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Original Article

COMPARATIVE STUDY BETWEEN PERIOSTIN AND OSTEOCALCIN AS BIOMARKERS FOR OSTEOPOROSIS AND FRACTURE RISK IN EGYPTIAN POSTMENOPAUSAL WOMEN

ALAA SALAM MOHAMED[1], ASHRAF ISMAIL KHALIFA[2], ASHRAF ABDEL-MONEAM ABOTALEB[3], NOHA ABDEL-RAHMAN ELDESOKY[4]

[1]Biochemistry Department, Faculty of Pharmacy (Girls), Al-Azhar University, Cairo, Egypt, [2]Rheumatology and Rehabilitation Department, Faculty of Medicine (Boys), Al-Azhar University, Cairo, Egypt, [3]Clinical Pathology Department (Boys), Al-Azhar University, Cairo, Egypt, [4]Biochemistry Department, Faculty of Pharmacy (Girls), Al-Azhar University, Cairo, Egypt
Email: alaa.salam2012.as@gmail.com

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ABSTRACT

Objective: This study aimed to compare between periostin and osteocalcin as biomarkers in Egyptian postmenopausal women with osteoporosis and to explore their possible relationship with fracture risk.

Methods: This study included 90 postmenopausal females recruited from Al-Hussein University Hospital, Cairo, Egypt; divided into three groups; 35 postmenopausal osteoporotic females with low fracture risk (group I), 35 postmenopausal osteoporotic females with high fracture risk (group II), and 20 apparently healthy controls. Serum periostin, osteocalcin, and estrogen were measured by Enzyme Linked Immunosorbent Assay (ELISA). Fracture risk assessment was calculated. Alkaline phosphatase (ALP), total and ionized calcium, Aspartate transaminase (AST), and Alanine transaminase (ALT) were measured spectrophotometrically.

Results: The diagnostic performance of periostin for discriminating high fracture risk from low fracture risk groups showed the specificity of (68.6 %) and sensitivity of (100 %), while for osteocalcin the specificity was (51.4 %) and the sensitivity was (68.6 %) respectively. Moreover, the multi Receiver Operating Characteristics (multi-ROC) curve for periostin and osteocalcin together revealed improved specificity and sensitivity of (100 %) each.

Conclusion: Periostin was superior to osteocalcin in discriminating high fracture risk from low fracture risk postmenopausal osteoporotic groups. Moreover, dual use of both markers gave the highest discriminative power between low and high fracture risk groups with 100 % specificity and sensitivity.

Keywords: Postmenopausal osteoporosis, Periostin, Osteocalcin, Estrogen, DXA, Fracture risk

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INTRODUCTION

Osteoporosis is a skeletal metabolic disorder characterized by micro-architectural deterioration of bone tissue, this leads to an increase in bone fragility and fracture risk [1]. It is the most common metabolic bone disorder worldwide [2]. It was estimated that nearly 1 in each 2 postmenopausal females above the age of 50 will suffer a fragility fracture at some point in their life-time [3].

Bone strength is a measure of the resistance to bone fracture, which is determined by a collection of many skeletal characteristics including: composition, microarchitecture, size, and shape [4]. Dual-energy X-ray absorptiometry has been used widely for BMD measurement, bone strength assessment, and diagnosis of osteoporosis [5]. However, there are some limitations of DXA important to be considered. Bone mineral density (BMD) can be affected by positioning errors or artifacts, including osteoarthritis, fractures, and jewelry [6]. There are also many other factors that could affect DXA results, including recently administered gastrointestinal contrast or radionuclides, implants, devices, or any foreign material in the measurement area, and pregnancy [7]. Moreover, alkaline phosphatase (ALP) that has been usually used as a biomarker for osteoporosis, isn't specific for bone, and originates from different organs as liver and kidney [8].

Bone turnover biomarkers usually result from the bone remodeling process and can be measured in urine or serum [9]. They are released throughout life to repair microfractures in bone and to maintain mineral homeostasis [10]. They are classified as markers of bone formation as total alkaline phosphatase, bone-specific alkaline phosphatase, osteocalcin, and procollagen type 1 N-terminal propeptide; and markers of bone resorption as hydroxyproline, deoxypyridinoline and pyridinoline [11].

