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Original Article

Impact of Bone Mineral Density on the Recurrent Urolithiasis

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H I G H L I G H T S

• Patients with calcium metabolism deficiencies are compatible for Urolithiasis.
• Reduction of bone density in patients with recurrent urinary stone can be the sign of bone metabolism deficiency.
• Patients with urinary stones are not recommended to use calcium.

A B S T R A C T

Introduction
As it seems, patients with urinary stones have calcium metabolism deficiencies which lead to excessive calcium absorption from their bones. This phenomenon may expose these individuals to osteoporosis. This study was performed to evaluate the bone mineral density (BMD) in patients with urinary stones in Iran.

Methods
This study is an analytical case-control study performed in Sina hospital from March 2016 to January 2018. Twenty-four male patients between the ages of 30 and 50, who had recurrent urinary tract stones were enrolled in the study. The control group was selected from the same age and sex group with no history of urinary stone formation. The diet was similar in the two groups. The sampling method was non-random. Age and body mass index (BMI) were considered as confounding variables. After completing the questionnaire, BMD of the lumbar spine (L4 L2) and the femoral neck were measured. The data were analyzed using linear regression and t-test.

Results
In both regions, BMD was significantly lower in patients compared to the control group (p-value<0.01). Besides, there was a significant correlation between duration of urinary stone and BMD in each of the mentioned areas (p-value<0.001, r=-0.73 in the lumbar spine, p-value<0.01 and r=-0.52 in the femoral neck). Additionally, BMD showed no association with age and BMI in any of the areas.

Conclusions
Reduction of bone density in patients with recurrent urinary stones may indicate a primary impairment in bone metabolism of these individuals. Considering that 30% of patients have osteopenia and, in general, patients with urinary stones are not allowed to use calcium, it is necessary to eliminate calcium from their diets only after complete analysis.

Keywords: Osteoporosis; Urine; Stone; Bone Mineral Density

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Introduction

The prevalence of urinary stones ranges from 2 to 3 percent in different communities (1). Calcium stones make up to 80 to 85 percent of urinary stones (2). The exact cause of the formation of these stones is unknown. Researches show that about 90 percent of patients with urinary stones have some form of metabolic disorder. These disorders which are involved in the development of urinary stones include hypercalciuria, hyperuricosuria, hyperoxaluria, and hypocitraturia (3).

Fass et al., showed that patients with urinary tract stones had a significantly lower bone mineral content (BMC) compared to healthy subjects. The exact cause of this phenomenon is unclear, however, it is obvious that patients with urinary tract stones also have severe skeletal problems. Primary disorder in bone metabolism is suggested as one of the mechanisms that explain bone density reduction in patients with urinary tract deficiency with low calcium diet (4).

Since no research has been done on the correlation of urinary tract stones with bone mineral density in Iran, we decided to conduct this study to determine the relationship between bone density and urinary stone disease duration.

Methods

We selected 24 male patients ages between 30 to 50 years from those patients who were referred to Sina Hospital's kidney stone removal section from March 2016 to January 2018 and were diagnosed with a recurrent urinary stone (diagnosed more than once) with imaging techniques (radiography or ultrasound). The patients had no confounding factors affecting bone mineral density (BMD) such as thyroid disease or corticosteroid usage. Patients who applied calcium restriction in their diet and those who had been in bed for a long time were excluded from the control study. To conduct an analytical case-control study, the control group which consisted of 24 men was selected from the patients who were referred to Sina Hospital at the same time interval and was in the same age group as the control group but without any history of urinary tract stones. The sampling method was non-random (Available samples).

Height and weight were measured for all the samples. Body mass index (BMI) was calculated by dividing the weight by the square of the height. BMD of lumbar spine L2-L4 (BMD LS) and femoral neck (BMD FN) were measured in patients and controls using the dual-energy x-ray absorptiometry (DXA) technique and expressed in milligram per square centimeter. The duration of the disease was calculated as the intervals between the first clinical presentation or the diagnosis of a stone presence until the BMD was measured and expressed in months.

Osteopenia and osteoporosis in the study group were determined according to the criterion T score which compares BMD with the mean BMD in the control group of 20-40 years. BMD values that were less than (-1) and (-2/5) standard deviation were considered as osteopenia and osteoporosis, respectively.

