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Determination of Vaspin, Visfatin and Nesfatin-1 levels in Postmenopausal Osteoporosis Women in Samarra City

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Abstract
This study is done in private clinics, from Samarra Salah-alddin governorate. the total of subjects are 55 female individuals, who volunteered to take part in the research, 20 individuals control group and 35 individuals patients group have hormonal assay (Vaspin, Visfatin and Nesfatin-1) there is a significant increase (P≤0.05) in the levels of (Visfatin, Vaspin, and Nesfatin-1) when compared with the control group. The results show that the mean ± SD of serum Vaspin levels are (2.292±0.678) ng/ml, and control group (1.166±0.367) ng/ml ,the mean ± SD of serum visfatin are (0.373±0.150) ng/ml, and control group (0.228±0.109) ng/ml and the mean ± SD of serum nesfatin-1 levels are (46.54±7.22) pg/ml, and control group (31.3±4.4) pg/ml.

Introduction:

Adipose tissue is a type of endocrine tissue that produces hormones and cytokines to sustain a variety of physiological roles [1]. Abnormalities of adipose tissue (such as obesity) have been shown to have a strong influence on the progression of metabolic bone diseases like osteoporosis [2, 3]. By secreting soluble substances, adipose tissue can connect with bone cells, termed adipokines (e.g. Vaspin, Visaftin, Nesfatin-1). This Adipokines are a crucial component of the complex network of soluble mediators implicated in the pathogenesis of chronic inflammatory and immunological driven diseases, such as rheumatic disorders, Osteoporisis, and Osteoarthritis, due to their pleiotropic activities. [4].

In osteoporosis, adipokines regulate bone It affects bone turnover and mineral density (BMD), as well as bone metastasis [5].

Osteoporosis (OP) is a multifactorial, complicated ageing condition with metabolic, hormonal, and biomechanical impacts [6], dual-energy X-ray absorptiometry (DEXA) is widely used to diagnose osteoporosis. when T-score 2.5[7]. Increased marrow adiposity is associated with significant loss, factors released by adipose tissue in the bone marrow might not only cause "fatty marrow," However, osteoblast differentiation and proliferation are also inhibited, leading to fewer osteoblasts, less bone formation, and, consequently, osteoporosis [8]. In

vitro, new research has discovered that vaspin is tightly connected with bone metabolism. Vaspin inhibits RANKL-induced osteoclast formation, reduces human osteoblast apoptosis, and regulates MC3T3-E1 osteogenic differentiation [9].

Numerous micro RNAs (miRNAs) have recently been shown to be implicated in the visfatin-mediated actions, especially in OP., visfatin dramatically decreased viability and promoted apoptosis of bone cells [10].

Furthermore, serum nesfatin-1 levels are linked to levels of high-sensitivity C-reactive protein, and synovial nesfatin-1 levels are linked to levels of IL-18 [11] These findings suggest that nesfatin-1 may play a key role in the pathophysiology of OP through the influence of nesfatin-1 on rat OP.

Materials and Methods

Patients and control

The study that included 90 of postmenopausal women, 20 of whom were healthy women who were considered as a control group, and 70 of them were represented by groups of patients with osteoporosis, who attended private clinics in Samarra city in Salah al-Din Governorate.

The study started from December 2019 to May 2020 on a study population whose ages ranged from 55-85 years.

Blood Sample Collection

A sample of 5 mL of blood was taken in a plane tube and left to clot for about 20–30 minutes before being centrifuged for about 5–15 minutes at 3000 rpm in a macro centrifuge. Fresh non-hemolysis serum was then obtained and maintained in deep freeze (- 20^{o} C). The serum was separated into three tubes for hormonal assays, which included:

Determination of Human serum Vsapin ,Visaftin and Nesfatin-1:

Serum Vaspin, Visfatin and Nesfatin-1 has been determined by using kit assayed according to the manufactured procedure (SunLong Biotech Co.,LTD, Cat. No. SL2458Hu, SL276Hu and SL274Hu, China).

Statistical analysis:

The statistical analysis was carried out using the statistical program (SPSS), and comparisons between groups were made using one-way analysis of variance (ANOVA), and arithmetic means for parameters were tested using the Duncan multiple ranges test to delimit significant differences, particularly between groups. The statistical significance threshold was set at (P 0.05).

Results and Discussion:

Levels of Vaspin in Osteoporosis and control group:

In the present study, Serum levels of Vaspin is significant increase($P \leq 0.05$) in postmenopausal osteoporosis women when compared with control group. the mean ± SD of serum Vaspin levels in postmenopausal osteoporosis women are (2.292±0.678) ng/ml, and control group (1.166±0.367) ng/ml respectively as shown in Table (1).

