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Metabolic and Anatomic Abnormalities Associated with Pediatric Nephrolithiasis: a Cross-Sectional Study

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Abstract

Background

Pediatric nephrolithiasis is a condition the prevalence of which varies geographically with multiple etiologies. The aim of this study was to determine possible concomitant anatomic and metabolic disturbances in children with nephrolithiasis and to answer the questions regarding the role of each metabolic and anatomic abnormality.

Materials and Methods

Between 2007 and 2015, 1,080 patients referred to our pediatric hospital of Hazrat Masumeh in Qom city, with the diagnosis of nephrolithiasis. Complete history from each eligible patient has taken using a prespecified data extraction form. Then, each child was referred for metabolic and anatomical evaluation using laboratory and imaging tests.

Results

According to the extracted data, 92% of our patients had at least one concomitant metabolic disorder and 12.5% had an anatomic abnormality. Recorded metabolic disorders in our series were hypocitraturia (56.9%), hyperuricosuria (21.4%), hypercalciuria (19.3%), hyperoxaluria (14.7%), phosphaturia (11.4%), and cystinuria (1.4%). According to data analysis, 12.5% of patients had an anatomical abnormality of which the ureteropelvic junction obstruction and vesicoureteral reflux were the most common.

Conclusion

The current study showed that the most common abnormalities in association with nephrolithiasis were metabolic disturbances, which highlight the importance of further metabolic study, even in patients with anatomical abnormalities.

Key Words: Anatomic abnormalities, Children, Metabolic abnormalities, Pediatric nephrolithiasis.

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1- INTRODUCTION

Pediatric nephrolithiasis, a condition the prevalence of which varies geographically with multiple etiologies, is being recognized as a relatively infrequent medical problem in developed countries, albeit it frequently considered in the evaluation of several childhood kidney disease (1-3).

The annual incidence in the United Kingdom has been estimated to be 2/1.000.000 in children (4), and accounts for 0.001 to 0.1% of hospital admission of children in the United States, and 7% in Asia (5, 6). There are several causative factors that can be considered as the etiology of disease including metabolic disorder, anatomical malformations, environmental and dietary factors (7).

Of these, however, metabolic disorder and developmental anomalies are known as the most common cause of nephrolithiasis. Multiple metabolic disturbances are contributing to the development of nephrolithiasis including hypercalciuria, hyperuricosuria, hyperoxaluria, cystinuria, hypocitraturia, hypomagnesiuria, and renal tubular acidosis (8, 9).

The most common anatomic abnormalities mentioned in the studies, which involved in the development of this condition are also including Ureteropelvic junction (UPJ) obstruction, duplicated ureter, Ureterovesical junction (UVJ) obstruction, neurogenic bladder and ureterocele (10).

Early recognition of the etiology of stone formation would be inevitable in terms of preventing further stone formation and complications (11).

Thus, in this study we aimed to find possible potential concomitant anatomic and metabolic disturbances in children with nephrolithiasis.

2- MATERIALS AND METHODS

2-1.Study design and population

Between 2007 and 2015, of 1,080 patients referred to our pediatric hospital of Hazrat Masumeh in Qom city with the diagnosis of nephrolithiasis, 95 patients were excluded due to incomplete data. Prespecified data extracting forms were completed, retrospectively, according to patients' hospital records.

2-2. Methods

Each child was referred to Hazrat Masumeh hospital for metabolic and anatomical evaluations. Metabolic screen had carried out with a plasma urea, creatinine, potassium, sodium, chloride, bicarbonate, magnesium, calcium, phosphate, alkaline phosphatase, albumin, uric acid, arterial blood gases, urine analysis, and culture, and in 24-h urine collection sodium, potassium, calcium, phosphorus, creatinine, oxalate, citrate, and cystine.

All blood samples were taken by experienced medical staff and under standard circumstances in terms of keeping sterilization and the health of samples for laboratory. Anatomical abnormality was defined to any structural abnormalities of the urinary tract using an imaging modality (12, 13).

2-3. Laboratory measurements

The definitions of metabolic disorders that are considered in this study are in accordance follows:

- Hypercalciuria is defined by a urinary calcium excretion of more than 4mg/kg per day in 24-h urine or Calcium/Creatinin (Cr)> 0.21mg/mg in child and >0.6mg/mg among infants.
- Hyperoxaluria> 40 mg/1.73m2/day or Oxalate/creatinine more than 0.3mg/mg in infants < 6 months or more than 0.15mg/mg in children <

4 years or more than 0.1mg/mg in children > 4 years of old.