The study was under the Tehran University of Medical Sciences Ethical Committee (IR.TUMS.VCR.REC.1398.835).

We utilized SPSS-12 software and the data were analyzed with t-test, and linear regression.

Results

Table 1 shows the mean values of age, duration of urinary tract stones, and bone density in each region. The bone density in patients was 11% lower than the control group. Femoral bone density showed a similar decrease (12%) in this group.

To evaluate the bone density in both of the groups, covariance analysis was used to adjust age and BMI which are confounding variables. The difference between BMD FN and BMD LS in patients and the control group was significant (p-value<0.01). Additionally, according to covariance analysis results, BMD FN and BMD LS were not influenced by BMI and age.

The findings of the present study showed that 8 and 9 patients had osteopenia in the lumbar spine and neck, respectively. In the control group, these numbers were 3 and 4, respectively. There was no osteoporosis in any of the subjects. Linear regression analysis showed a significant correlation between BMD LS values and duration of urinary stone (p-value<0.001, and r=-0.73).

Table 1. Mean and standard deviation of age, BMI, duration of urinary stone, BMD LS, and BMD FN in patients with urinary stone and control group

Evaluated parameters	Patients (Number=24)	Control (Number=24)	p-value
Age (Years)	38.4±6.7	39.3±6.8	--
BMI (Kg/m2)	26±3.75	25±4.5	--
Disease duration (Months)	26±2.5	--	--
BMD LS (mg/cm2)	1018±168	1153±155	0.0037
BMD FEM (mg/cm²)	888±117	1017±144	0.0018

BMI: Body Mass Index; BMD: Bone Mineral Density; BMD FN: Bone Mineral Density Femoral neck; BMD LS: Bone Mineral Density Lumbar Spine
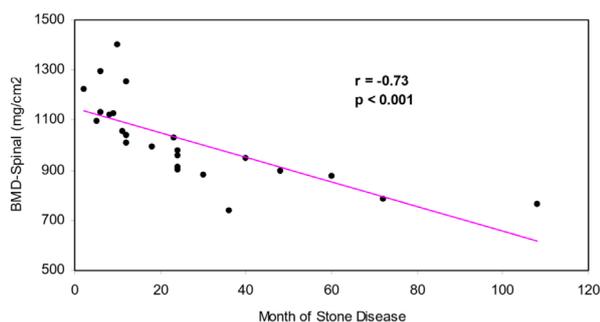
Figure 1. Correlation of BMD spine and duration of urinary stone in 24 patients with urolithiasis
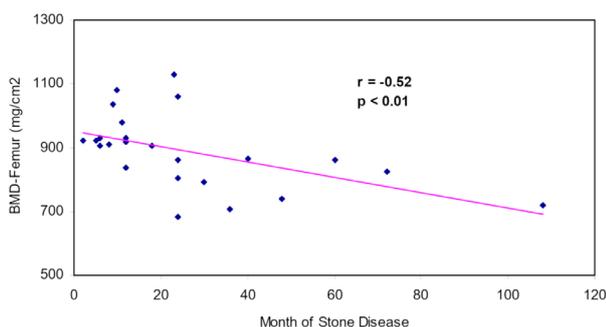

Figure 2. Correlation of BMD femur and duration of urinary stone in 24 patients with urolithiasis

In the case of BMD FN, this correlation was less notable (p-value <0.01, and r=-0.52) (Figure 1 and 2).

Discussion

Osteoporosis, the most common type of metabolic bone disease, is associated with a decrease in bone mineral and matrix. This disorder can be diagnosed by demonstrating typical fractures or by measuring bone mineral density. Multiple techniques are available to measure bone density in the axial and appendicular skeleton, but in most patients, the DXA method is preferred for measuring BMD. High accuracy, low radiation, low investigation time, and cost-effectiveness of DXA make this technique superior to other methods.

For the first time, Alhava et al., demonstrated a decrease in bone mineral density in patients with lithotripsy using a 2D gamma-ray attenuation technique (5). It is shown that Protease inhibitor-associated bone mineral density loss is related to hypothyroidism and related bone turnover acceleration (6).

