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Measurement of Serum Chemerin and Deoxyypyridinoline Levels in Iraqi Osteoporotic Postmenopausal Women with and without Metabolic Syndrome

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ABSTRACT



Metabolic syndrome is a cluster of medical conditions composed of abdominal obesity, hyperglycemia, hypertension, and lipid abnormalities, in which each can affect bone in different ways. We examine the association between metabolic syndrome and metabolic bone disease (osteoporosis) by measuring adipose tissue marker (chemerin) and bone resorption marker (deoxyypyridinoline) in the serum of osteoporotic postmenopausal women with and without metabolic syndrome. A case-control study included 112 postmenopausal women from 51 to 67 years of age. Women were selected from Osteoporosis Clinic-Al Yarmouk Teaching Hospital and were divided into two groups: group (1)- patients group included 57 postmenopausal women with osteoporosis (35 osteoporotic women with metabolic syndrome and 22 osteoporotic women without metabolic syndrome) and group (2)- control group included 55 postmenopausal women without osteoporosis and metabolic syndrome. A serum sample was taken from each woman and analysed for assessing chemerin, deoxyypyridinoline, fasting serum glucose, and lipid profile. We found a significant increase (p -value <0.001) in the mean value of serum chemerin and deoxyypyridinoline levels in patients compared to controls. In conclusion, chemerin is an adipose tissue marker associated with metabolic syndrome and may have an impact on bone turn over and development of metabolic bone disease which enhanced by the strong positive correlation between chemerin and bone resorption marker (deoxyypyridinoline).

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INTRODUCTION

Metabolic syndrome and osteoporosis are two common health problems worldwide. Metabolic syndrome is a cluster of medical conditions com-

posed of abdominal obesity, hyperglycemia, hypertension, and lipid abnormalities, in which each can affect bone in different ways (Wong et al., 2016).

Osteoporosis is a metabolic bone disease characterized by decreased bone mass and reduce bone strength leading to bone fragility and fracture (Sugimoto et al., 2016). Bone fragility is assessed by the micro-architectural quality which is determined by bone features, i.e. micro-architecture, micro-damage and remodelling rate which affect the ability of bone to resist fracture (Kuo and Chen, 2017, Amjed Haseeb Khamees, 2018).

Bone markers are produced during the bone remodelling process which involved bone formation markers, bone resorption markers, and bone turnover regulators. These markers may be enzymes,

proteins or byproducts during the bone remodelling process(Liu and Webster, 2016; Shawkat et al., 2018). Deoxyypyridinoline is a molecule act to stabilise collagen via cross-linking between collagen peptides(Seibel, 2005). During the degradation process, collagens-cross-linked are proteolytically broken down, and deoxyypyridinoline is secreted into the blood and then excreted to urine, so deoxyypyridinoline is regarded as bone resorption marker(Kuo and Chen, 2017).

Adipose tissue is an endocrine organ in which releases various adipokines. Thereby, enhance the linkage between adipose tissue and the metabolic function of other organs, i.e. bone(Waki and Tontonoz, 2007). Several adipokines have been assumed to be included in bone metabolism by various impacts on bone formation or resorption(Musso et al., 2013). In contrast, bone also represents the source of active molecules included in energy metabolism and then linked with the anabolism or catabolism of adipose tissue(Chen and Yang, 2015).

Chemerin is a molecule secreted by adipocyte, which has an important function in adipogenesis, adipocyte differentiation, insulin signalling pathway(Goralski et al., 2007) as well as linked with obesity and metabolic disturbance(Yilmaz et al., 2011). Additionally, chemerin acts as a pro-inflammatory factor that enhances releasing of pro-inflammatory cytokines which influences insulin sensitivity of adipose tissue and distal organs, i.e. liver and skeletal muscle(Bozaoglu et al., 2007). Bones and skeletal muscles interacted with each other and regarded as one unit. So, chemerin may have an important effect on the muscle-fat-bone axis(He et al., 2015). This study aimed to examine the association between metabolic syndrome and metabolic bone disease (osteoporosis) by measuring adipose tissue marker (chemerin) and bone resorption marker (deoxyypyridinoline) in the serum of osteoporotic postmenopausal women with and without metabolic syndrome.

MATERIALS AND METHODS

This case-control study included 112 postmenopausal women from 51 to 67 years of age. All women were selected from the Osteoporosis Clinic in Al- Yarmouk Teaching Hospital during the period from December 2017 to April 2018. Informed written consent was taken from each postmenopausal women.

Women were divided into two groups: group (1) patients group included 57 postmenopausal women with osteoporosis (35 osteoporotic women with metabolic syndrome and 22 osteoporotic women without metabolic syndrome), and

group (2) control group included 55 postmenopausal women without osteoporosis and metabolic syndrome.

Women with osteoporosis were diagnosed by dual-energy X-ray absorptiometry (DEXA). Women considered having osteoporosis when bone mineral density (BMD) is less than or equal to 2.5 standard deviations below that of a young adult reference population. This is translated as a T-score.