Osteocalcin (OC) is a small protein (consists of 49 amino acids) encoded by the BGLAP gene synthesized by osteoblasts. The serum concentration of total OC has been considered a biochemical marker of osteogenesis that reflects the number and activity of osteoblasts [12]. It is the major and most thoroughly characterized bone-specific non collagenous protein in bone extracellular matrix that has been conserved in bone through evolution. It has a high affinity for calcium and plays an important role in matrix mineralization [13, 14].

Periostin, also named osteoblast-specific factor (OSF-2), is encoded by POSTN gene. It is an extracellular matrix protein of 836 amino acids with a molecular weight of approximately 93 kDa [15]. Periostin exists in the basement membrane and lung's mesenchymal tissues. Its isomers are found also in the myocardium, skeletal muscle, heart valves, tendons, skin, periodontal ligaments, bones, and neoplastic tissues [16]. It is expressed predominantly in the periosteum , which covers the majority of bones and plays a vital role in regulating bone metabolism [17].

Periostin deficiency was related to osteoporosis and reduced bone strength [18]. The relationship between serum periostin, osteoporosis, and fracture risk in postmenopausal females is still unclear. Hence, the present work studies the possible relationship between serum periostin, BMD, estrogen, and fracture risk in Egyptian postmenopausal females compared to healthy postmenopausal controls. Moreover, the present study compares between periostin and osteocalcin performance as osteoporosis markers.

MATERIALS AND METHODS

Study population

This study was conducted on 90 postmenopausal females with age range (50–62) years old), divided into 70 osteoporotic females

recruited from Rheumatology and Rehabilitation Department, Al-Hussein University Hospital, Cairo, Egypt in the period from December 2016 till March 2018, and 20 healthy postmenopausal volunteers taken as control group. Osteoporotic women were categorized into two groups; 35 with low fracture risk (group I) and 35 with high fracture risk (group II) according to the American Association of Clinical Endocrinologists (AACE) recommendations [19]. The present study conforms to recognized standards including Declaration of Helsinki, US Federal Policy for the Protection of Human Subjects, and European Medicines Agency Guidelines for Good Clinical Practice; and was approved by Research Ethical Committee of Faculty of Pharmacy, girls, Al-Azhar University (REC number: 252). Written consents were taken from every participant prior to their enrollment in the study. Also, all participants have given written informed consent for publication.

Inclusion criteria

1) Inclusion criteria for high fracture risk patients:

a) Postmenopausal females with BMD T-score of–2.5 or below at spine and hip.

b) Postmenopausal females with BMD T-score-1 to-2.5 at hip or spine with FRAX® 10-year probability for major osteoporotic fracture ≥ 20 % or the 10-year probability of hip fracture ≥ 3 %.

2) Inclusion criteria for low fracture risk patients:

Postmenopausal females with BMD T-score-1 to-2.5 at hip or spine with FRAX® 10-year probability for major osteoporotic fracture<20 % or hip fracture<3 % [19, 20].

3) Inclusion criteria for control group

Postmenopausal females with BMD T-score of more than-1.

Exclusion criteria

1. Premenopausal and postmenopausal females with age more than 62 y.

2. Chronic diseases (Renal, Liver, Pulmonary, Cardiovascular, or any other major illness that could affect parameters.

3. Patient taking medications for osteoporosis.

4. Women who previously undergone a hysterectomy in young age.

All participants were subjected to physical examination, full clinical examination with particular attention if there were low back pain, pain in spine, forearm or femur, and DXA scan to assess BMD. Assessment of serum calcium levels (total and ionized) and alkaline phosphatase were done by colorimetric methods. Liver function tests, including ALT and AST were done by the kinetic ultraviolet method using (Biolis50i Superior, Japan) to ensure that any rise in ALP levels originate from bone. Osteocalcin and periostin were estimated by ELISA (Tecan A-5082, Austria). Estrogen was assessed by ELISA (Biotek, Japan).

Samples collection

Blood samples (8 ml) were collected by trained laboratory technicians under complete aseptic conditions and allowed to clot for 30 min then centrifuged at 3000 rpm for 15 min. The serum was aspirated and divided into three aliquots, kept at-80 °c until an assessment of calcium (Ca), alkaline phosphatase (ALP), alanine transaminase (ALT), aspartate transaminase (AST), estrogen (E2), osteocalcin (OC), and periostin.