Pietschmann F et al., measured BMD of the lumbar spine and trunk radius of patients with urolithiasis using DXA in 1992 (7). The BMD of lumbar vertebrae was much lower in patients with hypercalciuria than in non-hypercalciuric patients. This study confirms the osteopenia of trabecular bones in patients with hypercalciuria (8).

In our study, only male patients aged 30-50 years were studied, and therefore factors affecting bone density such as menopause or inadequate bone growth were excluded. The results showed a significant decrease in BMD LS and BMD FN in the patients compared to the control group (p-value<0.001). This reduction appears to be mainly due to bone metabolism abnormalities in these patients.

Other studies have similarly measured bone density in patients with urinary stones and showed a significant difference in bone mineral density of these patients compared to normal subjects (9). These studies have been performed using methods such as radiological photodensitometry, micro densitometry, calcium kinetic studies, neutron activation analysis, and histomorphometric analysis (10, 11).

Non-invasive techniques that make it easier to study bone density are currently available (12). Examination of bone density was also performed by single-photon absorption technique in forearm bones (13, 14), dual photon absorption (15, 16), dual-energy radiographic absorption (17, 18) and quantitative computed tomography (19), in the lumbar spine, and showed similar results to our study. Also, some of these methods such as dual photon absorption are applied to classify types of idiopathic hypercalciuria (20).

Some studies showed that the history of affection to urinary stone was significantly longer in people with reduced BMD in the lumbar spine than those with normal BMD (21, 22). We also found a similar result.

Wardle E et al., in 1985 described the increase in bone turnover as the scientific justification of osteopenia in patients with urolithiasis (23). Moreover, the correlation between osteoporosis and calcium urolithiasis in the adult population was highlighted (24).

Given that many of these people, based on an old belief, limit their consumption of dairy foods, they are unfortunately at high risk for osteoporosis and its associated complications. Therefore, therapeutically limiting diary regimes in patients with urinary stones is not recommended.

Conclusions

Various references recommend metabolic examinations for all the patients who are active in stone formation (which means that in a year stone excretion has happened more than once or a second stone has been formed or stone volume has increased). According to the result of these examinations, if calcium metabolism was impaired, bone density measurement should be performed for them. Also, their underlying disease needs to be carefully evaluated and appropriate treatment recommended to prevent stone formation and possible complications.

Authors' contributions

AM was responsible for study conception and design, EHN provided data, KNJ was responsible for statistical

analysis, FKH and FDT wrote the manuscript.

Ethical statement
The study was under the Tehran University of Medical Sciences Ethical Committee (IR.TUMS.VCR.REC.1398.835).

Data availability
Data will be provided by the corresponding author on request.

Abbreviation
BMC	Bone mineral content
BMD	Bone mineral density
BMI	Body mass index
BMD FN	Bone mineral density femoral neck
BMD LS	Bone mineral density lumbar spine
DXA	Dual-energy x-ray absorptiometry