The World Health Organization has established the following diagnostic guidelines(WHO, 1994):

- T-score -1.0 or greater is "normal".
- T-score between -1.0 and -2.5 is "low bone mass" (or "osteopenia").
- T-score -2.5 or below is osteoporosis.

However, women were classified to have metabolic syndrome if any three of the following were presented: Abdominal obesity (waist circumference >88 cm), triglycerides (TG) ≥ 150 mg/dL (1.7 mmol/L), high density lipoprotein-cholesterol (HDL-C) <50 mg/dL (1.29 mmol/L), fasting blood glucose (FBS) ≥ 110 mg/dL (6.1mmol/L), and blood pressure $\geq 130/85$ mmHg(ATPIII, 2001).

Regarding the selection of individual; both patients and controls with the following criteria were excluded from this study: Alcoholic, smoker, had disease that influence bone metabolism such as (Osteomalacia, Paget's disease, hyperparathyroidism, thyrotoxicosis, rheumatoid arthritis, ankylosing spondylitis, or renal, liver, and gastrointestinal tract diseases), and they were taking medication that influences bone turnover such as (Corticosteroid, L-thyroxine, anticoagulants, aluminium-containing antacids, and thiazolidinedione).

Serum specimens were drowning from each woman after overnight fast and were analyzed to assess chemerin by enzyme-linked immunosorbent assay (ELISA) kit (Ray Bio Company), deoxyypyridinoline by ELISA kit (Kamiya Biomedical Company), FBS by spectrophotometer using kit supplied by (Human Company), and lipid profile (total cholesterol, TG, and HDL-C by spectrophotometer using kits manufactured by (Human Company). However, low-density lipoprotein-cholesterol (LDL-C) and very low-density lipoprotein-cholesterol (VLDL-C) were calculated by the following equations:

$$LDL - c = total\ Cholesterol - (VLDL - HDL)$$

$$VLDL - c = \frac{TG}{5}$$

Furthermore, body mass index (BMI) was calculated as weight in kilograms per height (square

meter) [weight/ (height)²]. Women were considered as normal weight when BMI (18.5-24.9 kg/m²), overweight when BMI (25-29.9 kg/m²) and obese as BMI >30kg/m²(WHO, 2004).

Ethical Clearance

Informed written consent was obtained from all the participants in the study, and the study and all its procedure were done in accordance with the Helsinki Declaration of 1975, as revised in 2000. The study was approved by the College of the Medicine / University of Baghdad.

Statistical analysis

Analysis of data was achieved by using SPSS-20 (Statistical Packages for Social Sciences- version 20). Data were presented as a number, percentage, mean, standard deviation, and range. The significance of the difference of different means (quantitative data) was assessed by using Students t-test for difference between two independent means. However, the significance of the difference between different percentages (qualitative data) was assessed by using Pearson Chi-square test (χ^2 -test).

RESULTS

The results of this study showed that patients and controls were matching for age, BMI, and WC. However, a significant increase in the mean value of serum total cholesterol, TG, LDL-C, VLDL-C, FBS, chemerin, and deoxyypyridinoline with a significant decrease in mean value of serum HDL-C levels in patients compared to controls as demonstrated in Table1.

In addition, the mean value of age, BMI, WC, total cholesterol, TG, HDL-C, LDL-C, VLDL-C, FBS, chemerin, and deoxyypyridinoline was calculated according to patients have both osteoporosis and metabolic syndrome and patients with osteoporosis only as demonstrated in Table 3.

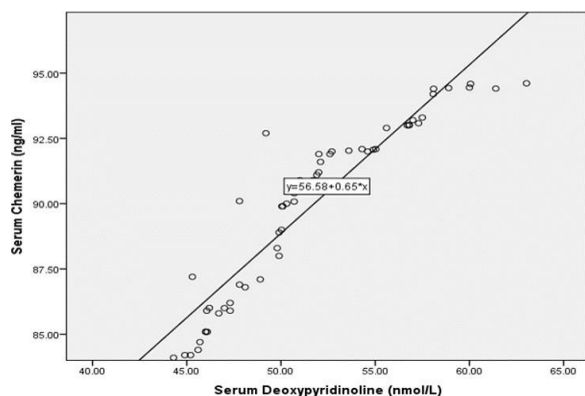


Figure 1: scatterplot between serum chemerin and deoxyypyridinoline in patients group

Moreover, a significant positive correlation was found between serum chemerin and serum deoxyypyridinoline ($r=0.867$, p -value <0.001) in the patient's group as illustrated in figure 1.

DISCUSSION

This study revealed that higher serum levels of chemerin and deoxyypyridinoline inpatient group than the control group. Also, after classification of patients according to have both osteoporosis and metabolic syndrome and having osteoporosis only, higher serum chemerin and deoxyypyridinoline levels were found in patients with osteoporosis and metabolic syndrome than in patients with osteoporosis only. Furthermore, serum chemerin levels positively correlated with serum deoxyypyridinoline inpatient group.

