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Study the Relationship of Dynamic Thiol/Disulphide Homeostasis and Bone Turnover Markers in Postmenopausal Osteoporosis

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Abstract

Osteoporosis is a skeletal disease differentiated by low bone density measured by dual-energy X-ray absorptiometry (DEXA). This study aimed to investigate the relationship between the levels of dynamic thiol and the procollagen type I N-terminal propeptide (PINP) in postmenopausal osteoporosis patients. The current study included a total number of 75 voluntaries (Individuals) divided into two groups: the first was the control group of apparently healthy individuals. This group consisted of 22 samples whose ages ranged between (46-65 years). The second group was the group of patients of postmenopausal women with osteoporosis, which consisted of 53 samples whose ages also ranged between (46-65 years),

The results of PINP, T-score, and Dynamic thiol showed significant variance between the studded groups ($P<0.05$). Serum levels of PINP showed a notable rise in osteoporosis patients compared to healthy individuals ($P<0.01$). Moreover, the serum level of Dynamic thiol showed a notable increase in the patient group when compared to the control group ($p<0.05$). Conclusion: according to the presented result PINP recommended indicator for bone turnover markers and a Dynamic thiol risk factors for fractures. Thiol /disulphide homeostasis shifted to the disulphide side.

Keywords: Dynamic thiol/disulphide, Procollagen type I N-terminal propeptide (PINP), homeostasis, bone turnover, postmenopausal osteoporosis.

Introduction

Bones have a role as scaffold and protection for muscles and organs; it is a tissue with a high level of constant remodeling. In adults, bone degradation is effect by osteoclasts and bone formation by osteoblasts (1). Bone homeostasis and remodeling need a balance between these two processes. Osteoblasts produce from mesenchymal stem cells; they build osteoid by synthesis special collagen and proteins like osteocalcin and osteopontin. Osteoclasts are huge, multinucleated cells that differentiate from the hematopoietic precursor of myeloid lineage, their function removing old or damaged bone matrix and resorbing bone (2). Osteoporosis is a skeletal disease differentiated by decreasing bone density leading to weaken bone strength and increase risk of fractures (3), Bone mineral density (BMD) as measured by Dual-energy X-ray Absorptiometry (DEXA). scan is strongly associated with fracture risk. A DXA-measured BMD T-score ≤ -2.5 is the WHO diagnostic criterion of osteoporosis (4,5). (4). It supplies information on variation in bone mineral contents and is beneficial for the follow up of bone mass and study of bone mass variation in the same patient (5), postmenopausal osteoporosis type considers primary osteoporosis where this disease is associated with estrogen reduction, which increases the bone loss with aging (6). Bone formation biomarkers, bone resorption biomarkers, and bone turnover regulators are all created by the bone remodeling process. (7) PINP starts off as a trimer of propeptides from type 1 collagen's three protein chains, but it's eventually transformed to monomeric forms in circulation. Levels of type 1 collagen osteoblasts (8). The fast drop in estrogen production during the first years after menopause causes accelerated bone remodeling, with enhanced bone creation (osteoblast activity) and resorption (osteoclast activity) (9). However, these mechanisms are no longer in balance, and bone resorption now outnumbers bone production, resulting in net bone loss and osteoporosis. (10) Oxidative stress (OS) is generated as a result of insufficient activity of the endogenous antioxidant defense system against reactive oxygen species (ROS). On the one hand, excessive ROS are able to exert oxidative damage to lipids, protein, and DNA (11). One of the important components of the basic defensive system in human body against the harmful effects of oxidative stress is the thiol-disulfide homeostasis and as a result of disturbances of this balance the increase level of S-S compound may lead to disorders in many human body's systems (12). The current study focusses to identify the correlation between PINP and Dynamic thiol for early diagnosis as novel biomarkers for the postmenopausal osteoporosis patients.

