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The Study on the Prevalence of Hypercalciuria and Hypercalcemia in patients with Urinary stones

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Urinary stones are one of the common diseases of urinary system. They can impose many clinical problems and complications, as pain, hematuria, urinary tract obstruction, infection, renal failure and hypertention. It is important to study the prevalence of the main metabolic disorders found in patients with diagnosis of urolithiasis in our Country. Appropriate management of these disorders can diminish the recurrence rate of urinary stone. We made a retrospective study on 193 patients with history of the urinary stone that referred to nephrology clinic and surveyed for metabolic disorders. Metabolic study consisted of blood calcium and creatinine levels, in addition to the volume of 24-hour urine creatinine and calcium. The blood parathormone level test was performed in patients suspected to hyperparathyroidism The number of men with urinary stone was 131 and the number of women was 62, the prevalence of disease in men was 2.1 fold than women. In our study the prevalence of hypercalciuria was different from studies in developed countries, where hypercalciuria is the most common disorder. The differences may be due to genetic and racial differences or different nutritional habits or environmental factors. We suggest more studies on genetic and racial factors and nutritional habits.

Key words: Urinary stones, Metabolic disorder, Hypercalciuria , Hypercalcemia .

Urinary stones are common disorders of the urinary system. The highest incidence is in 20 - 45 years age group. The prevalence of urinary stones is more in developed countries probably due to low fiber diet and high animal protein intake[1]. Urinary stones in 1974 in the United States were 36 cases per 100,000 for men, and 123.6 cases per 100,000 for women. Prevalence of the urinary stones has been 4% to 9% in men and 4.1% to 1.7% in women[2]. Positive family history of the urolithiasis is in many patients. People with a positive family history are at higher risk of developing urinary stones than those without a family history[3]. Urinary stone recurrence is common. About 50% of patients with urinary stone face the recurrence during the five years thereafter and almost 60% of those with one stone eventually build up another one within ten years later[2]. Average rate of new stone formation in patients with a previous history of stone is about a stone per two or three years[4]. Urinary stones can have severe pains and cause nausea, vomiting or urinary tract hemorrhage. Urinary stones complications include urinary outlet obstruction and renal failure. Infection with urinary tract stone can lead to deterioration of the patient's overall condition. Blockage of an infected kidney by stones may lead to sepsis and severe damage to the kidneys[5]. Kidney stones rarely can cause renal failure, but in the patients with abundant recurrent stones such as Cystine stones or other hereditary disorders of the stone formation, *stone blockage infection*, patients with multiple urologic measures taken to treat stones and patients with large sized stones are more susceptible to serious complication of the renal failure[6]. According to clinical

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appearances and physical difficulties imposed to the patient, some potential complications can occur. Moreover, the calculation of the required expenses to treat them and the cost of not working during the patient's clinical appearances encouraged us to study the factors predisposing the patient to develop the stone and the elimination of those factors to remove the stone recurrence rate or to minimize as possible[7]. Stones arise because of a phase change in which dissolved salts condense into solids, and all phase changes are driven by supersaturation. The ratio of their concentration in the urine to their solubilities determines the degree of supersaturation. The crystals are dissolved in the lower concentrations of a substance. At higher concentrations, the supersaturation of crystals can form and grow. Increased urine volume is a method to reduce the occurrence and the concentration of supersaturated materials[8].

In susceptible patients, the stone formation starts when the urine is supersaturated by a stone - forming material including calcium, uric acid, oxalate, cystine and *struvite* and also when other substances inhibiting the stone formation in the urine are reduced[9]. *Kidney stones* form in a process known as *nucleation.* Usually, cell debris and also other non-homogeneous crystals such as sodium hydrogen urate, uric acid, and hydroxyapatite crystals form a nucleus. Calcium and oxalate ions are then attach to the nucleus to create a mixed stone, which is known as heterogeneous nucleation[9]. The heterogeneous nucleation reduces the supersaturation level required for crystalization which is probably the main mechanism of urinary stone formation in humans[4]. When the nucleation occurred, the crystals grow and gather together, the phenomenon of the development and accumulation of nucleus is essential for the stone formation. Microscopic nuclei are smaller than that to cause the blockage and clinical symptoms. Citrate, pyrophosphate and magnesium are the most important inhibitors of nucleation with low molecular weight that provide the supersaturated urine with calcium at increased risk of urinary stones. Male with more than 300 mg calcium, and female with more than 250 mg calcium or more than 4 mg calcium excretion in both sexes per kg of body weight in 24 -hour urinary excretion are considered Hypercalciuria. The supersaturated calcium in the urine is present in many cases, and can be developed in hypercalciuria, primary hyperparathyroidism, sarkoidose, renal tubular acidosis, hyperthyroidism, tumors, excess vitamin D, Paget's disease, Cushing's syndrome or furosemide usage. Increased intestinal absorption of calcium and decreased tubular absorption of calcium are involved in the pathogenesis of hypercalciuria idiopathic. In cases of hyperparathyroidism, if the disease is diagnosed in its early stages, the stones frequently recur and are bilateral. In many cases, the urinary stone formation is the only appearance of hyperparathyroid disease. In case of hypercalciuria and hypercalcemia, parathormone test may lead to diagnosis[2]. Early diagnosis is important because parathyroidectomy should be diagnosed prior to developing kidney failure or bone disease[10].