Statistical analysis

The Statistical Package for the Social Sciences (SPSS) (V. 24.0, IBM Corp., USA, 2016) was used for data analysis. Date was expressed as Median and Percentiles for quantitative nonparametric measures.

The following tests were used; Wilcoxon Rank Sum was used for comparison between two independent groups, Kruskall Wallis was used for comparison between more than 2 patient groups, and Ranked Spearman correlation was used to study the possible association between two variables. The probability of error at 0.05 or less was considered significant, while at 0.01 and 0.001 was considered highly significant.

The Receiver Operating Characteristics (ROC) curves were constructed to obtain the most sensitive and specific cutoff values for each marker. Area under the curve (AUC) was calculated.

RESULTS

The Demographic data, clinical characters, and biochemical parameters of the control group, osteoporotic patients with low fracture risk (group I) and with high fracture risk (group II) were presented in table 1. Weight, body mass index and ALT were significantly increased in group I and group II compared to control group at $^{**}p \leq 0.001$ and $^{**}p \leq 0.01$, respectively. Total calcium and ionized calcium showed a significant decrease in group I and group II compared to control group ($^{**}p \leq 0.001$), while osteocalcin, ALP, and periostin showed a significant increase in group I and group II compared to control group ($^{**}p \leq 0.001$). Moreover, spine BMD T-score and total hip BMD T-score showed a significant decrease, while major osteoporotic (FRAX) (%) and hip fracture (FRAX) (%) showed significant increase in group I and group II compared to the control group ($^{**}p \leq 0.001$), as mentioned previously in inclusion criteria.

Table 1: Demographic, clinical, and biochemical parameters of all studied groups

Variables	Control (n = 20)	Group I (n = 35)	Group II (n = 35)	p value
Age (Years) (25Perc-75perc)	57.5 (50.25-60.75)	58.1 (53-59)	60 (57-62)	0.213
Height (Cm) (25Perc-75perc)	156 (153-158.75)	155 (151-159)	157 (149-160)	0.906
Weight (Kg) (25Perc-75perc)	64 (60-72.25)	77[a] (69-85)	80[a] (70-97)	0.001**
BMI (Kg/m^2) (25Perc-75perc)	26.85 (24.55-30.55)	32.4[a] (29.1-37.3)	35[a] (27.3-39.3)	0.001**
ALT (U/l) (25Perc-75perc)	6 (4-7)	7 (4-12)	11[a] (6-14)	0.016**
AST (U/l) (25Perc-75perc)	6.5 (4.25-9)	9 (6-13)	9 (5-14)	0. 135
Total Ca (mg/dl) (25Perc-75perc)	9.79 (9.6-10.2175)	6.04[a] (5.4-7.03)	5.48[a,b] (5.06-6.23)	0**
Ionized Ca (mg/dl) (25Perc-75perc)	4.62 (4.5925-4.6875)	4.59 (4.18-4.9)	4.18[a,b] (3.95-4.58)	0**
ALP (U/l) (25Perc-75perc)	108 (98.25-116.25)	350[a] (315-369)	454[a,b] (409-472)	0**
Spine BMD T-score (25Perc-75perc)	-0.1 (-0.3-0.675)	-2[a] (-2.8-(-1.1))	-2.2[a] (-2.7-(-0.3))	0**
Total hip BMD T-score (25Perc-75perc)	0.45 (0-1.075)	-1.7[a] (-2-(-1.4))	-2.3[a,b] (-2.4-(-1.4))	0**
Major osteoporotic (FRAX) (%) (25Perc-75perc)	2.2 (1.6-2.75)	6.3[a] (4.2-8.7)	15[a,b] (11.9-18)	0**
Hip fracture (FRAX) (%) (25Perc-75perc)	0.1 (0-0.1)	1.1[a] (0.9-1.9)	5[a,b] (3.9-6.4)	0**
Estrogen (pg/ml) (25Perc-75perc)	5.5 (3.25-8)	5 (3-10)	6 (3-11)	0.434
Osteocalcin (ng/ml) (25Perc-75perc)	7.15 (5.4-11.125)	26.2[a] (23.9-29)	27.7[a] (25.5-30)	0**
Periostin (ng/ml) (25Perc-75perc)	483 (411.75-564.75)	817.5[a] (710-886)	1102[a,b] (915-1340)	0**

a: Significant difference from control group, b: Significant difference from group I, $^{*}p \leq 0.05$ was considered significant, $^{**}p \leq 0.01$ and 0.001 were considered highly significant.