Subjects and methods

Study design:

The present study is a case-control one that conducted at the Biochemistry lab, after collecting samples from outpatient clinics in Baghdad Teaching Hospital - Medical City,

Patients' samples

The study Included adult women aged between 46 and 65 years who has been diagnosed with osteoporosis using DEXA (Dual-energy X-ray absorptiometry) in the period from (Jan. 2021 to Mar. 2021. The researcher included 22 control subjects as normal control cases and 54 patients diagnosed with osteoporosis.

Exclusion criteria were as: patients suffering from diabetes, hypothyroidism or hyperthyroidism, rheumatoid arthritis, and patients who treated with steroid drugs.

Ethical approval

This study obtained ethical approval from the College of Science for Women/ University of Baghdad in addition to securing informed consent from all participating patients.

Data Collection

Samples collection included withdraw ten milliliters from venous blood and put in a tube without anticoagulants at room temperature and then centrifugation it at 3000 cycles/ min, for less than 15 minutes. Serum was separated and transferred into an Eppendorf tube to collect it and stored in the freezing -20c° until assayed. PINP was estimated using enzyme-linked immune sorbent assay (ELIZA) technique, which works by coupling antibody or antigen to assay enzyme.

Dynamic thiol calculated their concentration by measured absorbance using a spectrophotometer. Dynamic disulfide bond (-S-S-) are reduced to function thiol group (-SH) by sodium borohydride (NaBH4), according to the (Erel and Neselioglu 2014), T score percentage calculated by DEXA which is described as bone mineral density and the body mass index is measured according to the specific equation: BMI= weight/ (height)2 (16).

Statistical analysis

Statistical analysis program (SPSS 25) has been performed for analysis the results. The general descriptive statistic was used to describe the main findings; Independent samples T-test has been used to identify the significant differences, Mann Whitney test has been used, ROC curve has been used too.

Results

The demographic characteristic of osteoporosis postmenopausal women and healthy (control) are summarized in Table (1).

Table (2) shows the mean ± SD of BMI [(32.13±0.74) (36.48±0.91)] for patient and control respectively. The result of BMI indicates significant difference (P<0.05) between patient and control. BMI is significantly decreased in patients as compared to control.

The mean ± of T-score (2.84±0.36)(0.58±0.09), for patient and control respectively. The T-score results indicated a significant difference (P < 0.001) between the patient group and the control group. Patients exhibited a significantly higher T-score (P < 0.001) compared to controls.

Additionally, the mean ± SD of PINP was reported as 182.4 ± 0.034 for patients and 127.4 ± 0.047 for controls. The PINP results showed a significant difference (P < 0.01) between the patient and control groups, with patients exhibiting a significantly higher PINP (P < 0.01) compared to controls.

Furthermore, Dynamic thiol level in osteoporosis patients was found to be (25.8), and in control was (38.5), Dynamic thiol appeared a significant difference between two groups (P<0.05), dynamic thiol level is significantly decreased in patients as compared to control.

The receiver operating characteristics curve (ROC)

ROC is a statistical study that uses a plot of the relationship between sensitivity and specificity to determine the optimum specificity and sensitivity for a diagnostic test. PINP test showed a cutoff value 120.2 as shown in table (3).

Table 1: Demographic elements for the donors

characteristics	Patients	Control
Number	54	22
Age	46-65	46-65

Table 2: Statistical distribution of some parameters level in serum of osteoporosis patients and control.

Parameters	Group	Mean ± SD	P-value
BMI (mean ± SD)	Osteoporosis	32.13±0.76	0.01
	Control	36.48±0.91	
T-score	Osteoporosis	2.84±0.36	0.001
	Control	0.58±0.09	
PINP	Osteoporosis	182.4±0.034	0.01
	Control	127.4±0.047	
Dynamic thiol (**Mean Rank)**	Osteoporosis	25.8	0.05
	Control	38.5	

*T-test independent was performed, Significant levels of both less than 0.01 and less than 0.05 are reported.

Table 3: Description of ROC result for PINP.