References

1. Robertson W, Peacock M, Baker M, Marshall D, Pearlman B, Speed R, et al. Studies on the prevalence and epidemiology of urinary stone disease in men in Leeds. British journal of urology. 1983;55(6):595-8.
2. Park S, Pearle MS. Pathophysiology and management of calcium stones. Urologic Clinics of North America. 2007;34(3):323-34.
3. Beara-Lasic L, Goldfarb DS. Recurrent Calcium Kidney Stones. Clinical Journal of the American Society of Nephrology. 2019:CJN. 02550319.
4. Fuss M, Gillet C, Simon J, Vandewalle J-C, Schoutens A, Bergmann PJEu. Bone mineral content in idiopathic renal stone disease and in primary hyperparathyroidism. 1983;9:32-4.
5. Alhava E, Juuti M, Karjalainen PJSjou, nephrology. Bone mineral density in patients with urolithiasis: A preliminary report. 1976;10(2):154-6.
6. Kinai E, Gatanaga H, Mizushima D, Nishijima T, Aoki T, Genka I, et al. Protease inhibitor-associated bone mineral density loss is related to hypothyroidism and related bone turnover acceleration. Journal of Infection and Chemotherapy. 2017;23(5):259-64.
7. Pietschmann F, Breslau NA, Pak CYJJoB, Research M. Reduced vertebral bone density in hypercalciuric nephrolithiasis. 1992;7(12):1383-8.
8. Schwaderer AL, Oduguwa A, Kusumi K. Urinary stone disease in pediatric and adult metabolic bone clinic patients. Urolithiasis. 2018;46(2):173-8.
9. Bartges JW. Feline calcium oxalate urolithiasis: risk factors and rational treatment approaches. Journal of Feline medicine and Surgery. 2016;18(9):712-22.
10. Westropp JL, Lulich J. Medical management of urolithiasis. BSAVA Manual of Canine and Feline Nephrology and Urology: BSAVA Library; 2017. p. 304-10.
11. D'Alessandro C, Ferraro PM, Cianchi C, Barsotti M, Gambaro G, Cupisti A. Which diet for calcium stone patients: A real-world approach to preventive care. Nutrients. 2019;11(5):1182.
12. Chapurlat R, Pialat J-B, Merle B, Confavreux E, Duvert F, Fontanges E, et al. The QUALYOR (QUalite Osseuse LYon Orleans) study: a new cohort for non invasive evaluation of bone quality in postmenopausal osteoporosis. Rationale and study design. Archives of osteoporosis. 2018;13(1):2.
13. Emer MÖ, İnce S, Arslan N. Bone Mineral Densitometry: Measurement and Evaluation Methods. Musculoskeletal Research and Basic Science: Springer; 2016. p. 197-212.
14. Wolman DN, Patel BP, Wintermark M, Heit JJ. Dual-Energy Computed Tomography Applications in Neurointervention. Journal of computer assisted tomography. 2018;42(6):831-9.
15. Mei K, Schwaiger BJ, Kopp FK, Ehn S, Gersing AS, Kirschke JS, et al. Bone mineral density measurements in vertebral specimens and phantoms using dual-layer spectral computed tomography. Scientific reports. 2017;7(1):17519.
16. Cherif R, Vico L, Laroche N, Sakly M, Attia N, Lavet C. Dual-energy X-ray absorptiometry underestimates in vivo lumbar spine bone mineral density in overweight rats. Journal of bone and mineral metabolism. 2018;36(1):31-9.
17. Fredenberg E. Spectral and dual-energy X-ray imaging for medical applications. Nuclear Instruments and Methods in Physics Research Section A: Accelerators, Spectrometers, Detectors and Associated Equipment. 2018;878:74-87.
18. Buckinx F, Landi F, Cesari M, Fieding RA, Visser M, Engelke K, et al. The Authors reply:"Dual energy X-ray absorptiometry: gold standard for muscle mass?" by Scafoglieri et al. Journal of cachexia, sarcopenia and muscle. 2018;9(4):788.
19. Lowitz T, Museyko O, Bousson V, Chappard C, Laouisset L, Laredo J-D, et al. Advanced Knee Structure Analysis (AKSA): a comparison of bone mineral density and trabecular texture measurements using computed tomography and high-resolution peripheral quantitative computed tomography of human knee cadavers. Arthritis research & therapy. 2017;19(1):1.
20. Sakhaee K, Maalouf NM, Poindexter J, Adams-Huet B, Moe OW. Relationship between urinary calcium and bone mineral density

in patients with calcium nephrolithiasis. The Journal of urology. 2017;197(6):1472-7.

21. TRINCHIERI A, NESPOLI R, OSTINI F, ROVERA F, ZANETTI G, PISANI EJTJou. A study of dietary calcium and other nutrients in idiopathic renal calcium stone formers with low bone mineral content. 1998;159(3):654-7.

22. Shavit L, Girfoglio D, Vijay V, Goldsmith D, Ferraro PM, Moochhala SH, et al. Vascular calcification and bone mineral density in recurrent kidney stone formers. Clinical Journal of the American Society of Nephrology. 2015;10(2):278-85.

23. Wardle E, Kurihara I, Saito T, Obara K, Shoji Y, Hirai M, et al. Bone mineral density in patients with hypercalciuric nephrolithiasis. Nephron. 1996;73(4):557-60.

24. Bijelic R, Milicevic S, Balaban J. Correlation of osteoporosis and calcium urolithiasis in adult population. medical archives. 2016;70(1):66.

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