ISSN: 1607-8322, e-ISSN: 2220-5799 **Anaesthesia, Pain & Intensive Care**
Vol 27(6); December 2023 DOI: 10.35975/apic.v27i6.2349

SHORT COMMUNICATION **PERIOPERATIVE MEDICINE**

Dual role of sclerostin and other parameters in postmenopausal women with osteoporosis

Narjis Hasan Ahmed[1], Haider Salih Jaffat[2], Mohauman Mohammed Alrufaie[3]

Authors affiliations:

1. Narjis Hasan Ahmed, Department of Biology, Faculty of Science, University of Kufa, Najaf, Iraq; E-mail: jww7gdef7@gmail.com
2. Haider Salih Jaffat, Department of Biology , Faculty of Science, University of Kufa, Najaf, Iraq; E-mail: hayder.alshafie@uokufa.edu
3. Mohauman Mohammed Alrufaie, Department of Chemistry, Faculty of Science, University of Kufa, Najaf 54001, Iraq; E-mail: muhaimin.alrufaie@uokufa.edu.iq

Correspondence: Mohauman Mohammed Alrufaie, **E-mail:** muhaimin.alrufaie@uokufa.edu.iq; **Phone:** 07809086646

ABSTRACT

Background & objective: Osteoporosis is a chronic progressive disease, characterized by decreased bone mass and damage to the microstructure of bone tissue, leading to decreased bone strength and increased risk of fractures. The main serious consequence of osteoporosis is fragility fracture. This case-control study was conducted to know the prevalence of osteoporosis in Iraqi postmenopausal women.

Methodology: One hundred female patients visiting Al-Sader Teaching Hospital in Al-Najaf province of Iraq, were included in the study. To determine the percentage of their bone density we used a dual energy x-ray absorptiometry (DEXA). Blood samples were taken after diagnosing the disease. In addition, serum estrogen and vitamin D3 were measured by enzyme linked immune sorbent assay (ELISA), while alkaline phosphatase was measured by spectrophotometer. Data were gathered by direct interviews with the women. The study excluded those who had chronic diseases.

Results: This study showed a significant increase ($P < 0.05$) in the concentration of sclerostin and alkaline phosphatase and non-significant differences in vitamin D3 concentrations between patients and healthy group.

Conclusion: Increased serum sclerostin and alkaline phosphatase levels in postmenopausal women with osteoporosis play an important role in the development of primary osteoporosis.

Key word: Osteoporosis; Sclerostin; DEXA

Citation: Ahmed NH, Jaffat HS, Alrufaie MM. Dual role of sclerostin and other parameters in postmenopausal women with osteoporosis. Anaesth. pain intensive care 2023;27(6):745−749; **DOI:** 10.35975/apic.v27i6.2349

Received: August 22, 2023; **Revised:** August 29, 2023; **Accepted:** September 11, 2023

1. INTRODUCTION

Osteoporosis is a serious public health concern that affects people all over the globe. The rise in osteoclast activity, which outweighs the increase in osteoblast activity, results in a decline in bone mass density in people over 30 y.[1] Women lose bone more rapidly, particularly during the first 5-10 y after menopause due to estrogen deficiency. Estrogen is a major sex-stimulating hormone in women, mostly produced in the ovaries; during menopause, estrogen levels rapidly decline.[2] Osteoporosis traditionally is classified as a primary disease, which is common in postmenopausal women due to decline in estrogen levels, and secondary type, which is caused by exogenous drugs or systemic disease affecting bone metabolism.[3] Bone mineral density (BMD) is used to express the amount of mineral matter per square centimeter in different bone segments, usually forearm, lumber spine and femur.[4] The most commonly used method of measuring BMD is dual energy x-ray absorptiometry (DEXA). Sclerostin is a glycoprotein encoded by the Sclerostin (SOST) gene, is mainly produced by mature osteocytes and is a critical regulator of bone formation through its inhibitory effect on Wnt signaling.[5] Wnt signaling is a main regulator of

skeletal development and homeostasis, so sclerostin negatively regulates osteogenic differentiation and bone formation, and promotes osteoclastogenesis and bone resorption.[6] Physiologically, alkaline phosphatase (ALP) in bones adheres to osteoblastic cell membrane with only small amount released in serum. Its concentration in serum rises only in cases of increased remodeling of bone while vitamin D is a steroid hormone classically involved in the calcium metabolism and bone homeostasis.[7,8] Clinically, it has been recognized that vitamin D deficiency leads to osteomalacia or osteoporosis in adults.[9]

2. METHODOLOGY

This study was conducted in Al-Sader Teaching Hospital in AL-Najaf province from DEXA unit in the Radiology Department and Fractures and Joints Department. Serum specimens were collected from 70 postmenopausal female patients with osteopenia and osteoporosis in addition to 30 healthy women (n=30) as a control group. The age of studied postmenopausal women patients was 50-65 y.

