausal women with type 2 diabetes are at a higher risk of developing osteoporosis symptoms as compared to women who do not suffer from diabetes. Diabetes control and the amount of healthcare should be well attended to for such patients to avoid fracture and further complications.

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