Correlation of osteocalcin with the other studied parameters revealed positive significant correlation with ALP in group I and group II ($r = 0.898$, $^{**}p \leq 0.001$) and ($r = 0.938$, $^{**}p \leq 0.001$) respectively. There were also positive significant correlations between osteocalcin and each of major osteoporotic (FRAX) (%) and hip fracture (FRAX) (%) in group II ($r = 0.791$, $^{**}p \leq 0.001$) and ($r = 0.922$, $^{**}p \leq 0.001$) respectively (table 2).

Table 2: Correlation of osteocalcin (ng/ml) with all studied parameters in controls, group I, and group II

Studied parameters	Correlation of osteocalcin (ng/ml)					
	Control (n = 20)		Group I (n = 35)		Group II (n = 35)	
	r-value	p value	r-value	p value	r-value	p value
Total Ca (mg/dl)	0.212	0.369	-0.128	0.465	-0.054	0.757
Ionized Ca (mg/dl)	0.132	0.579	-0.135	0.438	-0.235	0.175
ALP (U/l)	0.108	0.651	0.898	0**	0.979	0**
Spine BMD T-score	-0.289	0.216	-0.092	0.6	-0.266	0.192
Total hip BMD T-score	-0.443	0.051	-0.07	0.69	-0.249	0.15
Major osteoporotic (FRAX) (%)	0.681	0.001**	0.09	0.607	0.791	0**
Hip fracture (FRAX) (%)	0.601	0.005*	0.113	0.518	0.922	0**
Estrogen (pg/ml)	-0.45	0.046*	-0.342	0.045*	-0.066	0.706

*p ≤ 0.05 was considered significant, **p ≤ 0.01 and 0.001 were considered highly significant.

The correlation between periostin and the other studied parameters revealed positive significant correlation between periostin and ALP in group I and group II (r-value = 0.952, **p ≤ 0.001) and (r-value = 0.992, **p ≤ 0.001) respectively. There were also positive significant correlations between periostin and each of major osteoporotic (FRAX) (%) and hip fracture (FRAX) (%) in group II (r-value = 0.754, **p ≤ 0.001) and (r-value = 0.886, **p ≤ 0.001) respectively and negative significant correlation with estrogen in controls and group I (r-value =-0.648, **p ≤ 0.01) and (r-value =-0.356, **p ≤ 0.05) respectively. Moreover, periostin showed positive significant correlation with osteocalcin in groups I and II (r-value = 0.938, **p ≤ 0.001) and (r-value = 0.958, **p ≤ 0.001) respectively (table 3).

Table 3: Correlation of periostin (ng/ml) with all studied parameters in controls, group I, and group II

Studied parameters	Correlation of periostin (ng/ml)					
	Control (n = 20)		Group I (n = 35)		Group II (n = 35)	
	r-value	p value	r-value	p value	r-value	p value
Total Ca (mg/dl)	-0.239	0.311	-0.173	0.32	-0.141	0.419
Ionized Ca (mg/dl)	-0.071	0.768	-0.194	0.265	-0.076	0.663
ALP (U/l)	0.02	0.935	0.952	0**	0.992	0**
Spine BMD T-score	-0.042	0.859	-0.04	0.82	-0.284	0.099
Total hip BMD T-score	0.058	0.809	-0.003	0.986	-0.021	0.227
Major osteoporotic (FRAX) (%)	0.406	0.075	0.05	0.774	0.754	0**
Hip fracture (FRAX) (%)	0.433	0.057	0.074	0.672	0.886	0**
Estrogen (pg/ml)	-0.648	0.002**	-0.356	0.036*	-0.25	0.978
Osteocalcin (ng/ml)	0.406	0.075	0.938	0**	0.958	0**

*p ≤ 0.05 was considered significant, **p ≤ 0.01 and 0.001 were considered highly significant.