These results are agreed with [12], who showed revealed a significant positive association between vaspin serum levels and bone mineral density (BMD) in femoral neck & total hip in postmenopausal women and found that serum visfatin is higher in patients compared with healthy people and are related with the development of OP in inflammatory bowel disease (IBD). Vaspin's involvement in bone metabolism has been studied in vitro, with results showing that it has a bilateral impact on both bone-forming osteoblasts and bone-resorbing osteoclasts. Vaspin also protected human osteoblasts against apoptosis in a dose-dependent manner [13].

[14] discovered that vaspin suppressed receptor activator of nuclear factor-kB ligand (RANKL-induced osteoclastogenesis in bone marrow cells, suggesting that it may operate as a bone metabolism regulator and induced expression of nuclear factor of activated T cells cl (NFATcI) in bone marrow cells (BMCs), also vaspin inhibited the RANKL induced expression of up regulate of matrix metalloproteinase-a & cathapsin K and stimulate or pro inflammatory cytokines , As a result, it's possible that the action of vaspin bone metabolism is mediated in part by adipokines. [15].

Vaspin may also modify the actions cytokines including Tumor necrosis alpha (TNF-α) and interleukin 1 (IL1) mediated activation nuclear factor kappa B (NF-kB), so could modify the effects of pro-inflammatory cytokines actions in bone tissue [16], this relationships between vaspin & the above mentioned ostetropic agent , bone markers and cytokines of the RANKL /RANK/OPG system may all have a role in the development of OP in postmenopausal women.

Its seems obviously that vaspin is closely related to bone metabolism especially in human osteoblasts , [17] examined the effect of vaspin on human osteoblasts in relation to apoptosis , they noted there is a consistent decrease in apoptosis with increasing concentrations .Vaspin also increased BcI-2 protein expression which is a protein an inhibitor of apoptosis and decreased Bax protein expression which is an inducer of apoptosis, , this means that vaspin may anti-apoptotic roles by stimulating the mitogen activated protein kinase (MAPK/extracellular signal-regulated kinase (ERK)signaling pathway in human osteoblasts [17, 18].

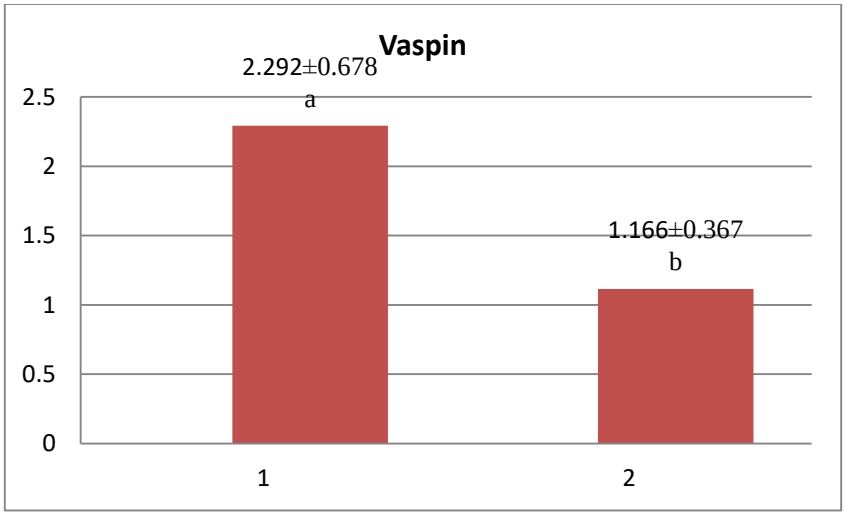

Figure1: The levels of Serum Vsapin Osteoporosis and Control group by(ng/ml)

--Different letters (a, b) in horizontal indicate that the means are different significantly at P≤0.05, among the studied groups.

Levels of Visfatin in Osteoporosis and control group:

In the present study, Serum levels of visfatin is significant increase (P≤0.05) in postmenopausal osteoporosis women when compared with control group.the mean ± SD of serum visfatin levels in postmenopausal osteoporosis women are (0.373±0.150) ng/ml, and control group (0.228±0.109) ng/ml respectively as shown in table (1).

The present study is agreed with [19] who concluded that visfatin are released by all human OA tissues in diametric enzymatically active confirmation and the activity of visfatin

Visfatin is abundantly expressed in human bone marrow, implying a role in bone homeostasis via prevention of induced aging in bone marrow-derived mesenchymal stem cells. (BM-MSCs) [20]. Inflammatory processes have been linked to OP and visfatin [21], Visfatin has caused bone loss and inflammatory responses [22], which are prevented by the particular visfatin inhibitor (FK868), which is further substantiated by animal studies. According to this, inhibiting visfatin (FK868) decreased pro-inflammatory factors (IL6,IL18) in osteoblasts. [23].

