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Association between Renal Stone, Bone Mineral Density and Biochemical Parameters

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Abstract

Background: To investigate the relationship between renal stone formation and osteoporosis.

Methods: Eight hundred thirty healthy subjects aged between 20 and 76 years were randomly selected from 50 clusters to take part in the study. Of these, 68 (8.2%) had a previous history of renal stone disease. All participants underwent clinical examination and bone mineral densitometry of the lumbar spine and femur using the dual-energy X-ray absorptiometry technique. Plasma levels of vitamin D3, calcium, phosphate, alkaline phosphatase, and parathyroid hormone were also measured.

Results: Data showed that patients with a history of renal stones had a higher prevalence of osteoporosis (16.7%) and osteopenia (53.3%) than the subjects without a history of renal stone disease (11.2% and 35.7%, respectively). For both men and women the mean age of patients with a history of renal stone disease was significantly lower than patients with no disease history (men: with history 44.27+/-14.8, without history 50.28+/-12.3; *P*= 0.02) (women: with history 43.21+/-11.8, without history 49.06+/-9.6; *P*= 0.02). Female patients with a history of renal stone disease also had a significantly lower (8.74%) mean spinal bone density (*P*= 0.02), but there were no other significant differences in either the biochemical parameters that were measured or in the hip bone density.

Conclusions: These data suggest that osteoporosis may be more prevalent in those patients that have had a history of renal stone formation.

Keywords: *Renal stone, Osteoporosis, Bone mineral stone*

Introduction

Renal stone formation (urolithiasis) is a common clinical disorder, and has afflicted mankind since antiquity. Its frequency has risen, however, with changes in lifestyle, and its overall prevalence is related to many factors (1, 2).

Studies of renal stone disease have revealed that 90% of patients have a metabolic disorder that could influence bone metabolism, potentially resulting in decreased bone mass and osteoporosis (3) e.g. disorders of calcium and phosphate metabolism (4, 5).

Approximately 75% of all renal stones are calcium-based and 50 to 60% of patients with recurring calcium renal stone formation are known to suffer from idiopathic hyper-calciuria (urinary calcium> 300mg/24 h) (6). Some studies have shown that calcium stone formation can be accompanied with a reduction in bone mass, although this is usually more evident in those with idiopathic hyper-calciuria (6-10). Other studies report a reduction in bone mass both in hyper-calciuric and normo-calciuric renal stone subjects (11-13). However the pathogenesis of bone loss in hypercalciuria patients is not entirely clear (14-16) and there is controversy as to whether these findings are relative to all hypercalciuric patients. Such discrepancies may depend on differences in the criteria used for hypercalciuria classification, different dietary conditions in the patients studied, and differences in the methods used in bone mass evaluation.

Previous studies suggested that a history of renal stone disease may have an important bearing on bone metabolism, and thus be a risk factor for osteoporosis. Recognizing this associa-

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tion could be important for an early diagnosis and prevention of bone loss in renal stone patients. We investigated the relationship between history of renal stone and osteoporosis in the Iranian population.

Materials and Methods

A cross section study was conducted on 830 healthy subjects aged between 20 to 76 yr randomly selected from 50 clusters in 2003 until 2005 in Tehran. 68(8.2%) of participations had a history of renal stones.

Exclusion criteria were any disease, condition or using drug that influence on bone metabolism. Inclusion and exclusion criteria were describe previously by IMOS study (17).

Ten ml of blood was taken from each subject at their home in the period late December to February (when reduced daylight results in lower vitamin D levels). The serum was separated immediately using a portable centrifuge and dispatched to the EMRC for immediate freezing. Serum 25-hydroxyvitamin D3 was measured by radioimmunoassay using an IDS kit (Immunodiagnostic Systems Limited, UK); intra and inter assay coefficients of variation (CV) were 5.2%, 7.5% respectively Parathyroid hormone was measured by immunoradiometric assay using a DiaSorin kit (DiaSorin Inc, Stillwater, USA), with intra and inter assay CV of 6.3%, 5.7% respectively. In the recall process subjects were invited to the EMRC in Shariati hospital where a clinical examination was performed (measuring height, weight, bone deformity (in particular lumbar spine deformity), and muscular sensitivity). A bone density evaluation of the lumbar spine and hip was carried out using the DXA method. If the subjects had been exposed to any radiation or calcium metabolism drugs within five days prior to the study, the BMD was postponed for at least 5 d. All subjects completed a questionnaire examining ethnicity, disease history, drug consumption, physical activity, and exposure to sunlight. An estimation of their calcium and vitamin D intake was based on a 2-day record of food consumption.