Table (4) and (fig. 1) represents the output data of the receiver operating characteristics (ROC) curve for each of serum periostin and osteocalcin. At cut off 602 for periostin, the specificity and sensitivity were (68.6 % and 100 %) respectively. At cut off 20.7 for osteocalcin, the specificity and sensitivity were (51.4 % and 68.6 %) respectively. Multi-ROC curve showed a huge improvement in the discriminative power of periostin and osteocalcin when used together as the sensitivity and specificity raised to 100 %, at cut off value of 850 for periostin.

Table 4: The discriminative power of serum periostin (ng/ml), osteocalcin (ng/ml), and combined (periostin/osteocalcin) between group I and group II osteoporotic patients

Variable	Cutoff	AUC	% Sensitivity	% Specificity	% Efficacy
Periostin (ng/ml)	850	1.000	100.0	68.6	84.3
Osteocalcin (ng/ml)	26.2	0.995	68.6	51.4	60
Multi-ROC: for periostin (ng/ml) at 850					
Osteocalcin (ng/ml)	32.5	1	100.0	100.0	100.0

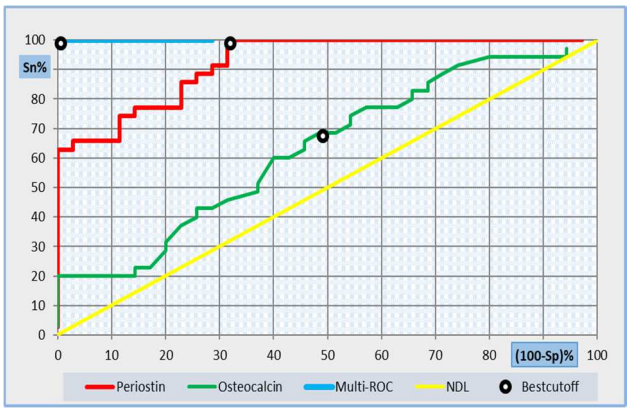

Fig. 1: ROC curve for discriminating patients with high fracture risk from those with low fracture risk showing the diagnostic performance of periostin (ng/ml), osteocalcin (ng/ml), and multi ROC for their combination

DISCUSSION

Osteoporosis is usually caused by altered bone micro-structure predisposing patients to fragility and fractures [21]. Introducing a biomarker that could predict the risk of bone fracture would help in the early therapeutic intervention, reducing future fractures, and complications.

In the current study, there were reductions in spine BMD T-score, total hip BMD T-score, and serum Ca in group I and group II compared to the control group (**p ≤ 0.001). This was matched with a study done by Tian *et al.* [22] who reported lower serum Ca and BMD in postmenopausal osteoporotic than non-osteoporotic females. Moreover, Qu *et al.* found lower BMD in the fracture group than in the non-fracture group; and in elder females than younger females. They stated that the risk of fracture increases with the reduction in bone density [23].

In the present study, major osteoporotic (FRAX) (%) and hip fracture (FRAX) (%) showed significant increases in group I and group II compared to control group. This result was similar to Tomasevic *et al.* who concluded that osteoporosis patients had a high risk of Major osteoporotic (FRAX) and hip fracture (FRAX) %. They indicated that patients suffering from osteoporosis and who had a history of fractures had higher fracture risk in comparison to those suffering from osteopenia without history of fractures [24].

In the present work, osteocalcin showed a significant increase in both patients' groups compared to the control group at **p ≤ 0.001 while no significant difference was obtained between groups I and II. This was matched with a study done by Alam *et al.* who reported a significant increase of osteocalcin in postmenopausal osteoporotic patients and explained it by accelerated osteoclastic activity due to the sudden depletion of estrogen which increases bone resorption on the expense of bone formation that is reflected in serum as increased osteocalcin levels [25].

Beg *et al.* reported that serum osteocalcin was significantly higher in postmenopausal females with osteoporosis than without (*p<0.05). They reported reduced osteocalcin levels after treatment with risedronate, an osteoporosis medication; and concluded that osteocalcin can be potentially useful in the diagnosis and the monitoring of response to therapy in osteoporotic patients [26].

