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Effect of urinary tract infection on the urinary metabolic characteristic as a risk factor in producing urolithiasis

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ABSTRACT

Urinary metabolic disorders are one of the most common causes of stone formation in children. The purpose of this study was to evaluate the effect of urinary tract infections in the urinary metabolic characteristics as a risk factor in the incidence of urolithiasis. This case-control study was conducted in 222 children with urolithiasis in the range of 6 months to 16 years old in Sanandaj, Kurdistan, Iran during 2012-14. Patients were divided into two groups based on those with urinary tract infection and without urinary tract infection. Then, urine samples were collected from both groups, and levels of calcium, oxalate, citrate, uric acid, creatinine, and cysteine were measured. The collected information was analyzed using software SPSS (version 16). The ratio Average levels of calcium, magnesium, oxalate, cysteine, uric acid to creatinine in urine showed no significant difference between two groups based on statistical analysis. However, the amount of citrate to creatinine in children with urinary tract infection and urolithiasis was clearly less P=0.01. The results of this study show that the urinary tract infection cannot change the urinary metabolic characteristics, but it can be considered as a risk factor in kidney stone formation due to the reduced amount of citrate in the urine.

Key words: Urolithiasis, Urinary tract Infection, Urinary metabolic characteristics

INTRODUCTION

Urolithiasis can be seen in all countries and regions of the world, but its prevalence in Asian countries and the Middle East is more than other regions of the world, and our country is endemic in this regard. Almost 7% of urolithiasis is in children under 16 years old [1].

Genetic factors, diet, and climate are the effective factors in the incidence of urolithiasis. Since the formation of urinary stones consists of several stages including the emergence of super-saturated urine, epistaxis and crystallization, crystals growth that should be over, thus the stone formation is a time-consuming process. Therefore, most of the researchers believe that the origin of stones in children, particularly at early ages is often associated with a metabolic disorder such as hyperuricosuria, hypercalciuria, hyperoxaluria, hypocitraturia and the cysteinuria. The mentioned metabolic disorders can be primary or secondary to systemic diseases. Such disorders are responsible for 90-85% of urolithiasis [2].

In many cases, children are symptom free. On the other hand, young children are not able to express their symptoms, so that stone formation can occurs at a young age. In recent years, due to the widespread use of imaging devices, especially usage of ultrasound during the investigation of urinary tract infections, many asymptomatic urinary stones are detected. Therefore, this question always arises whether the urinary tract infection has led to stones, or whether urinary stones cause urinary tract infections? [2 , 3]

Approximately 5-10% of urinary stones are made of Magnesium- ammonium phosphate (struvite). The reason is urease-producing bacteria, particularly Proteus. Because of the complications and risks of this type of stones in inducing chronic renal failure and recurrent urinary tract infections, this type of stone is considered as a serious kidney disease [3].

Although, the role of bacteria and urinary tract infection is detected in creating struvite stones, but the role of bacteria in causing other metabolic disorders, which are responsible for most urinary stones is less investigated. Therefore, we decided to compare urinary metabolic characteristics in children who have urolithiasis and urinary tract infections with children who have urolithiasis without urinary tract infections. Thus, we evaluated the role of urinary tract infection in change urinary metabolic characteristic as a risk factor in kidney stone formation.

MATERIALS AND METHODS

This research was a case-control study. Considering ethical considerations and after obtaining the consent of the patients' parents, urine samples were taken from children who had been referred to Pediatric Nephrology Clinic of Sanandaj, Kurdistan, Iran due to urinary stones during 2012-14. The final diagnosis of urolithiasis was the responsibility of Pediatric nephrologist. Patients who had abnormalities in the urinary tract and urologic disorders or underlying systemic diseases were excluded from the study. Finally, 222 children aged 6 months to 16 years old were studied and they were divided into two groups of 111 based on urine culture results.

The case group included children who had positive urine culture, in addition to urinary stones and the control group consisted of children who had urinary tract stones, but negative urine cultures. After treatment with suitable antibiotic, random urine samples were obtained in both groups and the levels of calcium, creatinine, oxalate, citrate, uric acid, and cysteine were measured. Given that urine samples had been taken randomly, the ratio of calcium and oxalate, citrate, uric acid and cysteine were measured simultaneously with creatinine to avoid the impact of urinary concentrations on the results. The results were analyzed using SPSS version 16 and they were analyzed using independent groups T-test.