Parameters	SE	Area	Cut off value	Sensitivity	1-Specificity
PINP	0.064	0.689	120.2	0.778	0.499

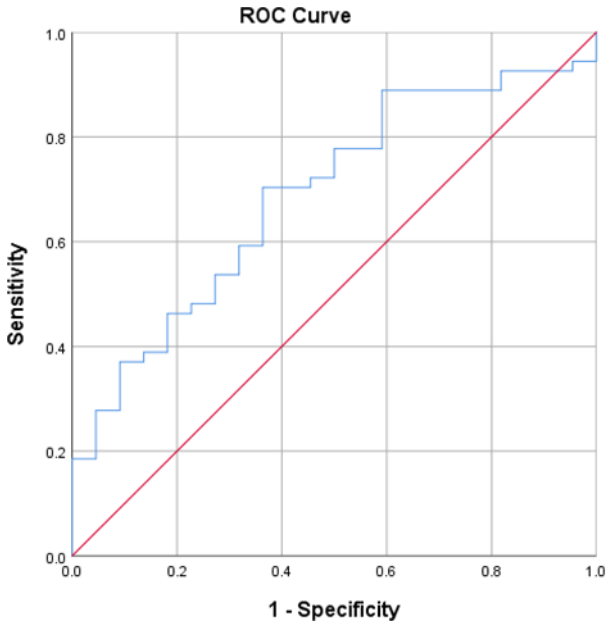

Figure 1: ROC curve of PINP

Discussion

Bone is a dynamic tissue that is crucial for maintaining the structural integrity of the human body. While it offers sufficient strength to guard against fractures, bone must also be lightweight to facilitate movement and agility. The strength is derived from the mineralization of the matrix through a combination of minerals. The mineralized component of bone is regulated and sustained by a process known as bone remodeling, during which osteoclasts resorb sections of old bone, and osteoblasts subsequently fill these resorption cavities with new bone through the deposition of collagen and minerals (17,18).

The current results indicate a significant difference ($P<0.05$) between the BMI of patients and control. Even thought that BMI showed significant deference the Obesity has not been established as a specific cause of osteoporosis but owing to its wide range of effects on several human body systems (19). It is reasonable to assume that obesity may be a cause of osteoporosis and bone fractures (20). Further study conducted by Azin et al. demonstrated that both BMI and femoral neck Bone Mineral Density BMD were increased, which was associated with a decreased risk of hip and other serious osteoporotic fractures in postmenopausal women (21). In addition, Felson et al. demonstrated the protective influence of higher body weight on BMD levels across various sites, especially in weight-bearing bones. T-score is the best a defining characteristic among patients' osteoporosis and control, this test was frequently used to diagnose osteoporosis by evaluating the central and axial

skeleton bone mineral density (BMD) to determine the T-score (22). Clinical guidelines for the prevention and treatment of osteoporosis:summary statements and recommendations from the Italian Society for Orthopaedics and Traumatology (23).

Additionally, the current findings show there is a significantly difference (P<0.05) between level of procollagen type I N-terminal propeptide (PINP) among the studying groups, that mean this parameter have a significant role in osteoporosis by consider PINP recommended indicator for bone turnover marker and a risk factor for fractures (24). The study of PINP as a biological response marker during teriparatide treatment for osteoporosis was carried out by J H Krege et al. Serum PINP concentrations reflect the integrated amount of skeletal new bone formation. Thus, diseases involving high bone turnover would be expected to be associated with high serum concentrations of PINP, and this was in agreement with our study (25,26).

Furthermore, the current findings indicate a significant difference between the Dynamic thiol level among both groups (P<0.05). Dynamic thiol level is significantly decreased in patients as compared to control. Dynamic thiol plays a role biochemical marker in the antioxidative pathway that counters oxidative stress. The thiol, which serves as a vital role in the antioxidant mechanism, interacts with disulphide, resulting in the reduction of thiol groups and achieving thiol/disulphide homeostasis (27). Petkats G, et al. Study Dynamic thiol/disulfide homeostasis in serum of patients with generalized vitiligo. They discovered a a substantial difference between patients and controls in the dynamic thiol/disulfide Patients with vitiligo have a lower level of thiol/disulfide homeostasis compared to healthy controls. and this was in agreement with our study (28).