On the other hand, there is a link between high levels of serum visfatin and bone anabolism [24]. Despite the minimal number of findings associating visfatin levels in the blood with bone anabolism, the preponderance of data suggests that visfatin plays a pro-anabolic role in osteoblast formation and function, as well as visfatin knock-down or inhibition in mice. (BM-MSCs) reduced osteoblastogensis, and alkaline phosphat activity, matrix mineralization and the expression of osteoblast differentiation markers [25], Because osteoblast metabolism and glucose metabolism are linked [26], Elevated levels of circulating visfatin may impair insulin signal in peripheral organs, it's possible that visfatin's anabolic effects on bone are due to its insulin-mimetic activity. In fact, visfatin is induced tyrosine phosphorylation of the insulin receptor substrate 1 (IRS1) and (IRS2), as well as the insulin receptor in human osteoblasts, It is also stimulated matrix mineralization in human osteoblasts without affecting ATP activity. [27,28].

Visfatin inhibitor (FK866) has decreased mineralization and accelerated adipogensis processes in mouse bone marrow stromal cells, ([29]. In addition, visfatin deletion and inhibition in mice pre-osteobalstic cells reduced osteoblastogensis and promoted adipogensis, moreover, several studies demonstrated that visfatin decreased osteoclastogensis mediated by the osteoclast receptor in mouse and human monocytes (RANKL) [30].

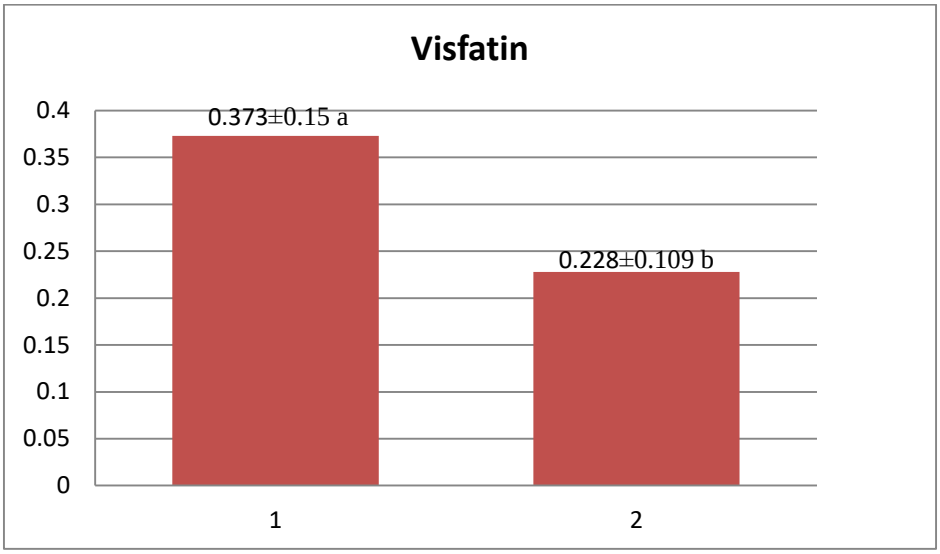

Figure 2: The levels of Serum Visfatin Osteoporosis and Control group by(ng/ml)

-Different letters (a, b) in horizontal indicate that the means are different significantly at P≤0.05, among the studied groups.

Levels of Nesfatin-1 in Osteoporosis and control group:

Serum levels of nesfatin-1 is significant increase (P≤0.05) in postmenopausal osteoporosis women when compared with control group, the mean ± SD of serum nesfatin-1 levels in postmenopausal osteoporosis women are (46.54±7.22) pg/ml, and control group (31.3±4.4) pg/ml respectively as shown in table (1).

In the present study, these results are agreed with [31,32].

In vivo and *in vitro*, nesfatin-1 increases osteoblast development and mineralization while inhibiting osteoclast differentiation because nesfatin-1 is involved in bone remodeling and the pathogenesis of OP, they are key regulators of osteoclastogenic activity and activate bone resorption, causing bone loss and negative changes in its structure and properties, it can be assumed that increased nesfatin-1 levels are a protective mechanism against changes in osteopenic bone structure and properties and can be used in the prevention of bone loss that leads to a reduction in bone strength[33,34].