RESULTS

In total, the data from 222 patients were analyzed.

113 were males and 109 were females. In the control group, there were 43 males and 68 females while in the patient group, there were 41 males and 70 females. The statistical analysis of the gender distribution in the two groups had no significant difference P = 0.7 (Table 1)

Table 1- Gender and Age Distribution

Groups	Gender		Age	
	Male	Female	>24 months	<24 months
Case	41	70	25	86
Control	43	68	24	87
P Value	0.7		0.87	

Also according to Table 1, the age distribution was similar in both groups and there was no difference between them (P = 0.87).

The results of surveying urines in terms of calcium and creatinine, oxalate, citrate, uric acid, and magnesium were collected in Table 2.

According to this table, the urinary excretion of calcium, uric acid, oxalate and cysteine and magnesium does not show any statistically significant difference between the two groups. However, the urinary citrate is clearly less in patients group compared to the control group (P = 0.01).

Table 2- Ratio of Means

Groups	Ca/Cr	Ox/Cr	Cit/Cr	Cys/Cr	UA/Cr	Mg/Cr
Case	0.35±0.35	0.42±2.5	0.88±2.04	0.001±0.09	1.04±0.6	0.19±0.16
Control	0.42±1.4	0.6±3.76	2.69±7.1	0.00±0.00	1.93±8.7	0.16±0.19
P Value	0.59	0.67	0.01	0.15	0.28	0.27

Ca=calcium Cit=citrate Cr=creatinine Cys=cysteine Mg=magnesium
UA=uric acid Ox=oxalate

DISCUSSION

Stone formation depends on four factors: 1. Matrix 2. Precipitation 3. Crystallization 4. Epistaxis and absence of inhibitors in the urine.

Matrix is a mixture of proteins, non-amine sugars, and organic materials. Matrix is formed inside the stone in concentric layers. In the next step, precipitation and crystallization occur in the presence of super saturation urine from specific ions under the influence of chemical and electrical forces, which leads to the stone formation and its growth. Epistaxis is the aggregation of crystals with different chemical structure, but the same crystalline form.
Crystals of calcium, oxalate and phosphate are the most common components of urinary stones. Crystals of uric acid, cysteine, and ammonium are other confounding materials for the formation of urinary stones. The risk of stone formation increases by increasing their concentration and decreases by increasing the concentration of inhibitors such as citrate and magnesium [7 , 8].

Tekin et al. concluded that the high concentration of oxalate and low citrate are effective in the formation of stones that correspond to some extent with the findings of our review [9].

Alpay et al. demonstrated that metabolic disorders including hypercalciuria, hypocitraturia, and Hyperoxaluria are effective in the incidence of urolithiasis [11].

Alemzadeh et al. conducted a research on urinary tract stones in children. They reported hypercalciuria and hypocitraturia as the most common metabolic disorder. This report was confirmed by Cambareri et al. [12-13].

In our study, there was no significant difference in the urinary metabolic parameters' mean such as calcium, oxalate, uric acid, and cysteine between children with stones and urinary tract infections and children with stones and without urinary tract infections. However, the amount of urinary citrate was significantly lower in children with urinary tract infection ($P = 0.01$).

CONCLUSION

According to the results of this study, it can be said that the urinary tract infection does not change the urine metabolic and chemical properties. However, urinary tract infection can act as a risk factor in the incidence of urinary stones due to the reduced amount of citrate in the urine, which is an important inhibiting substance in the formation of stones.

Due to the frequency of urinary tract infections in childhood, especially in females, it is recommended to measure the urinary citrate in these patients after the recovery of urinary tract infection, especially in cases where there is a family history of kidney stones. In the case of low urinary citrate, appropriate measures should be taken to prevent stone formation.

In the end, it is recommended to conduct similar studies with a larger sample size according to the frequency of urinary stones and urinary tract infection in children in order to confirm the relationship between urinary tract infection and the incidence of urolithiasis in children.

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