Singh *et al.* recommended the use of serum osteocalcin level as a screening tool for osteoporosis in postmenopausal females and advised only subjects having osteocalcin levels beyond osteocalcin cutoff point for DXA scan to grade the severity of osteoporosis [27].

Soroosh *et al.* discussed the relation between osteocalcin and bone formation by the following; Osteocalcin is produced by osteoblasts during bone formation process and binds to the c-carboxyglutamic acid (Gla) residues by its high affinity for calcium. This promotes the absorption of calcium to the hydroxyapatite in bone matrix and aids mineralization of bone. Decreases in bone mineralization (decreased hydroxyapatite crystal formation) in osteoporosis causes free osteocalcin to circulate in the blood and hence results in increased serum osteocalcin levels [28].

On the contrary, Rai *et al.* found very low levels of serum osteocalcin in postmenopausal females with fractures compared to the premenopausal females and linked it with reduced bone formation and increased resorption activity at late menopause [29].

Moreover, Liu *et al.* found no significant difference of the pooled serum osteocalcin in postmenopausal osteoporotic patients in comparison with postmenopausal controls. They recommended not to use serum osteocalcin as indicator for high bone turnover status in postmenopausal females unless new techniques for standardized circulatory osteocalcin evaluation are introduced in the future, since osteocalcin molecules are quite heterogeneous (different fragments and different carboxylation status) in the circulation, and can be influenced by many metabolic events [30].

The previously discussed controversy demonstrates that osteocalcin could not be considered as a reliable marker for osteoporosis diagnosis and monitoring; hence it appears the necessity of searching for new biomarkers.

Regarding the correlation of osteocalcin with other biomarkers, there were significant positive correlations with ALP in group I and group II. This was compatible with the results obtained by Singh *et al.* who stated that alkaline phosphatase had a strong positive correlation with serum osteocalcin level [27].

In the present study, there were no significant correlations between osteocalcin and each of (total hip BMD T-score and spine BMD T-score) in group I and group II. This was in accordance with a study done by Soroosh *et al.* who stated that serum osteocalcin levels did not correlate significantly with BMD in postmenopausal osteoporosis females [28].

In the current study, there were significant positive correlations between osteocalcin and each of (major osteoporotic (FRAX) % and hip fracture (FRAX) %) in group II. This was matched with Dai *et al.* who found a dose-dependent positive relationship between osteocalcin and the risk of hip fracture in Asian population [31].

In the current study, periostin showed a significant increase in both patients' groups compared to the control group at **p ≤ 0.001 and a significant increase in high fracture risk group than the low fracture risk group at **p ≤ 0.001. This means that high level of periostin was associated with an increased risk of fracture. These findings were agreed with a study done by Bonnet *et al.* who found periostin increased in females with incident fracture than those without [32]. Kim *et al.* and Sakellariou *et al.* found high serum periostin levels associated with increased fracture risk in postmenopausal females [33, 34].

Varughese*et al.* reported elevated serum periostin levels in response to bone injury and repair. They observed elevated periostin levels also in patients with radiological evidence of osteoporotic fracture [16].

Circulating periostin may reflect the adaptation of the metabolic activity of periosteum cells to the existing bone strains for maintenance of a stabilized bone quality. Women with lower bone mass and strength may have a higher mechanical strain in the remaining bone that would increase periostin expression. Thus, increased expression of periostin is reflected in serum by an increase of circulating periostin. However, at the level of bone, an increase of bone formation caused by an increased periostin expression is not enough to compensate the bone loss leading to fragility fractures [35].

De Lageneste *et al.* explained the role of periostin in bone regeneration by the activation of skeletal stem cells (SSCs) in the periosteum causing a high bone regenerative potential, reconstituting a pool of periosteal cells after injury [36]. Zhang *et al.* explained that mechanical activity and exercise may increase periostin production in osteoblasts, which in turn may inhibit the differentiation of osteoclasts by its effects on semaphorin-3A [37].

Kudo. explained that the cortical bone formation is regulated by the periostin-mediated blocking of random bone formation. They stated that, in response to mechanical stress, periostin expression is enhanced, and activates cellular functions to improve the irregular collagen fibrillogenesis and extracellular matrix organization to maintain tissue homeostasis [38].