It is possible that dynamic thiol/disulphide homeostasis influence the pathological and progression process of osteoporosis (29).

Conclusion:

The study's findings indicate that the serum concentration of PINP varied between patients and controls; this variation may serve as a diagnostic tool for bone turnover markers in postmenopausal osteoporosis. Dynamic thiol levels have an impact in process of osteoporosis.

Conflict of Interest: Non

Funding: Nil

References:

1. Bolamperti S, Villa I, Rubinacci A. Bone remodeling: an operational process ensuring survival and bone mechanical competence. *Bone Research*. 2022 Jul 18;10(1):48.
2. Šromová V, Sobola D, Kaspar P. A brief review of bone cell function and importance. *Cells*. 2023 Nov 5;12(21):2576.
3. Castellani C, De Martino E, Scapato P. Osteoporosis: Focus on Bone Remodeling and Disease Types. *BioChem.* 2025 Sep 11;5(3):31.
4. Gani LU, Sritara C, Blank RD, Chen W, Gilmour J, Dhaliwal R, Gill R. Follow-up bone mineral density testing: 2023 official positions of the International Society for Clinical Densitometry. *Journal of Clinical Densitometry*. 2024 Jan 1;27(1):101440.
5. Jain RK, Vokes T. Dual-energy X-ray absorptiometry. *Journal of Clinical Densitometry.* 2017 Jul 1;20(3):291-303.

6. Haseltine KN, Chukir T, Smith PJ, Jacob JT, Bilezikian JP, Farooki A. Bone mineral density: clinical relevance and quantitative assessment. *Journal of Nuclear Medicine*. 2021 Apr 1;62(4):446-54.

7. Voltan G, Di Giovannantonio G, Carretta G, Vianello S, Contessa C, Veronese N, Brandi ML. A novel case-finding strategy based on artificial intelligence for the systematic identification and management of individuals with osteoporosis or at varying risk of fragility fracture. *Archives of Osteoporosis*. 2024 May 31;19(1):45.

8. Kuo TR, Chen CH. Bone biomarker for the clinical assessment of osteoporosis: recent developments and future perspectives. *Biomarker research*. 2017 May 18;5(1):18.

9. Patel N, Ganti L. The treatment and monitoring of osteoporosis using bone turnover markers. *Orthopedic Reviews*. 2025 Jan 6;17:127772.

10. Greenblatt MB, Tsai JN, Wein MN. Bone turnover markers in the diagnosis and monitoring of metabolic bone disease. *Clinical chemistry*. 2017 Feb 1;63(2):464-74.

11. Ahmed DT, Hussein EA. The menopausal age and associated factors in a sample of Iraqi postmenopausal women. International *Journal for Sciences and Technology*. 2015 Jun;143(2492):1-6.

12. Mishra S, Nyomba BG. Estrogen deficiency plus type 1 diabetes: a double-dip for bone loss. *Endocrinology.* 2017 Jul 1;158(7):2066-7.

13. Zhou Q, Zhu L, Zhang D, Li N, Li Q, Dai P, Mao Y, Li X, Ma J, Huang S. Oxidative stress-related biomarkers in postmenopausal osteoporosis: a systematic review and meta-analyses. *Disease markers*. 2016;2016(1):7067984.

14. Korkmaz V, Kurdoglu ZE, Alisik M, Turgut E, Sezgın OO, Korkmaz HI, Ergun Y, Erel O. Thiol/disulfide homeostasis in postmenopausal osteoporosis. *Journal of endocrinological investigation*. 2017 Apr;40(4):431-5.

15. Kurhan F, Alp HH, Işık M, Atan YS. The evaluation of thiol/disulfide homeostasis and oxidative DNA damage in patients with obsessive compulsive disorder. *Clinical Psychopharmacology and Neuroscience*. 2022 May 31;20(2):240.

