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A comparative study of biochemical markers of bone turnover in postmenopausal women with type 2 diabetes mellitus

[1]Dr. Vinita Saini, Senior Demonstrator, Department of Biochemistry Dr SN Medical College, Jodhpur.

[2]Dr. Ranjana Mathur Senior Professor and Head**,** Government Medical College, Sirohi**.**

[3]Dr. Vijendra Saini, Medical Officer, Department of Pediatrics Umaid Hospital, Jodhpur

Corresponding Author: Dr. Vinita Saini, Senior Demonstrator, Department of Biochemistry Dr SN Medical College, Jodhpur

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Abstract

Background: Osteoporosis is a critical complication of menopause that increases the susceptibility to fracture. Advanced end glycation product produced in Type 2 Diabetes Mellitus also leads to bone depletion**.**

Aims: The aim of the study is to assess bone turnover in post-menopausal diabetic women.

Methods: t-score, serum calcium and serum phosphorus were assessed using QUS bone densitometer, End Point Arsenazo-Iii Method, UV End Point Method respectively

Results: Statistical analysis of T-score, serum calcium (mg/dl), serum phosphorus (mg/dl) among the group studied was done and p value was< 0.0001.

Conclusion: The Type 2 diabetic postmenopausal women in present study were observed to have decreased level of serum calcium and phosphorus as compared to the postmenopausal women without Type 2 diabetes. Also the bone loss velocity is high in the Type 2 diabetic postmenopausal women

Keyword: Osteoporosis, biochemical, postmenopausal

Introduction

Menopause is defined as the point of time when menstrual cycles permanently cease due to the natural depletion of ovarian oocytes from aging. The diagnosis is typically made retrospectively after the woman has missed menses for 12 consecutive months. It is characterized by hot flushes; night sweats and various other psychological and biochemical changes occur. It also leads to metabolic bone disorders.[1]

According to the WHO, Osteoporosis condition is recognized as a "silent global problem", which is characterized by a reduction in the bone mass and micro-architectural deterioration of bone tissue, leading to impaired skeletal strength with a consequent increase in

bone fragility and susceptibility to fracture and major increase in the incidence of osteoporosis.[2]

Diabetes mellitus is a common endocrine disease in most parts of the world. The chronic complications of diabetes include microvascular complications such as nephropathy, retinopathy, neuropathy, and macrovascular complications like acute coronary syndrome and stroke. Apart from above, 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.[3]

Recently, in a study performed by Li, Q et al, in Chinese population has revealed that,[4] the prevalence of premenopausal women with T2DM was 12.1%, while the prevalence in postmenopausal women was 19.4% and showed a statistical significance of $P < 0.05$. Recently, in India, menopausal women showed a prevalence ranging from 19.2% in premenopausal to 32.4% in postmenopausal women.[5]

Numerous investigations either in vitro or murine states the impact of several molecules derived from osteoblasts and osteocytes on glucose metabolism. In humans, these mechanisms are the strong determinant of the weak skeleton associated with type 2 diabetes.[6] In humans, biochemical markers and bone histomorphometry reveal a low bone turnover in T2DM. At a structural level, the accumulation of advanced glycation end (AGE) products under diabetic conditions has been proposed to alter collagen structure and contribute to impaired material properties[7]

Calcium and phosphate are important components of body inorganic matrix and major factors in maintenance of bone health. Calcium influences many extracellular and intracellular processes, is essential for the development, growth, and maintenance of bone, and for the stability of the cellular cytoskeleton. On the other hand, phosphorus homeostasis is regulated by three main hormones: PTH, 1,25(OH)2 D3, and FGF23 that is secreted by osteocytes.[8,9]

Bone Mineral Density (BMD) is an important factor linked to bone health and fracture risk. A bone mineral density (BMD) test measures the density of calcium and other types of minerals present in an area of the bone. With an increase in age, bones become thinner (Osteopenia) as they lose calcium, and also the deterioration of existing bone tissue occurs faster than the formation of a new bone. Bone mineral density tests are used to detect bone loss, Osteopenia, and osteoporosis. The results of the test are usually reported as T-score and Z-score.[10]

Thus, evaluation of these biochemical markers was done in the present study to make an assessment of bone turnover in post-menopausal diabetic women which provides with clear insight of osteoporosis and its progression.

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 Gynaecology 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.

The subjects selected for the study were group as follows:

- Group I – Post menopausal women without type 2 diabetes mellitus.(150)

- Group II –Post menopausal women with type 2 diabetes mellitus.(150)

Inclusion criteria

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]

Group 1 include post-menopausal women without type 2 diabetes mellitus.

Group 2 include post-menopausal women with type 2 diabetes mellitus.

Diabetes will 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)].[11]

Exclusion criteria

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 will be excluded.

An informed consent was taken from all the healthy control groups and study groups who participated in 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- $n = \frac{4P(1-P)}{L^2}$

Detailed personal and clinical history of all the subjects was taken and recorded in the Proforma under following headings:

1. Personal history [Name, age, dietary habits.]

2. Family history [Family members suffering from either obesity, hypertension, diabetes mellitus or thyroid abnormalities]

Collection of samples

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

1. Bone mineral density

Bone mineral density [BMD] was measured by QUS bone densitometer.