Statistical analysis was performed using SPSS (V 11.5), and results expressed as mean +/- standard deviation. The two-tailed t-test and the Mann- Whitney test were used to determine significant differences, and for the comparison of frequencies the X2 and Phisher test were used. The relationship between the mean values was evaluated using liner regression and logistic regression.

Results

Eight hundred thirty subjects participated in this study (39.2% men, 60.8% women) of which 68 (8.2%) had a history of renal stone formation (6.4% of women, and 11.2% of men; *P*= 0.002). furthermore, the frequency of renal stone was significantly higher among women. For both men and women, the mean age of patients with a history of renal stone disease was significantly lower than those without previous history of renal stone (men: with history 44.27+/-14.8, without history 50.28+/-12.3; *P*= 0.02) (women: with history 43.21+/-11.8, without history 49.06+/-9.6; *P*= 0.02). The vertebral bone mineral density in the women with a history of renal stone disease was significantly lower (with history 1.12+/-0.16, without history 1.03+/-0.13; *P*= 0.02). However, there were no other significant differences in the other measured variables, including serum calcium and vitamin D, parathyroid hormone, and bone density in the hip (Table 1).

In women with previous renal stone, ALP and serum vitamin D concentration were 191±75 U/l (*P*= 0.002) and 46 nmol/l (*P*= 0.03) respectively, that were higher than healthy women (54±71 U/l, 35 nmol/l, SD95% 40.05-30.56, respectively). In men there was not significant difference between ALP and serum vitamin D. In the women with previous renal stone frequency of osteopenia and osteoprosis was 53.3%, 16.7%, respectively (35.7% and 11.2% in healthy women respectively), that observed high frequency osteoporosis and osteopenia in the women with previous

renal stone (*P*= 0.04, X2= 6.04). In men no observed significant in the considering subgroups, also in the osteoporotic women was previous renal stone frequency 9.4% that was higher than women with normal BMD (*P*= 0.001). Whereas in the men no observed significant difference in considering subgroups.

In regression analysis after entire age and BMI, there was significant relation between previous history of renal stone and vertebral osteoporosis and osteopeni (*P*= 0.04), but there was not significant this association among the men both in the vertebral and hip area.

Table 1: Baseline characteristics of study participants

	Men			**Women**		
	Without history of renal stone	**with history of renal stone**	***P****	**Without history of renal stone**	**With history of renal stone**	***P****
Age(yr)	44.27±14.8	50.28±12.3	0.02	43.21±11.8	49.06±9.6	0.02
BMI(Kg/m2)	26.04±4.21	27.46±3.6	0.06	27.72±5.42	28.18±4.7	0.1
Vitamin D intake(IU/d)	53.54±59.4	46.7±51.3	0.5	46.5±64	50.4±52.9	0.6
Calcium intake(mg/d)	602.7±404	533.2±330	0.3	554.3±322	568.3±342	0.8
Serum vitamin D(nmol/l)	30.11±30	25.24±12.7	0.3	35.9±50	44.4±30	0.3
Serum calcium(mg/l)	9.7±0.6	9.6±0.54	0.3	9.5±0.58	9.8±0.83	0.1
PTH(pg/l)	26.31±14.9	28.1±12.8	0.4	31.8±21	30.8±19	0.7
Physical activity	11.8%	3.6%	0.16	6.75%	3.7%	0.31
Bone mineral density in spine(g/cm2)	1.16±0.16	1.15±0.17	0.7	1.12±0.16	1.03±0.13	0.02
Bone mineral density in hip(g/cm2)	1.018±0.15	1.014±0.13	0.8	0.95±0.13	0.94±0.11	0.1
Sun exposure(min/d)	77.3±76.5	68.5±59	0.5	44.4±48	53±46	0.3

* *P* value

Conclusions

The prevalence of renal stone disease has been reported as 1 to 5% in Asia, 5 to 9% in Europe, ~13% in North America, and ~20% in Saudi Arabia (18-20). In this study renal stone prevalence was slightly higher than general reported frequency in Asia but same as Middle East countries such as Pakistan and Saudi Arabia, and was consistent with studies performed in these countries (21).

