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Pediatric urolithiasis in a non-endemic country: A single center experience from The Netherlands

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Abstract *Objective:* To provide insight in causative factors of pediatric urolithiasis in The Netherlands, a non-endemic country.
Patients and methods: Data from 71 children with urolithiasis and stone analyses between 1996 and 2010 in the Radboud University Nijmegen Medical Centre were studied retrospectively. Patients (48 boys, 23 girls, ratio 2.1:1) were aged 0.5—18.3 years (mean 8.8, SD 5.6). All stone analyses were performed with FTIR spectroscopy.
Results: Of the 49 patients with metabolic analysis, 78% showed one ($n = 15$) or more ($n = 23$) metabolic abnormalities. Forty-seven percent had hypercalciuria ($n = 23$), 31% had hyperoxaluria ($n = 15$), 29% hypocitraturia ($n = 14$), 10% hyperuricosuria ($n = 5$), 10% cystinuria ($n = 5$), and 6% had hypomagnesiuria ($n = 3$).

Sixty-one percent of the stones were composed of calcium phosphate, calcium oxalate, or a combination of those. Twenty-six percent consisted of pure or mixed magnesium ammonium phosphate, 8.3% pure or mixed urate, and 8.3% cystine.
Conclusion: Children with urolithiasis in The Netherlands show stone composition similar to other Western European countries. However, a high percentage of metabolic abnormalities (78%) was found, indicating the need for extensive evaluation of pediatric urolithiasis to find underlying

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causes and thereby prevent stone recurrences. A close collaboration between a pediatric nephrologist and urologist is mandatory for optimal surgical and medical treatment.

Introduction

Pediatric urolithiasis is a serious disease for the children, parents, and doctors involved because it can cause permanent kidney damage and it has a high recurrence rate. The lifetime chance of an individual having a kidney- or bladder-stone is approximately 10–15% with a nearly 60% chance of recurrence within 10 years if not treated [1]. Although usually diagnosed between the third and fourth decade of life, urolithiasis can present at all ages, including childhood.

Several studies have shown an increase in incidence and prevalence of pediatric urolithiasis over the past decades. In 2007 Vandervoort et al. described a 4.6-fold increase in admittance in New York of children with urolithiasis, comparing data from 1994 to 1996 with 2003–2005 [2]. A recent study in the United States by Routh et al. [3] described a threefold increase in pediatric urolithiasis from 18.4 per 100,000 in 1999 to 57.0 per 100,000 in 2008. Annual incidences have been reported varying from 1.8 per 100,000 children per year in Kuwait 1996–2000 [4], 6.3 per 100,000 children under 16 years of age in an Icelandic study in 1995–2000 [5], up to a prevalence of 17% in patients under 14 years of age in endemic areas like Turkey, Tunisia, and the Far East [6].

Metabolic disorders, anatomical abnormalities, urinary tract infections (UTIs), intoxications (China), and dietary and climatic factors all contribute to the risk of developing kidney stones. Koyuncu et al. [7] found that, despite conservative measures, the risk of recurrence increases threefold if at least one metabolic abnormality is present. During metabolic evaluation in children with urolithiasis, 76% of patients showed at least one abnormality in the 24-hour urine collection as an explanation for the urolithiasis [2].

This illustrates the importance of proper management protocols to optimize treatment, reduce the recurrence risk and improve outcome. Because of the large geographic variation in incidence and etiologic factors, region-specific data are needed to develop adequate management protocols. Although much research has been done on etiologic factors, there is a paucity of published data from West European countries. This study was designed to provide insight in etiologic factors of pediatric urolithiasis in The Netherlands, and compare these data with other regions.

Patients and methods

Clinical evaluation studies

This study was performed at the Radboud University Nijmegen Medical Centre, a referral center for pediatric urolithiasis for the eastern parts of The Netherlands. We included all patients aged 0–19 years with a stone analysis between 1996 and 2010 according to the laboratory database. The year 1996 was selected for the start of inclusion, as the current stone analysis spectrophotometer has been in use since then. In addition, we included all children who were diagnosed with urolithiasis in this period according to the electronic patients charts system of our Medical Centre.

In total, 71 children were identified and their charts were studied retrospectively. Some of these patients were initially evaluated and/or treated elsewhere but eventually transferred to our Medical Centre for further investigation, treatment, and/or follow-up. Patients with urolithiasis were evaluated according to a standard protocol, which has been adjusted to up-to-date standards over the past 14 years. When the cause of urolithiasis was established before completing the analysis, further investigation was discontinued.

Complete evaluation included a full history, physical examination, two 24-hour urine collections, two separate urinalyses of freshly voided urine, blood chemistry studies, and, when available, stone analysis.

In the 24-hour urine collections, excretions of sodium, potassium, calcium, phosphate, magnesium, citrate, uric acid, creatinine, oxalate, amino acids, purines and pyrimidines were determined. The absolute excretion rate was considered as the most reliable marker to evaluate whether values were abnormal. If this excretion rate was not available, solute/creatinine ratios were used. In patients with hypercalciuria, the urine sodium excretion was measured as a marker of daily sodium intake [8]. Reference values used were adapted from previous publications [9–12].

All stone analyses were performed with Fourier transform infrared spectroscopy. Stones were divided in categories, based on the composition: 100% calcium oxalate, 100% calcium phosphate, mixed calcium oxalate and calcium phosphate, magnesium ammonium phosphate (pure + mixed), urate (pure + mixed), and cystine. Stones containing at least partly magnesium ammonium phosphate were accounted into that category because of the likeliness that a UTI was a causative factor in the urolithiasis. If urate was a stone compound, the stone was attributed to the urate category. Urate- and magnesium ammonium phosphate-containing stones could therefore be arranged in two categories, making the total percentage of stone analyses over a hundred percent. Stones were available for analysis in 67 of the 71 patients and 24 patients had more than 1 stone analyzed. If stones were of comparable composition (classified in the same stone category, Table 1), only the first stone analyzed was used in this study. Three patients had stones in two different categories, and one patient had stones in three different categories, resulting in a total of 72 stones. As these stones may have been caused by different underlying factors, they were all taken into account. Stone locations were divided in the following categories: kidney, ureter (combined as upper