- Uricosuria a urinary uric acid of >815mg/1.73m2/day in 24-h urine or >0.53mg/dl Glomerular filtration rate.
- Hypocitraturia urinary citrate of less than 400mg/g Cr in 24-h urine or Citrate/Cr < 0.51g/g.
- Cystinuria is defined by urinary cystine excretion of > 75mg/1.73m2/day, and
- Phosphaturia urinary phosphate of > 15mg/kg in 24-h urine (12).

2-4. Ethical consideration

As a retrospective study, university ethics committee supervised and corroborated the study in terms of ethical considerations, and patients' records remained confidential for analysis.

2-5. Data analysis

Data analysis was carried out using the statistical software of SPSS version 20.0 for windows (SPSS Inc., Chicago, IL). Results were presented as mean ± standard deviation (SD). P-value of 0.05 or less was considered to be statistically significant.

3- RESULTS

Hospital records of 1,080 patients with nephrolithiasis, who referred to our center for evaluation of metabolic and anatomic abnormalities, were reviewed. Of these, 95 (8.8 %) were excluded due to incomplete data. Of remaining 985, 57% were male and 43% were female (ratio of 1.33:1).

All patients were less than 16 years old; 3% neonate, 21% between 1 month to 1 year and 76% between 1-16 years old (**Fig.1**).

Of total 985 patients, 79.5% had experienced renal stone for the first time and remaining 20.5% had a history of nephrolithiasis.

Family history of renal stone was positive for 36.5% of patients, of those 21.8% were positive in father, 12.4% in mother and remaining in other first and second degree family members. In 91.6% of patients, stones were located in pelvis and 8.4% in urethra.

Only 10 cases of bladder stone were recorded (out of total 985). Some degree of hydronephrosis was associated with nephrolithiasis in 12.8% of patients of which 1.5% were bilateral.

According to the extracted data, 92% of patients had at least one concomitant metabolic disorder and 12.5% had an anatomic abnormality. Of these, 630 patients (63.9%) suffered from multiple metabolic disorders, and in 28% there was only one metabolic disorder.

Recorded metabolic disorders in our series were hypocitraturia (56.9%), hyperuricosuria (21.4%), hypercalciuria (19.3%), hyperoxaluria (14.7%), phosphaturia (11.4%) and cystinuria (1.4%) (**Figure.2**).

According to data analysis, 12.5% of patients had an anatomical abnormality of which the urethropelvic junction obstruction and vesicourethral reflux were the most common (data not shown). The average number of stone was 2.5 per each patient and in 78% of children the stone size was less than 5mm.

Statistical analysis, however, revealed no significant differences between anatomical abnormalities and any metabolic disorder with numbers of stones, location, size and history of prior renal stone formation in patients and their family.

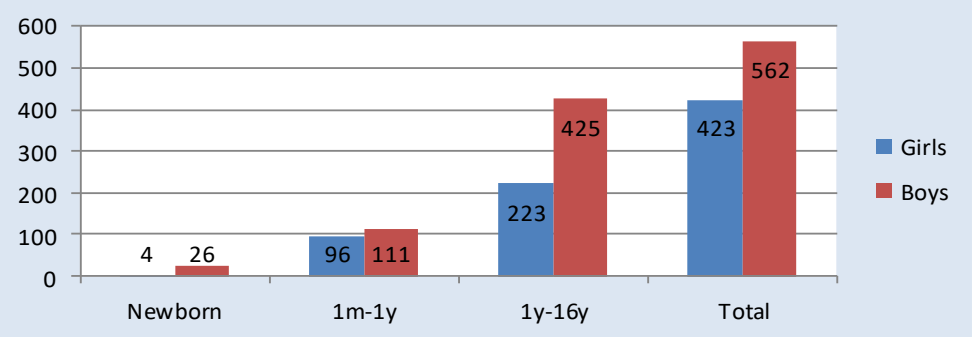

Fig.1: Age and gender distribution among patients participating in the project (2007-2015).

