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Association between serum uric acid level and bone mineral density in postmenopausal Iraqi women.

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Abstract

Background: Uric acid is the final product of purine metabolism and is synthesized mainly in the liver and intestine, from xanthine, by the action of xanthine oxidoreductase. The serum uric acid concentration is the result of equilibrium among various factors: dietary intake, endogenous synthesis, and renal excretion. **Objective:** This study was evaluated the association between serum uric acid level and bone mineral density in postmenopausal Iraqi women in whom the risk of cardiovascular disease is increased. **Patients and methodologies:** In this study, a descriptive cross-sectional study was applied to study the association between serum uric acid level and bone mineral density in postmenopausal Iraqi women from 2nd March 2021 to 5th June 2022. Data were collected for 190 patients in different hospitals in Iraq, where the patients were divided into three groups, the first group of patients, which included patients Q1, which included 72, and the second group, which have 53 patients, called the Q2 group, as well as in the third group Q3 that contain 65 patients. A statistical study was conducted for patients using the SPSS program. **Discussion and analysis:** The last consequence of purine metabolism is uric acid, which was formerly thought to be a waste byproduct. The possibility of an independent relationship between hyperuricemia and BMD and fractures suggests that serum UA plays a protective function in bone diseases. Hypouricemia and multiple sclerosis are related. Both a trend toward BMD modifications according to blood uric acid levels in the spine and femoral neck, as well as no significant connection among baseline, which are levels into serum uric acid as well as BMD, were discovered. The average serum uric acid levels did not differ between HRT users and nonusers or between users and non-users of bisphosphonates. Our study shown that serum Ca, Cr, and Tc positively impact on patients at least osteopenia while negatively impact on Osteopenia patients.
Additionally, in postmenopausal women, a favorable correlation among serum Ca concentrations and BMD was found. In T2DM patients, an antioxidant activity played a significant mediating role between calcium levels and BMD. **Conclusions:** our results showed that levels of Serum Ca, Cr, and TC were negatively related to osteopenia in hospital-based T2DM patients, which may be useful on osteopenia patients. According to this study, there is no connection between postmenopausal women's levels of blood uric acid and BMD. Future studies would face difficulty in determining the impact and mode of the effect of bisphosphonates are upon serum uric acid in postmenopausal women using HRT.

Keywords: Uric acid; T2DM; Serum Ca; Serum Ua; Spine; and BMD.

Introduction

Uric acid is the final product of purine metabolism and is synthesized mainly in the liver and intestine, from xanthine, by the action of xanthine oxidoreductase [1]. The serum uric acid concentration is the result of

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equilibrium among various factors: dietary intake, endogenous synthesis, and renal excretion. Because human beings are incapable of catabolizing it into compounds with greater solubility due to the lack of the enzyme's urate oxidase or uricase, its concentration is higher compared to other mammals. This characteristic facilitates its antioxidant properties because it neutralizes different pro-oxidant molecules: hydroxyl radicals, hydrogen peroxide, and peroxynitrite. However, under certain conditions, it acquires pro-oxidant properties. [2,3]

A bone disorder known as osteoporosis causes abnormally weak bones, which increases the risk of bone breakage. Postmenopausal women are more susceptible to this illness. Aging, reduced physical activity, caffeine and alcohol use, smoking, steroid usage, thyroid illness, diabetes, and a lack of estrogen [4], particularly in menopausal women, are risk factors for the onset of osteoporosis. A research study using an experimental animal model found that antioxidants might stop bone loss because estrogen insufficiency is linked to oxidative stress. [6,7]

Humans include a variety of natural antioxidants, such as albumin, bilirubin, and uric acid. According to studies, bilirubin inhibits oxidation, albumin maintains the overall antioxidant state, and uric acid neutralizes free radicals. Uric acid is the most prevalent of these natural antioxidants and eliminates two-thirds of the free - radicals of plasma [7,8]. Much research has looked at the connections between uric acid, oxidative stress, and osteoporosis. The difference in uric acid levels between postmenopausal and perimenopausal women had an impact on osteoporosis development. Moreover, uric acid has a stronger antioxidant impact than vitamins or even other enzymatic antioxidants. [9,10]

The high concentrations of uric acid and its low solubility facilitate the formation of crystals in the joints and, thus, the appearance of gout, which is characterized by pain and inflammation in the affected area. The sustained elevation of acid concentrations of uric acid can induce kidney damage. Increased levels of uric acid are related to various risk factors for cardiovascular disease: insulin resistance, systemic inflammation, oxidative stress, obesity, hypertension, and dyslipidemia. Prospective studies have been published showing the association between baseline hyperuricemia and cardiovascular and all-cause mortality. [11,12]

Uric acid concentrations are higher in men than in women; they remain stable throughout life. In women, they increase with spontaneous or surgical menopause, independently of age [13]. Everything seems to indicate that estrogens promote more efficient renal clearance of urate, which leads to a lower serum uric acid concentration.8 It has also been identified that Most women with gout are postmenopausal and that hormone therapy lowers uric acid levels. [14,15]

