Evaluation of LRRC17 and Periosten for Osteoporosis Patients

Noor Ali Nemaha[1], Dr. Hanan Jassim Hammod[2]
[1], College of Health and Medical Techniquse/Kufa/Al-Furat Al-Awsat Technical University/Iraq
[2], Babylon Technical Institute/Kufa/Al-Furat Al-Awsat Technical University/Iraq
E-male: dr.hanan.jh@gmail.com

Abstract
Osteoporosis is a metabolic bone disease that results, at the cellular level, in osteoporotic bone resorption that is irreplaceable by osteogenesis of osteoblasts. This leads to weak bones and causes osteoporosis, which leads to an increased risk of fractures. **Aim of Study:** the current study aimed to detected biomarkers in patients with osteoporosis and it association with some physiological status have been a study because increase incidence of osteoporosis, for both genders which might also help in early diagnosis of case of osteoporosis to prevent development of complication, this achieved by: Estimation of some biomarkers include Leucine-rich repeat-containing 17 and Periostin .Result , The study, higher serum periostin levels have been reported to be associated with increased fracture risk in postmenopausal women The perostin parameter in the current study was highly significant increase in osteoporosis age group (41-50 y) patients (27.81±5.86) than in control age group (41-50 y) (14.91±0.52) according to p-value (0.002) , demonstrated that postmenopausal women in the lowest plasma lrrc17 tertile had higher, The LRRC17 parameter in the current study was highly significant increase in osteoporosis age group (41-50 y) patients (712.33±60.68) than in control age group (41-50 y) (311.22±21.64) according to p-value (0.001).
Keywords: Periosten; osteoporosis patients; LRRC17

1. Introduction

Osteoporosis is the most common chronic metabolic bone disease, and it is characterized by increasing osteoporosis. It affects people of all ages, genders, and gender identities, but it is more common among elderly individuals and women. With the aging of the population and the extension of life spans, several variables that impact bones, such as aging and menopause, are becoming more prevalent. According to the International Osteoporosis Foundation, one in every three women over 50 and one in every five men over 50 may suffer a bone fracture as a result of osteoporosis at some time in their lives. Osteoporosis is growing more prevalent throughout the world (14). Osteoporosis can be primary or secondary to other diseases that lead to bone loss. Type I osteoporosis in rare cases, the process of bone formation is normal in this type of osteoporosis, which leads to more bone loss (13). Periostin is an extracellular matrix protein produced by periosteal osteoblasts and osteoblasts (8). Periostin has been found to play a role in bone strength and microstructure maintenance. It has a protein structure that includes an amino-terminal EMI domain, a tandem repeat of four Fas 1 domains, and a carboxyl-terminal domain with a heparin-binding site. Function Periostin (POSTN) regulates the recruitment and binding of bone activators from primary sources such as bone marrow and blood (12). Leucine-rich repeat-containing 17 (LRRc17) is a 37 kDa protein with secretary feature containing five putative LRR domains. Previous experimental study well characterized the role of LRRc17 in bone metabolism as an inhibitor of RANKL induced osteoclast differentiation (6).

2. Materials and Methods

1-Patients

The research was carried out at Al-Sadr Teaching Hospital's Physiotherapy Center-Osteoporosis Department from December 1 to January 9. The study included 90 participants, including 45 osteoporosis patients and 45 healthy adults who served as controls. Patients were diagnosed by specialists based on their family histories, age, height, weight, and a few unambiguous clinical criteria, which were then confirmed by the DXA (dual-energy x-ray absorptiometry) instrument and other tests. As shown in Appendix 1, various vitamin D and calcium laboratory tests

2 -Control

The controls provided blood samples that were equivalent to those of the patients in terms of sex and age, but they did not have any hereditary illnesses, infections, or chronic conditions.

3- Exclusion criteria

When the samples were taken from patients and controls, some of them were left out since they could change the results. In this study, samples with (heart failure, vitamin deficiency, warfarin intake, chemotherapy, kidney failure, surgery, removal of the small intestine, drug treatment, cephalosporin antibiotics) were included because these conditions could affect the results of protein S1P, LRRC17, GSN, and protein Perostin in the

doi.org/10.31838/hiv22.02.560 Received: 19.07.22, Revised: 31.08.22, Accepted: 13.08.22

samples.

Methods

1 -Sample Collection

Each control and osteoporosis patient had 5 mL of venous blood drawn in this investigation. Ethyl alcohol was used to sanitize the skin. The patient was being readied for a blood transfusion at this time. Blood was drawn and deposited in tubes as follows: The tube included a separating gel in which 3 ml was poured and left to clot for 10-15 minutes at room temperature before being centrifuged for 5 minutes at 5000 rpm to obtain the serum. The serum was collected for testing purposes (LRRC17 and periosten).

