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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-

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

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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.



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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 effected 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 -20°C 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 (NaBH_4), 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: $\text{BMI} = \text{weight} / (\text{height})^2$ (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 $\pm$ SD of BMI $[(32.13 \pm 0.74) (36.48 \pm 0.91)]$ 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 $\pm$ of T-score $(2.84 \pm 0.36) (0.58 \pm 0.09)$, 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 $\pm$ 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 $\pm$ SD	P-value
BMI (mean $\pm$ SD)	Osteoporosis	32.13 $\pm$ 0.76	0.01
	Control	36.48 $\pm$ 0.91	
T-score	Osteoporosis	2.84 $\pm$ 0.36	0.001
	Control	0.58 $\pm$ 0.09	
PINP	Osteoporosis	182.4 $\pm$ 0.034	0.01
	Control	127.4 $\pm$ 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



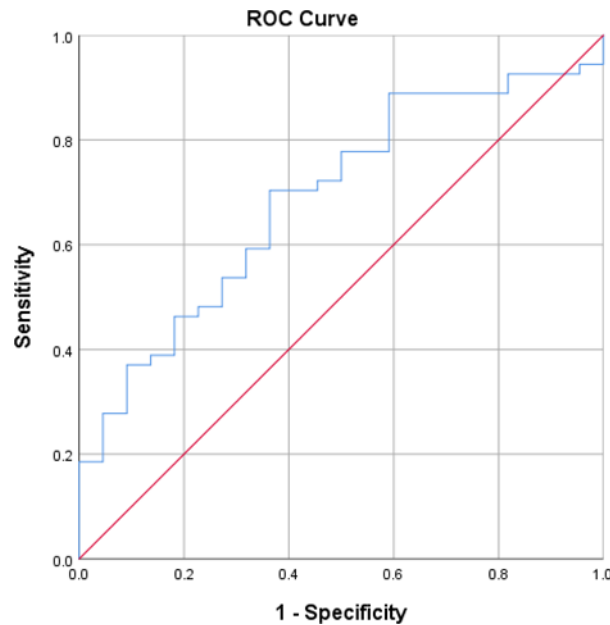


Figure 1: ROC curve of PINP

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 though BMI showed significant difference, 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 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/disulphide homeostasis in serum of patients with generalized vitiligo. They discovered a a substantial difference between patients and controls in the dynamic thiol/disulphide Patients with vitiligo have a

lower level of thiol/disulphide 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

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