With menopause, impacts and changes of the body composition which occur into favor of within the accumulation of fat to the abdominal region, a circumstance that increases the risk of cardiovascular disease. This redistribution is accompanied by changes in the secretion of various hormones produced in adipose tissue: leptin and adiponectin. [16,17,18]

There is a relationship between intra-abdominal visceral fat and uric acid. The mechanisms that explain this relationship are increased production of uric acid together with increased triglyceride synthesis and decreased excretion due to the effect of insulin in the urinary tract. [19,20]

Based on the above, the objective of this study was: to evaluate the Association between serum uric acid level and bone mineral density in postmenopausal Iraqi women in whom the risk of cardiovascular disease is increased

Patients and Methods

In this study, a descriptive cross-sectional study was applied to study the association between serum uric acid level and bone mineral density in postmenopausal Iraqi women from 2nd March 2021 to 5th June 2022. Data were collected for 190 patients in different hospitals in Iraq, where the patients were getting by three groups, where the first group of patients, which included patients Q1, which included 72, and the second group, which have 53 patients, called the Q2 group, as well as in the third group Q3 that contain 65 patients. This study was examined and analysis by the program SSPS. This study was progressed with baseline features of the women patients, which have Age (mean ±SD), Body mass index (kg/m^2), Abdominal obesity, Body fat mass, and Comorbidities that include diabetes, hypertension, asthma, as well as health complications associated with osteoporosis that contain fractures and deformities, osteoporosis, and heart failure, and Economy level which are low, middle, high and all these features can be seen in **Table 1**. To follow-up, this study was examined laboratory data of women patients which represent Serum Ca, Serum phosphate, Hb1AC (%), Cr, TC, TG,

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HDL, LDL, AST, WBC, and HGB that, can be shown in **Table 2**. Besides to that, our study was added to check of the healthy results related to women patients, where can present with three UA quantiles which are Q1, Q2, and Q3 can be check in **Table 3**.

Furthermore, this study included distributions of BMD based on the levels of serum uric acid with two parameters, spine and femoral neck where it, was shown in **Figure 1**. As well as our data was evaluated with a logistic evaluation of outcomes related to women patients were based on the basic parameters, which are Q1, age, Q3, Q2, and obesity, which it shown in **Table 4**. Finally, our study was evaluated to the evaluation of disadvantage outcomes for women patients, where see all these in **Table 5**.

Results

Table 1: Baseline features of the women patients.

Variables	**Q1 group (n=72)**	**Q2 group (n=53)**	**Q3 group (n=65)**
Age (mean ±SD)	3.43 ± 0.55	4.43 ± 0.23	5.64 ± 0.67
Body mass index (kg/m^2)	21.5 ± 2.75	23.1 ± 3.0	23.7 ± 2.4
Abdominal obesity	0.83 ± 0.055	0.83± 0.055	0.87 ± 0.034
Body fat mass	32.4 ± 6.44	35.4 ± 6.3	34.2 ± 5.7
Comorbidities			
diabetes	27 (37.50%)	14 (2.14%)	16 (24.62%)
Hypertension	23 (31.94%)	12 (1.84%)	21 (32.31%)
asthma	22 (30.56%)	27 (4.13%)	28 (43.08%)
Health complications associated with osteoporosis			
Fractures and deformities	15 (20.8%)	13 (24.53%)	17 (26.15%)
Osteoporosis	26 (36.11%)	18 (33.96%)	25 (38.46%)
Heart failure	31 (43.06%)	22 (41.51%)	23 (35.38%)
Economy level			
Low	18 (25.00%)	14 (26.42%)	16 (24.62%)
Middle	25 (34.72%)	20 (37.74%)	19 (29.23%)
High	29 (40.28%)	19 (35.85%)	30 (46.15%)

Table 2: Laboratory data of women patients

Variables	**Q1 group**	**Q2 group**	**Q3 group**
Serum Ca (mmol/L)	2.325 ± 0.13	2.331 ± 0.13	2.345 ± 0.13
Serum phosphate (mmol/L)	1.132 ± 0.142	1.132 ± 0.142	1.172 ± 0.142

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Hb1AC (%)	6.855 ± 1.33	6.725 ± 1.11	6.87 ± 1.11
Cr (μmol/L)	72.731 ± 19.66	76.33 ± 17.86	81.72 ± 15.43
TC (mmol/L)	4.72 ± 1.15	4.62 ± 1.01	4.67 ± 1.21
TG (mmol/L)	1.834 ± 3.734	1.76 ± 1.66	1.862 ± 1.52
HDL (mmol/L)	1.273 ± 0.34	1.247 ± 0.35	1.182 ± 0.284
LDL (mmol/L)	2.932 ± 0.87	2.90 ± 0.88	2.968 ± 0.87
AST (U/L)/ALT (U/L)	1.033 ± 0.375	0.997 ± 0.33	1.02± 0.34
WBC	6.44 ± 1.66	6.57 ± 1.65	7.01 ± 1.62
HGB (g/L)	145.44 ± 13.86	147.84 ± 14.17	148.77 ± 14.33

Table 3: The healthy results related to women patients.