2.1. Collection of blood sample

Five milliliters of blood were taken from a vein using aseptic technique. Sample was placed in a labelled gel tube to enable blood to clot at room temperature for 10 min. The samples were centrifuged @6000 rpm for 15 min, and then serum was separated and frozen at −80 ºC until time to perform the laboratory analysis for study.

2.2. Dual Energy X-ray Absorptiometry (DEXA)

The measurement of bone density (defined as the amount of bone mineral divided by the area of the bone).[10] BMD is reported using 2 scores based on SD measurements: - the Z score and the T score.

- Osteoporosis: T-score −1 to −2.5; Severe osteoporosis: T-score ≤ −2.5 plus the presence of at least one fracture.
- Osteopenia: Is a BMD T-score between −1 and −2.5
- Normal bone density: Is a BMD less than −1

2.3. Statistical analysis

The statistical system SPSS v.24 was used, and the analysis of variance by using T-test for the comparison between the groups was done. P < 0.05 was considered statistically significant.

3. RESULTS AND DISCUSSION

The results reveal statistically significant differences of postmenopausal women with osteoporosis and osteopenia compared with the Control group. There was significantly decreased (P < 0.001) BMD and t-scores in patients compared with the Control group in postmenopausal women, while the age showed a significant difference when compared between patients and control group in postmenopausal women (P = 0.009). The result of the same Table indicates that there was no significant difference (P = 0.06) in BMI between control and patient groups.

Table 1: Comparisons of age, BMI, BMD and T-score between two groups

Parameter	Patients Group (n = 70)	Control Group (n = 30)	p-value
Age (y)	60.7 ± 7.60	54.2 ± 7.25	**0.009**
BMI (kg/m^2)	28.01± 4.33	30.38± 3.82	0.06
BMD (g/cm^2)	0.73 ± 0.09	0.97 ± 0.08	**< 0.001**
T-score	-2.44 ± 0.72	0.05± 0.82	**< 0.001**

Data presented as mean ± SD; P ≤ 0.05 considered significant; BMI: body mass index; BMD: bone mineral density

3.1. Comparison of biomarkers

There was a significant increase (P < 0.001) in serum levels of SOST, ALP between osteopenia / osteoporosis patients compared with control postmenopausal women, while, there was a significant decrease in serum estrogen (P < 0.001) (Table 2).

There was no significant difference (P = 0.18) in vitamin D3 between patients group compared with the control group (Table 2).

Table 2: Comparison of biomarkers in patient with osteoporosis, and control group in postmenopausal women

Biomarkers	Patients Group (n = 70)	Control Group (n = 30)	p-value
Sclerostin (pg/ml)	2870 ± 160	2500 ± 83.84	< 0.001
Estrogen (pg/ml)	14.3 ± 3.53	22.3 ± 1.78	< 0.001
ALP (U/l)	177.5 ± 50.08	110.13 ± 13.42	< 0.001
Vit-D3 (ng/ml)	23.08 ± 4.77	26.77 ± 9.74	0.18

Data presented as mean ± SD; P ≤ 0.05 is significant; ALP- Alkaline phosphatase.

3.2. Sclerostin

The levels of sclerostin (SOST) influenced by a variety of factors, including the environment, age, sex, body mass index, and total body fat contents. Increased sclerostin production in osteocytes, followed by a decrease in Wnt-catenin signaling in bone cells, is associated with declining bone mass with aging.[10] Sclerostin negatively regulates canonical Wnt signaling pathways by binding to low-density lipoprotein receptor-related protein (LRP) 5/6 so that it is crucial to both bone development and regulation of bone mass.[11,12] Recent studies have reported that serum estradiol levels are inversely associated with serum levels of the key inhibitor of Wnt signaling produced by osteocytes, sclerostin, and estrogen treatment of postmenopausal women reduces circulating sclerostin levels.[13] As estrogen levels decline at menopause the result of this study indicated, that there was a significant positive correlation(r = 0.540 & P = 0.002) between age and SOST concentrations in postmenopausal women. Studies showed that vitamin D is one of the most important vitamins for bone metabolism and mineralization, according to the same study vitamin D deficiency has been related to osteoporosis, poor bone mineral density, and muscle problems.[14]