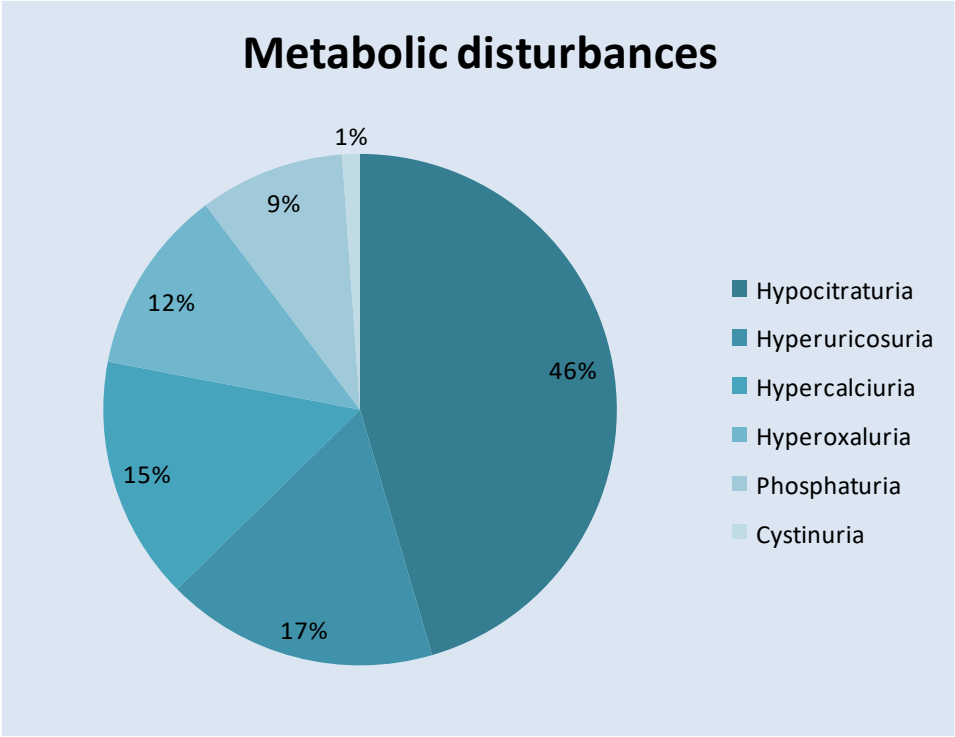

Fig.2: Metabolic disturbances among patients participating in the project (2007-2015).

4- DISCUSSION

Stone formation in urinary system is a complex process, which is impresses by several biochemical and anatomical factors. Urinary supersaturation, pH, and biochemical composition as well as anatomical malformations of urinary tract are well established factors, which were commonly taken into consideration in this context. In the current study, we have investigated the frequency of anatomic and metabolic disturbances in children suffering from nephrolithiasis. We have found a male to female ratio of 1.33:1 among total of 985 patients enrolled in this study, which is consistent with previous studies (14-19). Our data showed that 20.5 % of patients had a prior history of renal stone. It has been also observed that more than one-third of our patients had a positive family history of the disease, which predominantly occurred in the father. Our data analysis revealed 92% of participants had an underlying metabolic disturbance and 12.5% had a developmental anomaly. Of these, 63.9% had multiple predisposing factors and in

26.3% there was only one risk factor. Hypocitraturia and hyperuricosuria were the most frequent metabolic disturbance (56.9% and 21.4%, respectively). Phosphaturia was detected in 11.4 % of patients, albeit no isolated phosphaturia was found and was always concomitant with other factors. Our results were in consistent with other studies, in which the metabolic abnormalities were considered as the major risk factor for developing renal stones (20, 21).

Percontra, there are some evidences showing almost identical causality effect of metabolic and anatomic abnormalities (10); among the metabolic risk factors, hypercalciuria has been recognized as the most common predisposing factor of pediatric urolithiasis. This is despite the fact that hypercalciuria is the third common metabolic abnormality in our series (19.3%). Nonetheless, the difference in our results with the findings of other studies that considering hypercalciuria as the most frequent risk factors could be due to geographic differences, diet, underlying genetic susceptibility and the age distribution of patients evaluated in these studies. Indeed, hypocitraturia was the prevailing metabolic disturbance among our participants. Urinary citrate represents multiple effects on stone formation. Citrate can reduce urinary calcium saturation through binding to ionized calcium. Citrate also impedes stone formation via disturbing the accumulation of calcium oxalate and preventing growth of calcium phosphate crystals. However, numerous studies have recognized hypocitraturia as the most common metabolic risk factors for nephrolithiasis (22).

Anatomical malformations included other influencing factors which evaluated in the current study. ureteropelvic junction obstruction and vesicoureteral reflux were the most involving anatomical anomalies in our series. There is widely accepted traditional belief which states that the causative effect of anatomic abnormalities on nephrolithiasis is associated with urinary stasis and subsequent infection as well as delayed washout of the stoneforming substances. However, this assumption was challenged for some reasons, suggestive of the probable role of underlying metabolic abnormalities (23). Our findings also emphasize the impressive role of metabolic disorders in developing nephrolithiasis.

4-1. Limitations of the study

Our study might be restricted by some limitations, albeit it provides the outstanding information regarding the etiology of nephrolithiasis. Common to all retrospective studies, there is a chance for bias in hospital recordings. Therefore, it would be better if the analysis carried out prospectively.

5- CONCLUSION

In current study, results showed that the most common abnormalities in association with nephrolithiasis are metabolic disturbances, which highlight the importance of further metabolic studies, even in patients with anatomical abnormalities. Hence, given the high rate of recurrence, we recommend that the metabolic study should be carried out routinely in all patients.

6- CONFLICT OF INTEREST: None.

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