UA quantile	**Osteopenia**	**Osteoporosis**	**At least osteopenia**
Q1	7 (9.72%)	4 (13.50%)	17 (18.75%)
Q2	5 (9.43%)	2 (17.80%)	15 (33.58%)
Q3	4 (6.15%)	1 (9.47%)	12 (14.57%)

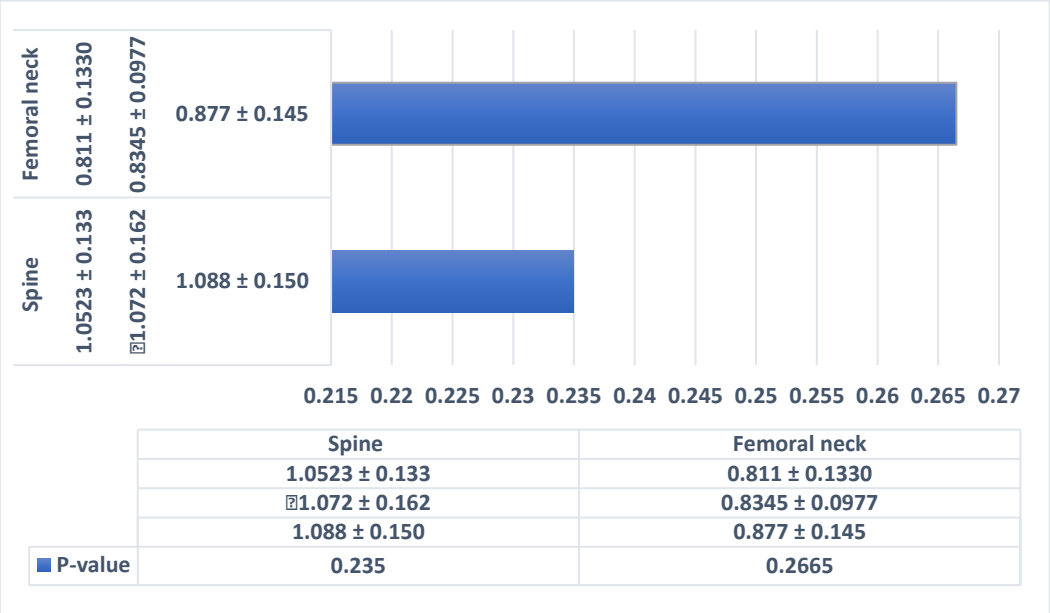

Figure 1: Distributions of BMD based on the levels of serum uric acid.

Table 4: Logistic evaluation of outcomes related to women patients.

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UA quantile	Patients	P-value
Q1	(3.9-8.1) 5.8	0.0002
Age	(2.5-6.3) 4.4	0.0001
Q3	(0.9-1.3)1.1	0.621
Q2	(0.85-1.45) 1.56	0.063
Obesity	(0.773-1.56) 1.44	0.0611

Table 5: Evaluation of disadvantage outcomes for women patients.

	Disadvantages outcomes	Q1	Q2	Q3
R correlation	1	0.9	0.8	0.652
Sig	1	0.009	0.04	0.613

Discussion

The last consequence of purine metabolism is uric acid, which was formerly thought to be a waste byproduct. The possibility of an independent relationship between hyperuricemia and BMD and fractures suggests that serum UA plays a protective function in bone diseases. [21,22,23]

Hypouricemia and multiple sclerosis are related. Both a trend toward BMD modifications according to blood uric acid levels in the spine and femoral neck, as well as no significant connection among which are the baseline of levels of serum uric acid as well as BMD, were discovered. The average serum uric acid levels did not differ between HRT users and nonusers or between users and non-users of bisphosphonates. [24]

In a hospital- a group of T2DM patients, this study found a negative correlation between increased blood Ca, Cr, and TC levels at osteopenia, and this connection was unrelated to other potential risk factors.

Numerous researchers have hypothesized the association between serum UA, diabetes, and at least osteopenia based on earlier investigations, but there hasn't been agreement on this issue. One study found no evidence that increased serum UA had a protective impact on bone health. Although our study presented the previous studies of other studies about serum UA and its effect on diabetes for patients with at least osteopenia, however, our study shown that serum Ca, Cr, and Tc positively impact on the patients with at least osteopenia while negatively impact on Osteopenia patients. [25,26]

Our investigation has confirmed similar findings. The unfavorable correlation between serum UA and at least osteopenia can be attributed to a number of causes [27,28]. In humans, purine nucleosides and free bases are degraded by the enzyme serum calcium, which contributes for around half of the antioxidant qualities of human plasma [29]. Its antioxidant properties might be a significant factor in its ability to protect against osteopenia. [30]

Additionally, in postmenopausal women, a favorable correlation among serum Ca concentrations and BMD was found. In T2DM patients, an antioxidant activity played a significant mediating role between calcium levels and BMD.

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Conclusions

In conclusion, our results showed that levels of Serum Ca, Cr, and TC were negatively related to osteopenia in hospital-based T2DM patients, which may be useful on osteopenia patients. According to this study, there is no connection between postmenopausal women's levels of blood uric acid and BMD. Future studies would face difficulty in determining the impact and mode of the effect of bisphosphonates are upon serum uric acid in postmenopausal women using HRT.

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