Caudarella et al. reported prevalence of osteopenia and osteoporosis in this group of idiopathic calcium stone formers was 54% and 14% respectively (22), which is consistent with our results. Garcia-Nieto et al. reported that idiopathic hypercalciuria was associated with a decreased Bone Mineral Density (BMD) both in children and adults. Also it was being increasingly recognized that idiopathic hypercalciuria may be a contributing factor to osteopenia and/or osteoporosis in adults (23). The results of our study confirm the previously reported significant reduction in bone mass in patients with renal stones and idiopathic hypercalciuria. This bone loss occurs often in the lumbar spin that consistent some of the other studies (9, 10, 24- 26). In our study the vertebral bone mineral density in the women with a history of renal stone disease was significantly lower than healthy women. Tsuji and et al reported a decrease in bone mineral density was observed in about 27% of patients with lithiasis in both men and women compared to control sub-

jects but there were no significant differences between the patients and the control groups. In female patients with hyper-calciuria, the frequency of low BMD reached 40.5%, showing a significant difference compared to the female normocalciuria group (27).

Consequently, a defective tubular reabsorption of calcium with secondary hyperparathyroidism or a defective tubular reabsorption of phosphate with a low serum phosphate stimulating 1, 25 (OH) vitamin D synthesis could be a possible explanation for the low bone mineral density observed in some patients with calcium kidney stone, but a reduced bone mineral content is also found in calcium renal stone formers without signs of secondary hyper-parathyroidism or alterations of phosphate levels (28). Some of the studies by applying photodensitometric to the proximal radius showed that bone mineral content in patients with previous renal calculi and hypercalciuria was less than one standard deviation below the normal average, whereas the difference between hypercalciuric and normocalciuric renal stone formers was not significant (29, 30), and other studies reported a reduced bone mineral content in calcium renal stone formers without primary hyperparathyroidism (7). In present study one of the exclusion criteria was known endocrine disorders such as hyperparathyroidism. Therefore it is in concordance with studies which analysis this diseases with calcium renal stone formers without primary hyperparathyroidism (24, 29). Epidemiologic studies have demonstrated an increased incidence of kidney stones in individuals with low calcium intake. More recently, a 5-year clinical study showed that the recurrence of kidney stones is higher in stone-formers on a low dietary calcium intake (31).

In agreement with previous studies, some studies reported that the restriction of dietary calcium to prevent kidney stone relapse is a risk factor for negative calcium imbalance and bone demineralization (25, 28, 29). Also these studies suggested that moderate dietary protein restriction proved to be beneficial not only in reducing calcium excretion but also in limiting the entire lithogenic potential in the urine of patients with idiopathic hyper-calciuria and calcium kidney stone. In the present study there significant differences between calcium intake in the people who have previous renal stones and control group. Of course it seems that this difference is due to difference calcium intake and low consumption of this nutrient in the investigation society. In present study daily mean calcium consumption was less than 600 mg, whereas in most studies regarding efficacy of calcium and its association correlation with renal stone and BMD, means daily calcium consumption is higher than 800 and 1000 mg.

Trinchieri et al. in the study on 52 male, with idiopathic calcium renal stone, reported these bone mineral density of lumbar spine, was significantly lower in the group consuming less than 600 mg/day of calcium than in the group consuming more than 1000 mg/day, as so were unable to demonstrate any significant differences in calciotropic hormones and in markers of bone resorption (urinary pyridinium crosslinks and hydroxyproline) between patients on a low calcium diet and patients consuming a normal calcium diet, although 1,25 vitamin D levels tend to be higher in patients on a low calcium diet. In conclusion, long-term dietary calcium restriction may lead to negative calcium balance and bone loss in presence of slightly increased levels of 1,25 vitamin D (28). Also in the present study in patients with previous renal stone BMD in the lumbar spine lower than normal people, so that after adjusting age and BMI, there was a correlation between renal stone with osteoporosis and osteopeni that is consistent with other studies (28).

Totally in the several studies, negative effects of low calcium diets on recurrence of renal stone have been reported.

On the other hand, it is still a common practice to recommend a restriction of oxalate and calcium intake in patients with calcium stones. The prolonged adoption of this diet can lead to a negative calcium balance in the presence of

various pathological conditions related to calcium stone disease: renal hypercalciuria, hypophosphataemia, high levels of 1, 25 vitamins D. It has been observed that in these patients, following a prolonged reduced calcium intake, an increase in alkaline phosphatase levels and urinary excretion of hydroxyproline occurs in the presence of normal values of serum PTH and urinary cAMP (32, 33).

In conclusion it seems that previous renal stone disease is associated with high prevalence of bone loss. Thus we recommend, bone loss evaluation for these patients.

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