2 -BMI (Body Mass Index)

The BMI is a metric that uses a person's weight and height to assess how lean or obese they are. It is used to determine the weight of tissue.

3- ELISA (Enzyme Linking Immunosorbent Assay)

The amounts of the proteins LRRC17 and POST in the plasma of healthy controls and osteoporosis patients were measured using ELISA kits.

4-Human protein ELISA kit (LRRC17)

The Bioassay Technology Laboratory provided a specific kit for testing human Leucine-rich Repeat-containing protein 17 concentrations in serum

5-Human Protein Periostin ELISA Kit

The level of human protein periostin was measured using the enzyme-linked immunosorbent assay (ELISA) method, as directed by the manufacturer. Bioassay Technology Laboratory, E3226Hu, China

3. Results and Discussion

4.1 Results

This study was conducted on a total 90 person composed of two groups. The first group was the patient group, which consists of 45 patients with Osteoporosis, were collected from patients attended to " Physiotherapy Center - Osteoporosis Department in AL-Sadder medical city in Al-Najaf Governorate/ Ministry of Health/Iraq, in the period from 1st of December to the 9th of January. with an age ranging between (34-68) years old; and the second group is the control group (non-osteoporosis), which consists of 45 with no osteoporosis, also from the same place with age ranging (30-68) years old. Patients were diagnosed by specialist physicians based on family histories, age, height, weight and some clear clinical parameters and confirmed by the DXA (dual-energy x-ray absorptiometry) device.

Table (.1) General characteristics of patients and healthy groups.

Group		Patient		Healthy		*p*-value
		N	%	N	%	
Gender	Male	10	22.2	13	28.9	0.03*
	Female	35	77.8	32	71.1	
Age	20-40	7	15.6	15	33.3	0.04*
	41-60	25	55.5	15	33.3	
	<60	13	28.8	15	33.3	
BMI (kg/M^2)	Normal	12	26.7	11	22.4	0.023*
	over-weight	17	37.8	13	28.9	
	Obesity	36	35.6	21	46.7	
Smoking	No	28	62.2	24	53.3	0.039*
	Yes	17	37.7	21	46.6	
Menopause	Pre-menopause	14	31.2	21	65.6	0.001**
	Post-menopause	31	68.8	11	34.3	
Hypertension	Yes	33	73.3	26	57.7	0.043*
	No	12	26.6	19	42.2	

*Significant different at($p<0.05$)
**Significant different at($p<0.01$)

2-Biochemical Results

Table.2: Biochemical parameter in patient and control in study on osteoporosis.

Group Parameter	Patient	control	P-value
LRRC17 ng/ml	739.62±55.30	328.77±12.31	0.0001**
Periosten pg/ml	29.204±3.76	15.45±0.284	0.0001**
BMD ng/ml	0.63±0.014	1.02±0.021	0.0001**
V.D ng/ml	19.67±0.42	33.63±1.93	0.05*

**Significant different at($p<0.01$)

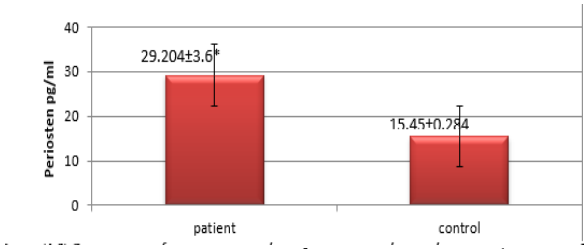

Figure (4-3) Comparisons of serum periosten between patient and control groups in osteoporosis

The Periosten parameter in the current study was highly significant increase in osteoporosis patients (739.62±55.30) than in control group (328.77±12.31) according to *p*-value (0.0001).

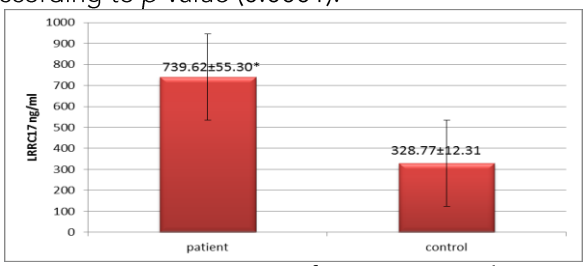

Figure (4-2) Comparisons of serum LRRC17 between patient and control groups in osteoporosis.