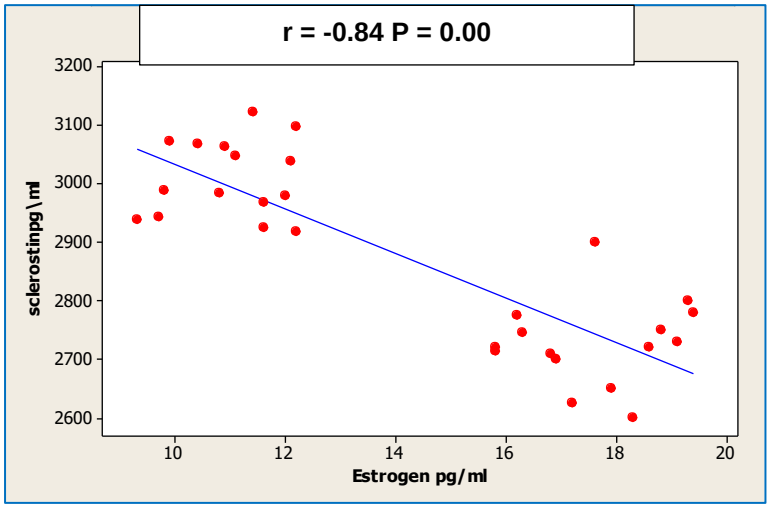

Figure 1: Correlation between serum SOST and serum estrogen levels in (osteopenia-osteoporosis) postmenopausal women.

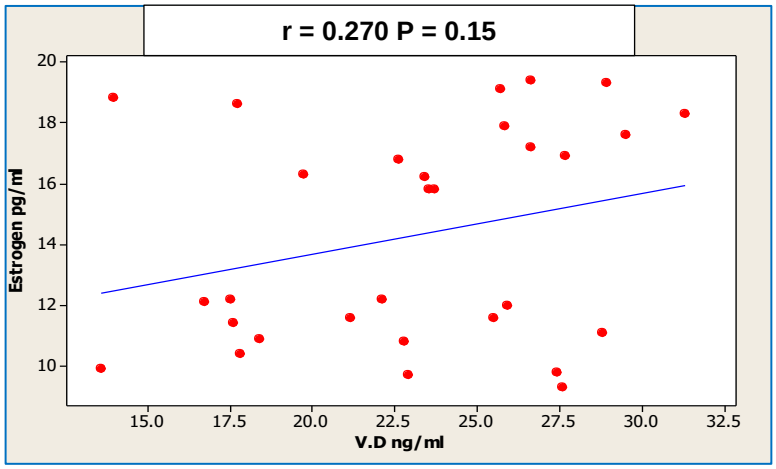

Figure 2: Correlation between serum estrogen and vit D3 levels in (osteopenia-osteoporosis) postmenopausal women

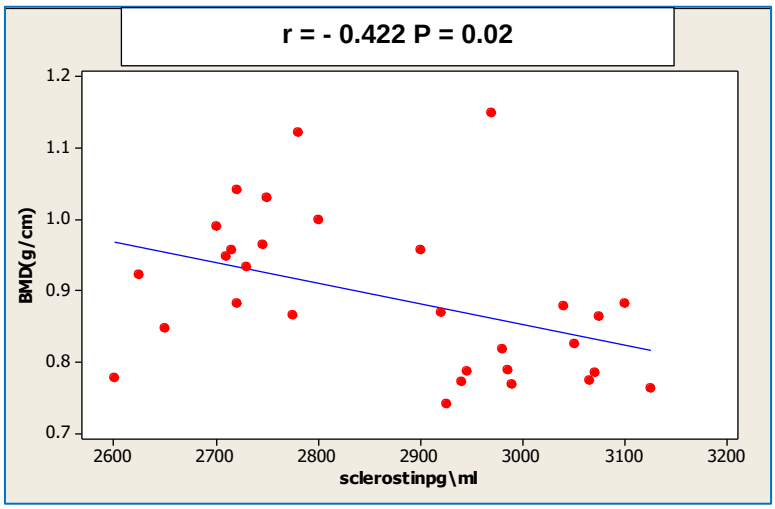

Figure 3: Correlation between BMD and SOST in (osteopenia-osteoporosis) postmenopausal women.