In the bone tissue, [31] were the first to reveal that the nucleobindin (NUCB) protein, which later found out to be a precursor to nesfatin-1, had intracellular and extracellular localization.

Nesfatin-1 may act as a modulator of matrix maturation in the bone mineralization process [31], so it can be considered an indicator of processes occurring in bone tissue during the development and evolution of the skeleton, allowing for the characterization and determination of the intensity of changes related to bone formation and resorption, as [35] explained. The strength of the immune-histochemical reaction for nesfatin-1 in the growth plate increased in tandem with the degree of chondrocyte maturity, suggesting that nesfatin-1 may be used as a biomarker of maturation if the matrix in bone mineralization changes. [32].

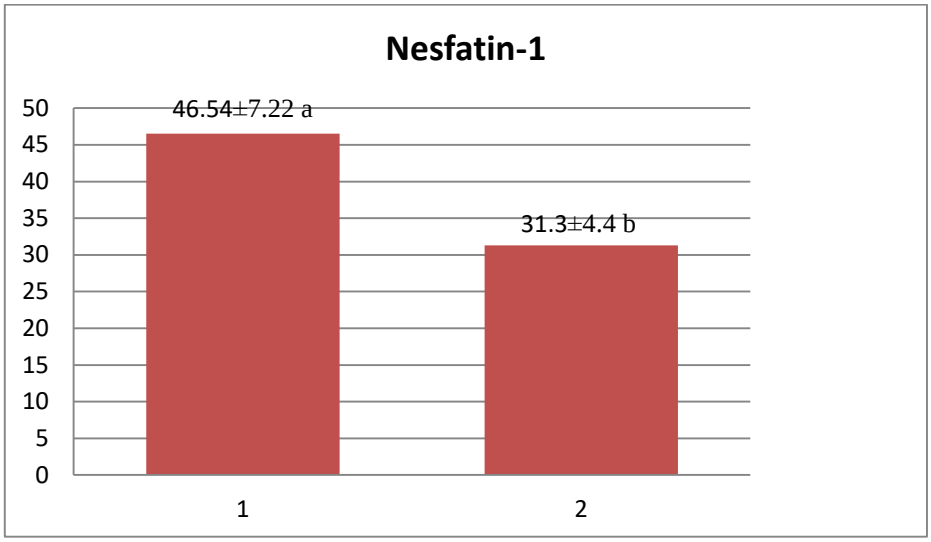

Figure 3: The levels of Serum Nesfatin-1 Osteoporosis and Control group by(pg/ml)

-Different letters (a, b) in horizontal indicate that the means are different significantly at P≤0.05, among the studied groups.

Conclusion:

The mean value of serum Vaspin, Visfain and Nesfatin-1 in postmenopausal osteoporosis women was significantly higher compared to control group. It was noted that adipose tissue that secret this hormones had a main effect in the pathogenesis of osteoporosis and could be used as a biomarkers to diagnosis the patients with osteoporosis.

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قياس مستويات هرمون الفاسبين، الفسفاتين والنيسفاتين-1 لدى النساء ما بعد سن اليأس المصابات بهشاشة العظام في مدينة سامراء

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فاسبين، فسفاتين، نيسفاتين-1، ما بعد سن اليأس، هشاشة العظام

معلومات المؤلف

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الخلاصة:

أجريت هذه الدراسة في العيادات الخاصة في سامراء بمحافظة صلاح الدين. كان إجمالي الأشخاص 55 أمراة ما بعد سن اليأس، تطوعن للمشاركة في البحث، 20 منهن سليمات اعتبرن كمجموعة سيطرة و 35 امرأة مصابات بهشاشة العظام خضعوا لفحص هرموني تضمن قياس مستويات (فاسبين، فسفاتين، نيسفاتين-1) وكانت هناك زيادة معنوية ($P\leq0.05$) في مستويات (فاسبين، فسفاتين، نيسفاتين-1) عند مقارنتها بمجموعة السيطرة. أظهرت النتائج أرتفاع معنوي في مستويات فاسبين (2.292 ± 0.678) نانوغرام / مل ، ومجموعة السيطرة (1.166 ± 0.367) نانوغرام / مل ، وارتفاع معنوي في مستويات الفازفاتين (0.373 ± 0.150) نانوغرام / مل. ، مقارنة بمجموعة السيطرة (0.228 ± 0.109) نانوغرام / مل وكذلك اظهر هرمون نيسفاتين-1 ارتفاع معنوي في مستواه حيث بلغ (46.54 ± 7.22) بيكوغرام / مل ، مقارنة بمجموعة السيطرة (31.3 ± 4.4) بيكوغرام / مل.