The LRRC17parameter in the current study was highly significant increase in osteoporosis patients (739.62±55.30) than in control group (328.77±12.31) according to p-value (0.0001

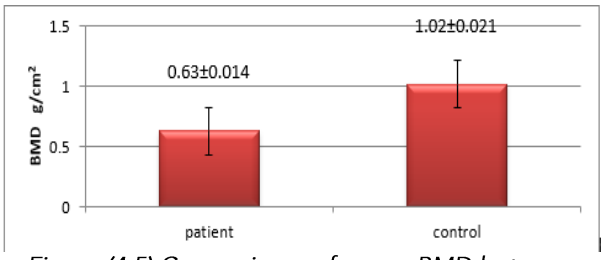

Figure (4-5) Comparisons of serum BMD between Patient and control groups in osteoporosis

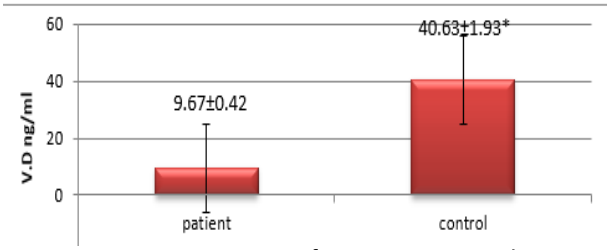

Figure (4-6) Comparisons of serum vitamin D between patient and control groups in osteoporosis

The VitD parameter in the current study was highly significant decrease in osteoporosis patients (9.67±0.42) than in control group (40.63±1.93) according to p-value (0.0001).

Table.4: Biochemical parameter in patient and control in study on osteoporosis as age groups **comparison.**

Tabl:3 Biochemical parameter in patient and control in study on osteoporosis as pre-menopause and post-menopause groups comparison.				
Parameter	group	20-40 y	41-50 y	<60 y
LRRC17 ng/ml	patient	697.92±89.19	712.33±60.68	924.82±214.74
	control	360.85±23.72	311.22±21.64	314.24±16.93
	P-value	0.001	0.001	0.0001
Periosten pg/ml	patient	25.71±4.78	27.81±5.86	42.75±13.14
	control	15.24±.42	14.91±0.52	16.20±0.49
	P-value	0.042	0.002	0.046
BMD g/cm	patient	0.63±0.02	0.63±0.0	0.64±0.02
	control	0.95±0.04	1.03±0.03	1.08±0.03
	P-value	0.0001	0.0001	0.0001
V.D ng/ml	patient	10.23±0.68	9.42±0.64	8.91±0.89
	control	37.46±3.59	43.40±3.91	41.01±2.38
	P-value	0.0001	0.0001	0.0001

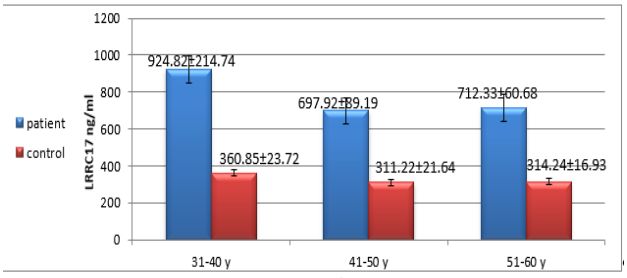

Figure (4-17) Comparisons of serum LRRC17 between patient and control groups age in osteoporosis

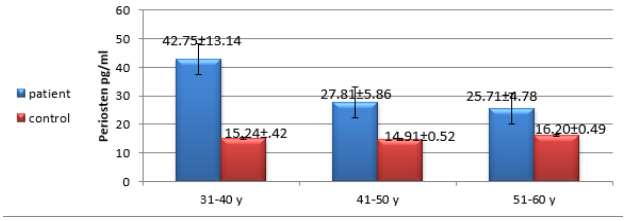

Figure (4-19) Comparisons of serum Periosten between patient and control groups age in osteoporosis

The LRRC17 parameter in the current study was highly significant increase in osteoporosis age group (20-40 y) patients (697.92±89.19) than in control age group (20-40 y) (360.85±23.72) according to p-value (0.001). The LRRC17 parameter in the current study was highly significant increase in osteoporosis age group (41-50 y) patients (712.33±60.68) than in control age group (41-50 y) (311.22±21.64) according to p-value (0.001). The current study agreed with a study that found a significant increase in patients, the LRRC17 parameter in the current study was highly significant increase in osteoporosis age group (<60 y) patients (924.82±214.74) than in control age group (<60 y) (314.24±16.93) according to p-value (0.0001). The Perostin parameter in the current study was highly significant increase in osteoporosis age group (20-40 y) patients (25.71±4.78) than in control age group (20-40 y) (15.24±.42) according to p-value (0.042).

The perostin parameter in the current study was highly significant increase in osteoporosis age group (41-50 y) patients (27.81±5.86) than in control age group (41-50 y) (14.91±0.52) according to p-value (0.002). The perostin parameter in the current study was highly significant increase in osteoporosis age group (<60 y) patients (42.75±13.14) than in control age group (<60 y) (16.20±0.49) according to p-value (0.046)

Tabl:3 Biochemical parameter in patient and control in study on osteoporosis as pre-menopause and post-menopause groups comparison.