MATERIAL AND METHODS

This research is descriptive and the information contained in the records of patients admitted to Nephrology clinic is used. It seems that a careful study on the metabolic of individuals with kidney stone disease, the metabolic disorder causing the stone formation can be discovered in the high percentage of patients. In our study, 193 patients, referred to the nephrology clinic with a recent history of urolithiasis which has been removed spontaneously, by lithotripsy procedure or surgery, were studied. The evaluation was conducted in terms of metabolic disorder, which the results are studied.

The blood tests were performed in terms of urea, Creatinine and calcium level, in which the unit of measurement was mg/dL, and 24-hour urine of patients was also studied in terms of urine volume during the time in the Cm^3, and also the 24-hour urine Creatinine and calcium in mg.

Hypocalcaemia is considered in case of the blood calcium level more than 10.5 mg/dl, and Hypercalciuria is considered in male with more than 300 mg calcium, and female with more than 250 mg calcium or more than 4 mg calcium excretion in both sexes per kg of body weight in 24 -hour urinary excretion[2, 4].

In our study, 193 patients, referred to the nephrology clinic with a recent history of

urolithiasis which has been removed spontaneously, by lithotripsy procedure or surgery, were studied. The metabolic disorders were carried out and the results are mentioned. The history of urinary stone in the patients was proved by stone excretion or sonography or radiology methods. Patients, who were studied in case of metabolic features, were included in the study. The cases suspected to have urinary stones, or with incomplete tests or tests conducted in another laboratory were excluded. The individuals aged from 20 to 60 years were considered. In this study, the following criteria were taken into consideration in order to remove the patients from the study:

1) Children and people under 20 years and over 60 years.
2) Pregnant women due to physiological changes in kidney function and also in calcium and uric acid homeostasis.
3) Patients treated with calcium and vitamin D.
4) Patients treated with thiazide diuretics which may affect the calcium level in blood and urine and blood acid uric
6) Patients treated with loop diuretics such as furosemide which may affect the calcium level in blood and urine and blood acid uric
7) Patients with renal insufficiency and creatinine clearance less than 60 mL per minute.

RESULT

The metabolic of 193 patients with a history of urinary stone proved by stone excretion or imaging observations such as sonography or radiography were studied. Each patient was identified by a number and the information about age, sex, weight, blood calcium level, blood creatinine level, and blood Parathormone, in addition to 24 -hours urine in terms of calcium volume were extracted from the file. In the patients under study, the patient's mean weight was 87.8 kg, with standard deviation of 10.47 and *variation Range* of 62, the minimum weight of 58 and maximum weight of 120 Kg. However, in female patients, the mean weight was 66.6 kg, with standard deviation of 8.73, *variation Range* of 40, minimum weight of 50 kg and maximum weight of 90 Kg. In terms of the blood calcium level in all patients under study, the mean calcium was 9.64 mg/dl, with standard deviation of 0.48 and *variation Range* of 3.3. The minimum blood calcium was 8.2 mg/dl and the maximum was 11.5 mg/dl. In male patients, the mean blood calcium level was 9.65, with standard deviation of 0.52, *variation Range* of 3.3, minimum level of 8.2 mg/dl and maximum level of 11.5 mg/dl. In female patients, the mean blood calcium level was 9.61, with standard deviation of 0.40, *variation Range* of 1.9, minimum level of 8.7 mg/dl and maximum

Table 1. Variables and measurement scales

Definition	The Unit of measure	The Scale of measure	The Type of Variable	The Name of Variable
Based on the information in the file	mg/dl	Continuous quantitative	Dependent	Blood Calcium
Based on the information in the file	mg/dl	Continuous quantitative	Dependent	Blood creatinine
Based on the information in the file	mg	Continuous quantitative	Dependent	24-hour urine calcium
Based on the information in the file	Based on year	Continuous quantitative	Background	*patient's age*
Based on the information in the file	Female Male	Nominal quantity	Background	*patient's sex*
	Yes - No	Nominal quantity	Independent	urinary stone
Based on the information in the file	ng/l	Continuous quantitative	Independen t	blood Parathormone in patients with hypercalcemia

Table 2. Metabolic disorders found in the patients' blood tests

Percentage of patients with this disorder	The number of patients with the disorder	Metabolic disorder
4.70%	8	Hypercalcemia
3.10%	6	*Hyperparathyroidism*