QUS bone densitometer [Gluer C.C.et al 1994][12]

The skeletal health status was evaluated using Quantitative Ultrasound Scan (QUS) measurements to determine the prevalence of BMD at the heel bone (calcaneus) and these measurements was carried out by the SONOST 3000 clinical bone densitometer. Quality assurance tests were run on a daily basis according to the manufacturer's protocol with the standard phantom before each data collection session to ensure the stability of QUS measurements.

- BMD values was measured in terms of QUS device specific T-score criteria which is similar to WHO's criteria. T-score is the number of standard deviation relative to the standard speed of sound (SOS) value of the young age group.
- T-score 1.0 or higher is normal
- T-score between −1.0 and −2.5 is "osteopenia"
- T-score − 2.5 or lower is "osteoporosis".[13]

Estimation of serum calcium was done by end point arsenazo –III method:[Thomas L. et al 1998][14]

Estimation of serum phosphorus was done by UV end point method:[Tietz NW et al 1995][15]

Results

Table 1: Mean T score of the subjects studied.

Sr. No.	Studied Group (n=150)	Mean±SDRange
1	Post-menopausal women without type 2 diabetes mellitus	-1.06±0.10 (-1.99-1.95)
2	Post-menopausal women with type 2 diabetes mellitus	-2.83±0.41 (-3.82--1.08)

Table 2: Statistical analysis of T score among the group studied.

Sr. No.	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	19.78	<0.0001(HS)

(Students t test applied, HS= Highly significant)

Graph 1:

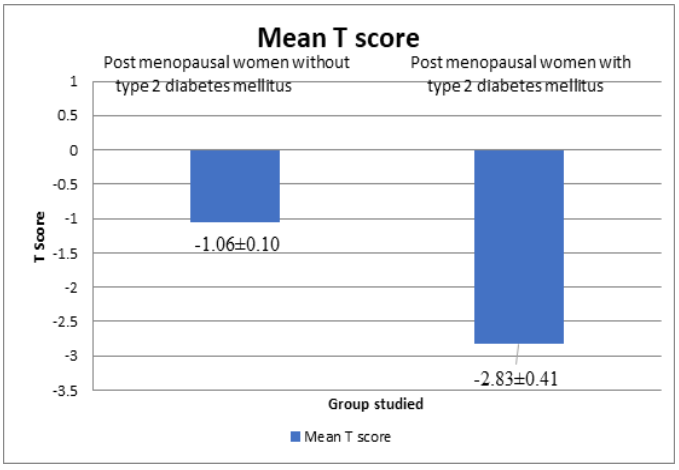


Table 3: Mean serum calcium (mg/dl) of the subjects studied.

Sr. No.	Studied Group (n=150)	Mean±SD (Range)
1	Post-menopausal women without type 2 diabetes mellitus	9.39±0.54 (8.3-10.6)
2	Post-menopausal women with type 2 diabetes mellitus	8.65±0.40 (8.1-9.9)

Table 4: Statistical analysis of serum calcium (mg/dl) among the group studied.

Sr. No.	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	13.54	<0.0001(HS)

Students t test applied, HS= Highly significant

Graph 2:

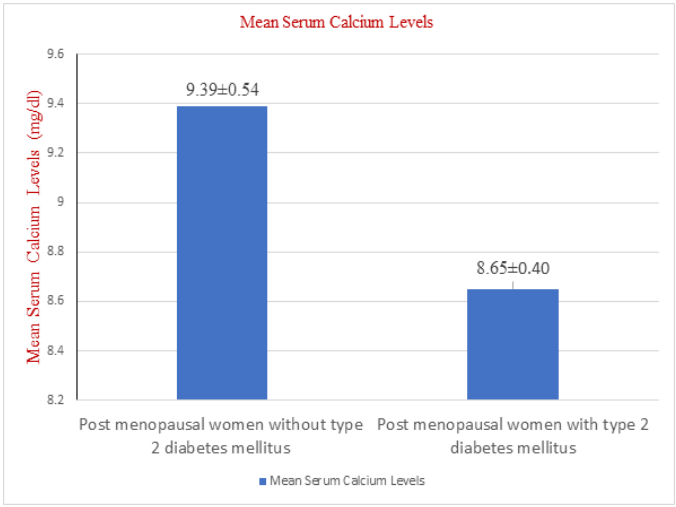


Table 5: Mean serum phosphorus(mg/dl) level in both subjects studied

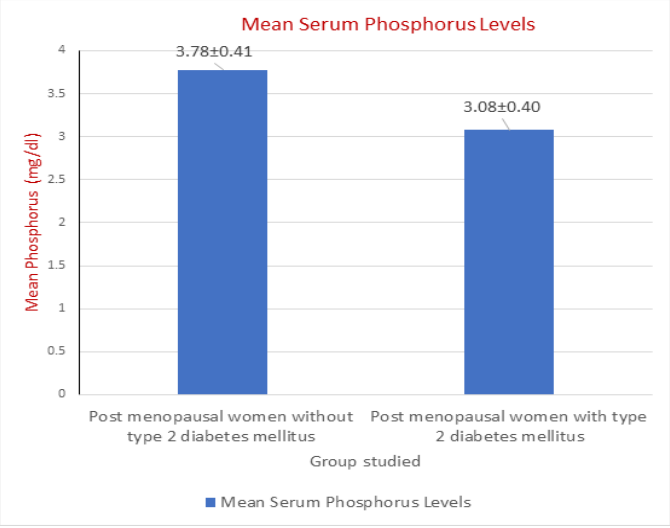
Sr. No.	Studied Group (n=150)	Mean± SD (Range)
1	Post-menopausal women without type 2 diabetes mellitus	3.78±0.40 (2.61-4.6)
2	Post-menopausal women with type 2 diabetes mellitus	3.08±0.41 (2.11-3.95)

Table 6: Statistical analysis of serum phosphorus (mg/dl) among the group studied.

Sr. No.	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	14.83	<0.0001(HS)

Students t test applied, HS= Highly significant

Graph 3:



T Score

Mean T-score was -1.06±0.1.02 and -2.83±0.41 in post-menopausal women without type 2 diabetes mellitus and with type 2 diabetes mellitus which varied from (-1.99-1.95) and (-3.82--1.08) respectively. [Table: 1, Graph: 1]

On analysing statistically value of mean T score between post-menopausal women without type 2 diabetes mellitus v/s post-menopausal women with type 2 diabetes mellitus (t-value =19.78, p-value = <0.0001) was found to be Highly-Significant**.** [Table: 2]

Serum Calcium

The mean serum calcium levels were observed in post-menopausal women without type 2 diabetes mellitus and with type 2 diabetes mellitus groups was 9.39±0.54 varied from 8.3-10.6 and 8.65±0.4 varied from 8.1-9.9 respectively [Table: 3, Graph 2].

On analysing statistically value of mean serum calcium level between post-menopausal women without type 2 diabetes mellitus v/s post-menopausal women with type 2 diabetes mellitus (t-value =13.54, p-value = <0.0001) was found to be Highly-Significant**.** [Table: 4]

Serum Phosphorus

In both the groups of post-menopausal women without type 2 diabetes mellitus and with type 2 diabetes mellitus, the mean serum phosphorus levels was estimated to be 3.78±0.40 ranged from 2.61-4.6 and 3.08±0.41 ranged from 2.11-3.95 respectively [Table:5, Graph 3].

A statistically highly significant elevated serum phosphorus level was observed in post-menopausal women without type 2 diabetes mellitus subjects (t= 14.83, p<0.0001) when results was compared with post-menopausal women with type 2 diabetes mellitus subjects**.** [Table: 6].

Discussion

The results of T score were in agreement with those of the Abdelmonem Fathy Zeid et al[16] in year 2020 they also observed that type 2 diabetic patients have significantly lower T score values and more frequent osteoporosis than healthy postmenopausal women. In another study done by Al-Matouq et al.[17] in year 2018 about prevalence of osteoporosis among postmenopausal females with type 2 diabetes mellitus in Saudi Arabia that also observed decreased T score among diabetics. Yijun Zhou et al[18] in year 2010, also reported that Postmenopausal women with type2 diabetes have lower BMD levels and higher osteopenia/osteoporosis rate than BMI-matched control subjects. Impaired bone formation may occur in Chinese postmenopausal women with type 2 diabetes.

In contrast to our study, Hadzibegovic et al.[19] in year 2008 and many studies on white women in year 2003 showed that postmenopausal women with type 2 DM had higher BMD among them and another study of Thakur and Dash et al[20] in year 2018 study showed no significant difference in bone mineral density among post-menopausal women with and without type 2 diabetes mellitus in Western Odisha.

The results of serum calcium and phosphorus were in agreement with those of the Amira Shoukry Ahmed et al[21] in year 2020, they also observed that statistically highly significant difference of mean values of serum calcium and phosphorus between these two main groups: diabetics post-menopausal women and non-diabetics post-menopausal women.

Meena Varma et al[22] in year 2005 showed that in postmenopausal diabetic women the serum alkaline phosphatase tends to be higher, while serum calcium and phosphorus levels are decreased. Also suggest that hyperglycaemia in postmenopausal women affect the bone related biochemical parameters. These results were contrary to the results of Nada M Alselami et al[23] in year 2015they had estimated a significant elevation in 1,25(OH)2 Vitamin D3, Ca and Pi levels in diabetic postmenopausal patients group compared to the healthy group. However, a non-significant change was observed in serum PTH level between these groups.

Conclusion

The type 2 diabetic postmenopausal women in present study were observed to have decreased level of serum calcium and phosphorus as compared to the postmenopausal women without type 2 diabetes and also concluded that bone disease is frequently overlooked as a complication of diabetes and osteoporosis (OP) is a common bone illness that affects post-menopausal women and is characterized by reduced bone mineral density (BMD) and deteriorated bone tissues, making the bones fragile. The findings of present study aids in early diagnosis and better management of bone loss and further reducing the complications related to osteoporosis.

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