Parameter	Cycle	Patient	Control
LRRC17 ng/ml	Pre	710.30±63.27	307.07±17.35
	Post	740.93±157.66	317.66±35.92
	P-value	0.421	0.641
Periosten pg/ml	Pre	27.07±4.36	15.16±0.43
	Post	37.76±14.57	15.80±0.75
	P-value	0.057	0.822
BMD g/cm^2	Pre	0.63±0.02	1.01±0.03
	Post	0.67±0.03	1.00±0.03
	P-value	0.213	0.123

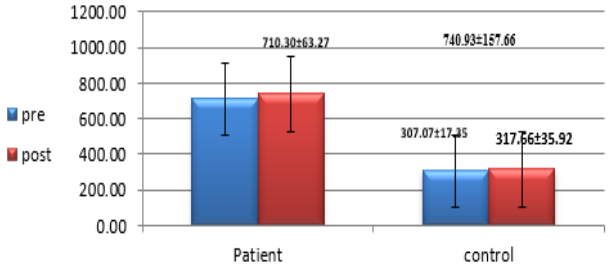

Figure Comparisons of serum LRRC17

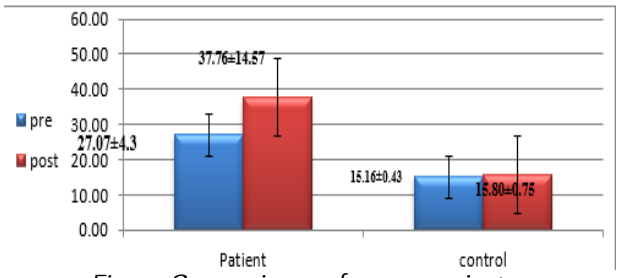

Figure Comparisons of serum periosten

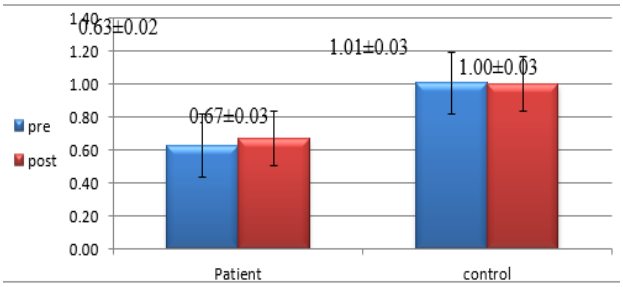

Figure Comparisons of serum BMD

4. Discussion

In bone, periostin is mainly expressed by periosteal osteoblasts and osteocytes (2). The present study shows that hip fracture women had higher serum periostin (sPostn) levels. The elevation of sPostn is associated with bone density loss yet fracture itself may even increase sPostn levels during early healing phase (11). The current study agreed with a study that found a significant increase in patients, which contradicts his study that *LRRC17* negatively regulates *RANKL* to inhibit bone degradation. Later, Kim *et al* demonstrated that postmenopausal women with lower *LRRC17* level had a 3.32-fold higher odds ratio for osteoporotic fracture and associated with a 46% higher risk of osteoporotic fracture than the group with higher LRRC17 levels, suggesting LRRC17's potential as a marker for osteoporotic fracture (7). The BMD parameter in the current study was highly significant decrease in osteoporosis patients (0.63±0.014) than in control group (0.63±0.014) according to p-value (0.0001). Clinically, BMD is a strong relevant marker of osteoporosis, as well as a key indicator for its diagnosis and treatment (4). The current study agreed with a study that found a significant decrease in patients, Vitamin D is a pro-hormone that regulates Ca and P balance and skeletal structures and has an adverse impact on skeletal health and neuromuscular function. Vitamin D deficiency increases the risk of osteoporosis. Serum 25OHD level lower than 20 ng/mL was reported to be associated with defective bone mineralization (12) These findings suggest that low circulating lrrc17 level may be a risk factor for OF. In fact, Hong et al. Demonstrated that postmenopausal women in the lowest plasma lrrc17 tertile had higher odds ratio (OR) for OF than those in the highest tertile and that each log-unit decrease in plasma (3). The study, higher serum periostin levels have been reported to be associated with increased fracture risk in postmenopausal women from the Os des Femmes de Lyon cohort study independently of age, bone turnover markers, and BMD (9) clinical studies have also demonstrated that circulating periostin levels were positively correlated with non-vertebral fractures after adjustment for BMD and potential confounders in Korean postmenopausal women (5).There is little if any change in BMD in midlife pre- or early peri-menopausal women. BMD loss increases substantially in the late perimenopause and remains rapid in the first few postmenopausal years. Body weight is an important determinant of the rates of BMD loss during the menopause transition. These findings suggest that healthcare providers should consider screening for osteoporosis when women enter the late stages of the menopause transition, particularly if they have relatively low body weight (1).

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