3.3. Correlation Study

Results of the association indicate:

1. Figure 1 indicates, there was a significant negative correlation (r = -0.841) between SOST and estrogen concentrations in postmenopausal women.

2. Figure 2 indicates that there was a significant positive correlation (r = 0.270) between estrogen and vitamin D3 concentrations in postmenopausal women.

3. Figure 3 indicates that there was a significant negative correlation (r = -0.422) between BMD and SOST concentrations in postmenopausal women.

4. 4. Figure 4 indicates that there was a significant positive correlation (r = 0.593) between BMD and estrogen concentrations in postmenopausal women.

Figure 5 indicates that there was a significant positive correlation (r = 0.540) between age and SOST concentrations in postmenopausal women.

4. CONCLUSION

Both osteoporosis and osteopenia are considered dangerous indicators, as they lead to fractures and other complications which may even lead to death. In addition to DEXA scan method, osteoporosis can be clinically confirmed by several methods including measurement of some parameters such as sclerostin, estrogen, ALP, vitamin D3.

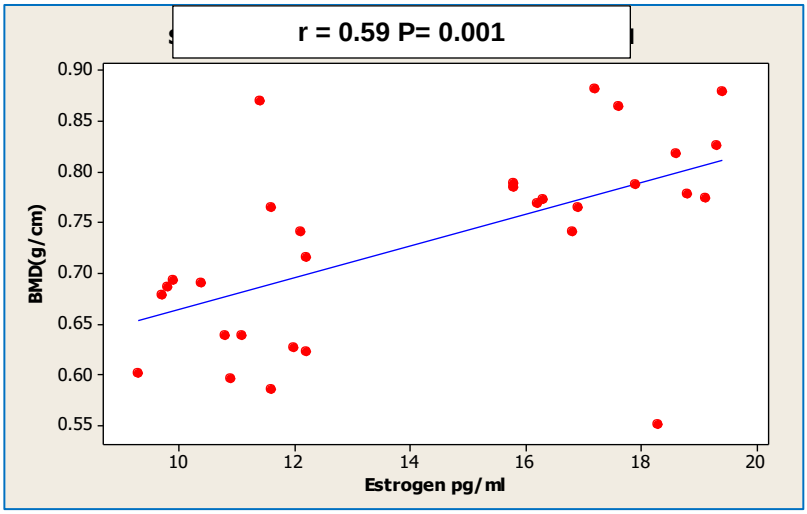

Figure 4: Correlation between BMD and estrogen in (osteopenia-osteoporosis) postmenopausal women

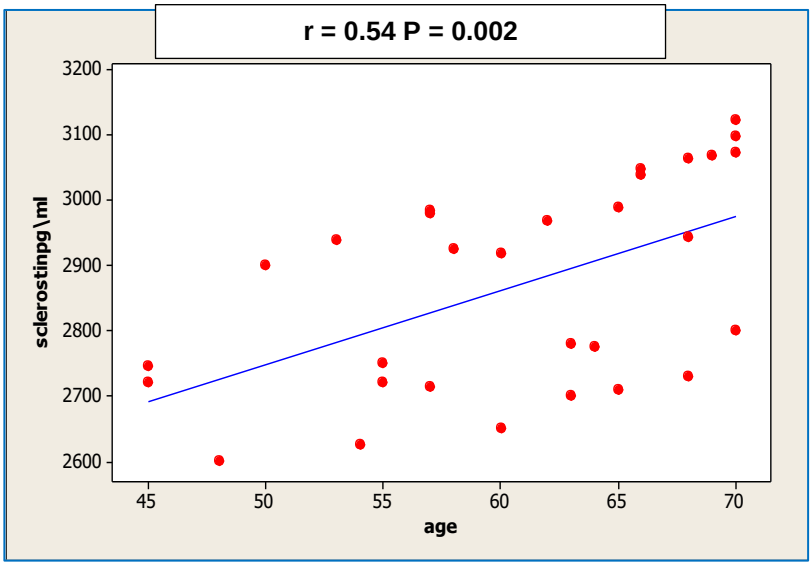

Figure 5: Correlation between SOST and age in (osteopenia-osteoporosis) postmenopausal women.

5. Data availability

The numerical data generated during this research is available with the authors.