The present study also found that the occurrence of osteoporosis was higher among postmenopausal women with metabolic syndrome in agreement with other studies(Jeon et al., 2011, Yilmaz, 2012, Moon et al., 2012). Because of adipocytes and osteoblasts are mainly derived from a mesenchymal stem cell in the bone marrow, osteoporosis and metabolic syndrome could have a common relation(Sharma et al., 2014). Adipocytes secrete adipokines such as chemerin, resistin, leptin, and visfatin that affect bone metabolism, mineral metabolism, and activity of osteoblast and osteoclast(Muruganandan and Sinal, 2014, Oh et al., 2005). Prior studies reported that adipokines might linked with a metabolic bone disease such as osteoporosis(Lubkowska et al., 2014; Mohiti-Ardekani et al., 2014).

Also, previous researches studied the linkage between bone health and metabolic syndrome. Lower vertebral, femoral neck and hip BMD were found in individuals with metabolic syndrome in relation to those without metabolic syndrome(Hwang and Choi, 2010, von Muhlen et al., 2007) suggested that metabolic syndrome might be another risk factor for osteoporotic fracture(Hwang and Choi, 2010).

A study by Yaturu et al. observed that both metabolic syndrome and diabetes are independently related to lesser BMD and higher prevalence of osteoporosis(Yaturu et al., 2009). Besides, an experiment performed by Pirih et al. showed that decreasing in the bone surface and bone volume in hyperlipidemic mice, assuming the occurrence of impaired bone remodelling (Pirih et al., 2012).

The association between metabolic syndrome and osteoporosis may be explained by increasing fat mass due to an increase in body weight led to a high risk of osteoporosis. Adipose tissue act as energy storage and release a variety of hormones

Table 1: Mean value of age, BMI, WC, total cholesterol, TG, HDL-C, LDL-C, VLDL-C, FBS, chemerin, and deoxy pyridinoline in patients and controls

Parameters	Patients (n=57)	Controls (n=55)	p-value
Age (years)	60.12±5.09	59.31±3.55	0.327
BMI (kg/m ²)	30.66±1.93	30.39±1.43	0.396
WC (cm)	96.53±5.12	96.2±4.3	0.716
Cholesterol (mg/dl)	207.15±27.88	178.44±7.1	<0.001
TG (mg/dl)	152.76±16.55	134.66±5.03	<0.001
HDL-C (mg/dl)	47.26±7.44	58.42±1.93	<0.001
LDL-C (mg/dl)	129.35±31.57	93.09±7.04	<0.001
VLDL-C (mg/dl)	30.55±3.31	26.93±1.01	<0.001
FBS (mg/dl)	137.62±39.1	92.39±2.76	<0.001
Chemerin (ng/ml)	89.87±3.35	77.65±1.43	<0.001
Deoxy pyridinoline (nmol/L)	51.57±4.83	36.62±1.18	<0.001

Table 2: Number and percentage of osteoporotic women with and without metabolic syndrome

Osteoporotic Women with Metabolic Syndrome		Osteoporotic Women without Metabolic Syndrome		p-value
No	%	No	%	
35	61.4%	22	38.6%	<0.001

Table 3: assessment of demographic and laboratory parameters in osteoporotic women with and without metabolic syndrome

Parameters	Osteoporotic Women with Metabolic Syndrome (n=35)	Osteoporotic Women without Metabolic Syndrome (n=22)	p-value
Age	59.97±5.16	60±4.95	0.984
BMI	30.9±2	30.3±1.82	0.26
WC	96.8±5.33	95.95±4.95	0.552
Cholesterol (mg/dl)	226.79±13.47	175.39±7.52	<0.001
TG (mg/dl)	165.45±5.52	132.98±3.27	<0.001
HDL (mg/dl)	41.63±2.13	56.2±1.93	<0.001
LDL (mg/dl)	152.07±13.76	92.59±6.87	<0.001
VLDL (mg/dl)	33.09±1.1	26.6±0.65	<0.001
FBS (mg/dl)	152.07±13.76	92.59±6.87	<0.001
Chemerin (ng/ml)	92.27±1.56	86.13±1.5	<0.001
Deoxy pyridinoline (nmol/L)	54.8±3.75	47.14±1.73	<0.001

and inflammatory mediators such as adipokines, tumour necrosis factor- α , interleukin-1 β , interleukin-6, and C-reactive protein (Calder et al., 2011). So, elevation of pro-inflammatory cytokines enhances osteoclast differentiation and bone degradation via activation of receptor activator of NF- κ B ligand (Rankl)/receptor activator of NF- κ B (Rank)/osteoprotegerin (OPG) pathway (Khosla, 2001, Campos et al., 2012).

In addition, lipid abnormalities may cause high levels of oxidised lipids. Lipids oxidation enhances the upregulation of peroxisome proliferator-activated receptor- γ (PPAR- γ). This is a member of the nuclear receptor family of transcription factors that found in adipocytes and stimulate adipocyte differentiation and proliferation as well as suppress osteoblast formation (Lecka-Czernik et al., 2002).

CONCLUSION

Chemerin is an adipose tissue marker associated with metabolic syndrome and may have an impact on bone turn over and development of metabolic bone disease which enhanced by the strong positive correlation between chemerin and bone resorption marker (deoxy pyridinoline).

Conflicts of interests

The author has none to declare

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