Table 3. Hypercalciuria disorder found in the patients' blood tests

Percentage of patients with this disorder	The number of patients with the disorder	Hypercalciuria disorder
28.50%	55	Hypercalciuria

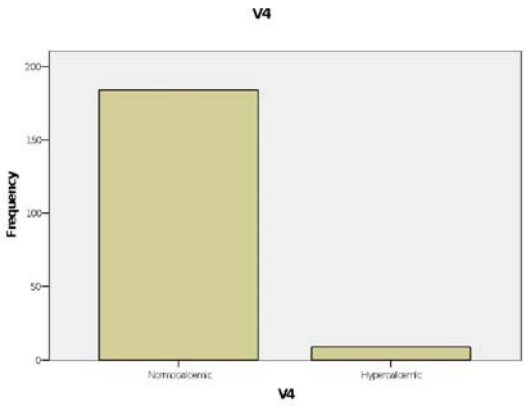

Fig. 1. The frequency of hypercalcemic and Normocalcemic in patients

level of 10.6 mg/dl. Given that the blood calcium level more than 10.5 mg/dl is considered hypercalcemia, 9 out of 193 patients (4.7%) were hypercalcemia, which is shown in Table 2 and Figure 2.

The prevalence in our study included hypercalciuria 28.5%, hypercalcemia 4.7%, hyperparathyroidism 3.1%.

DISCUSSION

Stones are most common in urinary tract diseases that have high recurrence rate in white women. The prevalence of urinary stones is mentioned 10% in American white men and 4% in American black men[11]. About 60% of the urinary stones recur within a few years later (12). We do not have exact statistics on the prevalence and the incidence of urolithiasis in the general population of our country. In this study, we examined the medical records of patients who had a proven history of urolithiasis and referred to the nephrology clinic for metabolic studies. In our study, 28.5% of patients had hypercalciuria, however, in western societies about 60-50% of patients with the history of urinary stone had hypercalciuria[13-16]. The question is whether these differences are due to genetic and racial differences or different nutritional habits or environmental factors? In the case of calcium, the consumption in normal diet and the absorption in the gastrointestinal tract should be studied carefully. It is better that the mineralization rate of bones in our people and other communities to be investigated. Whether, while our patients and the patients in other countries have the same amount of calcium and the same bone conditions, they have less urinary calcium excretion? Whether our people, with lower levels of calcium excretion, are at increased risk of urinary tract stones? We may need to revise the definition of hypernatremia as a risk factor for urinary stones in our society and consider smaller amounts of calcium excretion in the urine as a risk factor for kidney stone rather than amounts greater than 300 mg of calcium in the 24 - hour urine in men and 250 mg in women. Hypernatremia may be associated with hypocalcemia, in which, the possible causes particularly hyperparathyroidism should be sought. A proper action should be done in cases where a special reason is present for the high urinary calcium excretion. In case of hyperparathyroidism, surgical procedure for parathyroidectomy is needed to prevent further

damage to kidneys and bones. In many cases, the hypercalciuria is associated with normal blood calcium levels. In the case of idiopathic hypercalciuria, the consumption of plenty of fluids to increase the urine volume and decrease calcium concentration in the urine, the reduction of salt consumption to reduce calcium excretion in the urine, and the administration of thiazide diuretics, with potassium citrate or Potassium-sparing diuretics, reduce the recurrence rate of urolithiasis[17]. In our study, 19.7% of patients had hypocitraturia that its frequency was similar to other studies. Citrate prevents the process of converting the crystals to kidney stones. Low level of the urinary citrate is a risk factor for urinary stone disease. Hypocitraturia increases the risk of calcium and uric acid stones. In these cases, the administration of potassium citrate prevents the crystallization of calcium salts and to a large extent reduces the risk of urinay stone recurrence in patients[19].

CONCLUSION

Unfortunately, in our country many patients have been treated as symptomatic and just for kidney stones, moreover, metabolic study is not carried out to identify the primary metabolic disorder. Therefore a proper treatment is not performed to deal with it, and the patient will still be at the high risk of urolithiasis recurrence and its complications. We recommend that following the stone treatment, the patient be referred to a nephrologist to perform metabolic evaluation and necessary treatments to prevent or reduce the recurrence of stones. This study showed a lower incidence of hypercalciuria in our patients. Further evaluation in terms of genetic and racial differences and careful analysis of diet and gastrointestinal disorders can increase the accuracy of study. About calciuria, the determination of dietary calcium intake and also bone mineral materials and probably the incidence of osteopenia and osteoporosis are recommended. The question is that whether the lower prevalence of hypercalciuria in our people is resulted from the lack of calcium in the diet or is associated with a higher incidence of bone problems? Or our people excrete less calcium in the urine due to their genetic and racial characteristics?

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