16. Peterson CM, Thomas DM, Blackburn GL, Heymsfield SB. Universal equation for estimating ideal body weight and body weight at any BMI. *The American journal of clinical nutrition*. 2016 May 1;103(5):1197-203.

17. Georgescu B, Cristea AE, Oprea D, Lupu AA, Stanciu LE, Borgazi E, Caraban BM, Ciortea VM, Irsay L, Iliescu MG. Current evidence on and clinical implications of vitamin D levels in pain and functional management of knee osteoarthritis: a systematic review. *Clinics and Practice*. 2024 Sep 26;14(5):1997-2012.

18. de Villiers TJ. Bone health and menopause: osteoporosis prevention and treatment. *Best Practice & Research Clinical Endocrinology & Metabolism*. 2024 Jan 1;38(1):101782.

19. Gkastaris K, Goulis DG, Potoupnis M, Anastasilakis AD, Kapetanos G. Obesity, osteoporosis and bone metabolism. *Journal of musculoskeletal & neuronal interactions*. 2020;20(3):372.

20. Piñar-Gutierrez A, García-Fontana C, García-Fontana B, Muñoz-Torres M. Obesity and bone health: a complex relationship. *International journal of molecular sciences*. 2022 Jul 27;23(15):8303.

21. Shayganfar A, Farrokhi M, Shayganfar S, Ebrahimian S. Associations between bone mineral density, trabecular bone score, and body mass index in postmenopausal females. *Osteoporosis and sarcopenia*. 2020 Sep 1;6(3):111-4.

22. Chiu CT, Lee JI, Lu CC, Huang SP, Chen SC, Geng JH. The association between body mass index and osteoporosis in a Taiwanese population: a cross-sectional and longitudinal study. *Scientific Reports*. 2024 Apr 12;14(1):8509.

23. Tarantino U, Iolascon G, Cianferotti L, Masi L, Marcucci G, Giusti F, Marini F, Parri S, Feola M, Rao C, Piccirilli E. Clinical guidelines for the prevention and treatment of osteoporosis: summary statements and recommendations from the Italian Society for Orthopaedics and Traumatology. *Journal of Orthopaedics and Traumatology*. 2017 Nov;18(Suppl 1):3-6.

24. Gillett MJ, Vasikaran SD, Inderjeeth CA. The role of PINP in diagnosis and management of metabolic bone disease. *The Clinical Biochemist Reviews*. 2021 Feb;42(1):3.

25. Hussein E. Menopausal symptoms and related factors among women in Baghdad City. *Int J Adv Res*. 2016;4(9):1670. doi:10.21474/ijar01/1670

26. M, Gao C, Luan X, Fan C, Hao M, Jin C, Zhao J, Li H, Zhao J, Luan J, Lin Y. Analyzing the factors associated with efficacy among teriparatide treatment in postmenopausal women with osteoporosis. *BMC Musculoskeletal Disorders*. 2024 Feb 3;25(1):109.

27. Owegie OC, Kennedy QP, Davizon-Castillo P, Yang M. Thiol Isomerases: Enzymatic Mechanisms, Models of Oxidation, and Antagonism by Galloylated Polyphenols. *Antioxidants*. 2025 Sep 30;14(10):1193.

28. Fidan F, Alkan BM, Uğurlu FG, Bozkurt S, Sezer N, Bicer C, Erel Ö, Ardiçoğlu Ö, Akkuş S. Dynamic thiol/disulphide homeostasis in patients with fibromyalgia. *Archives of rheumatology*. 2017 Jan 18;32(2):112.

29. Mert SA, Dilbaz B, Kinay T, Dilbaz S, Kayikcioglu F, Neselioglu S, Erel O, Ustun YE. Evaluation of Oxidative Stress with" Dynamic Thiol/Disulfide Homeostasis" in Cases with Endometrioma. *Medical Science and Discovery*. 2022 Aug 24;9(8):458-64.