Yan *et al.* found the initial levels of periostin after fracture significantly higher in osteoporotic patients than controls revealing that high periostin level was an independent predictor of femoral neck BMD in elderly females presenting with acute hip fracture. They declared that increased periostin levels during early healing phase may imply that periostin play a role in bone repair [39].

Luo and Deng. found no significant differences in serum periostin levels between postmenopausal females with normal and abnormal BMD T-score, and reported that periostin is not a predictor of early-stage bone deterioration in Chinese postmenopausal females. However, during the course of their study, BMD data at one year after baseline indicated that the femur neck bone mineral content (BMC) and T-score became lower in women with higher baseline serum periostin [40]. This indicates a powerful relation of periostin and BMD.

In the present work, no significant correlations were obtained between periostin and bone mineral density in the three groups. This result is compatible with Walsh *et al.* who reported that there were no significant correlations between serum periostin and BMD at the lumbar spine or total hip, when analyzed as a group and within each group [41].

However, Gossiel *et al.* revealed that the changes in periostin levels were positively correlated with the changes in total hip BMD and femoral neck BMD in postmenopausal females with osteoporosis after treatment with teriparatide [42].

In the present work, there was a significant positive correlation between periostin and each of (major osteoporotic (FRAX) (%) and hip fracture (FRAX) (%)) in group II. This was matched with Terpos *et al.* who stated that periostin was elevated in the bone marrow plasma and in the serum of newly diagnosed symptomatic multiple myeloma patients and correlates with extensive bone lytic lesions, bone fractures and extensive osteolysis [43].

Also, there were no significant correlations between periostin and each of (total hip BMD T-score and spine BMD T-score) in both patients' groups in the present study. This was as the findings of Rousseau *et al.* who reported that serum periostin was not significantly associated with BMD of the spine or the hip [44]. Yan *et al.* reported that serum periostin level was negatively correlated with femoral neck BMD, an acute hip fracture was associated with a transient change of serum periostin levels in older females, and that measurement of serum periostin around the time of bone healing phase may include assessment of response to fracture therapy [39].

In the current work, there was a significant positive correlation between periostin and ALP in group I and group II. This result is compatible with Anastasilakis *et al.* [45] and in contrast with Hu *et al.* [46].

In the current work, there was a significant positive correlation between osteocalcin and periostin in group I and group II. However, the diagnostic performance of periostin and osteocalcin in discrimination between group I and group II using ROC curves revealed a more powerful discriminating capability of periostin than osteocalcin. The best cutoff value of periostin was taken at 850 ng/ml with specificity and sensitivity (100 % and 68.6 %), respectively, while the best cutoff value of osteocalcin was taken at 26.2 ng/ml with specificity and sensitivity (68.6 % and 51.4 %) respectively. Moreover, a multi ROC curve was performed for periostin and osteocalcin together and revealed improved specificity and sensitivity of 100 % for each at the cut off values (850 and 32.5), respectively.

CONCLUSION

The present study implies a potential role of periostin as a promising biomarker for the prediction of fracture risk in postmenopausal osteoporotic females. Moreover, periostin was superior to osteocalcin in discrimination of high fracture risk from low fracture risk patients. On top of that and according to the studied Egyptian population, Dual assessment of osteocalcin, and periostin seemed to be more efficient in identifying high fracture risk from low fracture risk osteoporosis patients than the use of each of them alone.

LIMITATIONS AND RECOMMENDATIONS

- The number of participants in the present study was the maximum number that authors could afford financially as this study was completely self-funded, so further studies are recommended on large scale to confirm our results.

- The present study involved only postmenopausal women so further studies are recommended to examine the role of periostin as a biomarker for senile osteoporosis in both sex groups and in different age groups.

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AUTHORS CONTRIBUTIONS

AI, AA and NA were involved in paper idea, protocol development and data analysis.

AI and AS were responsible for patient recruitment and clinical records.

NA and AS were responsible for gaining ethical approval and writing the manuscript.

All authors reviewed and edited the manuscript and approved the final version of the manuscript.

CONFLICTS OF INTERESTS

None

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