6. Acknowledgement

We gratefully thank staff and Faculty of Medicine, DEXA unit in the Radiology Department and Fractures and Joints Department, Al-Sader Teaching Hospital in AL-Najaf province for their valuable help, as well as the patients who consented to participate in this study.

7. Conflict of interest

The study utilized the hospital resources only, and no external or industry funding was involved.

8. Authors' contribution

NHA: Writing the manuscript

HSJ: Conduct of the study work and manuscript editing

MMMA: Final evaluation and sending the manuscript

9. REFERENCE

1. Mathew A, Lukachan GA, Varughese D, Raju N, Mathai AS, Johnson AS. Impact of frailty and comorbidity index on postoperative complications and functional outcomes among elderly patients undergoing hip fracture surgeries under regional anesthesia techniques. Anaesth. pain intensive care 2023;27(2):161−169. DOI: 10.35975/apic.v27i2.2132
2. Störk S, van der Schouw YT, Grobbee DE, Bots ML. Estrogen, inflammation and cardiovascular risk in women: a critical appraisal. Trends Endocrinol Metab. 2004 Mar;15(2):66-72. [PubMed] DOI: 10.1016/j.tem.2004.01.005
3. Amin S, Rahman H, Ismail S, Abidin E. An overview of osteoporosis and heath promotional strategies for community-based osteoporosis prevention in Malaysia. Int J Public Health Clin Sci. 2017;4(1):28-40. [FreeFullText]
4. Vezzoli G, Soldati L, Mora S. Calcium-sensing receptor polymorphisms and human disease. In: Molecular, Genetic, and Nutritional Aspects of Major and Trace Minerals. Academic Press; 2017. p. 3-13. DOI: 10.1016/B978-0-12-802168-2.00001-4
5. Omran A, Atanasova D, Landgren F, Magnusson P. Sclerostin: From Molecule to Clinical Biomarker. Int J Mol Sci. 2022 Apr 26;23(9):4751. [PubMed] DOI: 10.3390/ijms23094751
6. Marini F, Giusti F, Palmini G, Brandi ML. Role of Wnt signaling and sclerostin in bone and as therapeutic targets in skeletal disorders. Osteoporos Int. 2023 Feb;34(2):213-238. [PubMed] DOI: 10.1007/s00198-022-06523-7

7. Jean G, Souberbielle JC, Zaoui E, Lorriaux C, Mayor B, Hurot JM, et al. Total and bone-specific alkaline phosphatases in haemodialysis patients with chronic liver disease. Clin Biochem. 2012 Apr;45(6):436-9. [PubMed] DOI: 10.1016/j.clinbiochem.2012.01.018

8. Saponaro F, Saba A, Zucchi R. An Update on Vitamin D Metabolism. Int J Mol Sci. 2020 Sep 8;21(18):6573. [PubMed] DOI: 10.3390/ijms21186573

9. Ives R, Brickley M. New findings in the identification of adult vitamin D deficiency osteomalacia: Results from a large-scale study. Int J Paleopathol. 2014 Dec;7:45-56. [PubMed] DOI: 10.1016/j.ijpp.2014.06.004

10. Mödder UI, Hoey KA, Amin S, McCready LK, Achenbach SJ, Riggs BL, et al. Relation of age, gender, and bone mass to circulating sclerostin levels in women and men. J Bone Miner Res. 2011 Feb;26(2):373-9. [PubMed] DOI: 10.1002/jbmr.217

11. Burgers TA, Williams BO. Regulation of Wnt/β-catenin signaling within and from osteocytes. Bone. 2013 Jun;54(2):244-9. [PubMed] DOI: 10.1016/j.bone.2013.02.022

12. Tanaka S, Matsumoto T. Sclerostin: from bench to bedside. J Bone Miner Metab. 2021 May;39(3):332-340. [PubMed] DOI: 10.1007/s00774-020-01176-0

13. Mirza FS, Padhi ID, Raisz LG, Lorenzo JA. Serum sclerostin levels negatively correlate with parathyroid hormone levels and free estrogen index in postmenopausal women. J Clin Endocrinol Metab. 2010 Apr;95(4):1991-7. [PubMed] DOI: 10.1210/jc.2009-2283

14. Hadi SM, Ouda MH, Alboaklah HKM. Association of vitamin D3 deficiency and osteoporosis. Review. Kerbala J Pharm Sci. 2022;1(20). [FreeFullText]

