CHILDREN'S HOSPITAL

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Kidney Stone Disease in Children

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Objectives

At the end of this activity, the participant should be able to:

1. Describe the different types of kidney stones in children
2. Discuss the etiology and risk factors associated with kidney stone disease in children
3. Discuss the evaluation and management of kidney stone disease in children

Introduction

There has been a growing incidence and prevalence of kidney stone disease in children in recent decades. This trend may be attributed to improved screening techniques, changes in nutrition (increased intake of salty foods), increasing sedentary lifestyles and global obesity, and changes in environmental factors. Kidney stone disease in children is associated with considerable morbidity and recurrence burden. The majority of children with kidney stones have identifiable metabolic and/or genetic risk factors, unlike adults. Also, kidney stone disease in children differs from adults in presentation and treatment. Whereas adults may present with acute onset of severe flank pain radiating to the groin, symptoms in children are often non-specific. Indeed, many children are asymptomatic, and kidney stones may be diagnosed incidentally in the course of evaluation for other medical problems. Children who present with kidney stones must be thoroughly evaluated to uncover underlying risks. Appropriate treatment must be instituted to prevent stone recurrence.

Epidemiology

The incidence of kidney stones in children varies worldwide. In Europe, kidney stones occur in one to two children per million population per year. In the United States, there has been a significant increase in the number of children diagnosed with kidney stones in the last several decades. A recent study of the Pediatric Health Information System database indicates that stones now account for 1 in 685 pediatric hospitalizations across the United States. In this study, most patients were white and younger than 13 years of age. Several studies show a slightly higher prevalence of kidney stones in boys than in girls, although studies from other regions show a female preponderance. In general, kidney stones are more common in adults than in children. The southeastern United States (The 'Stone Belt') has recorded the highest prevalence of kidney stones in adults (Fig. 1).

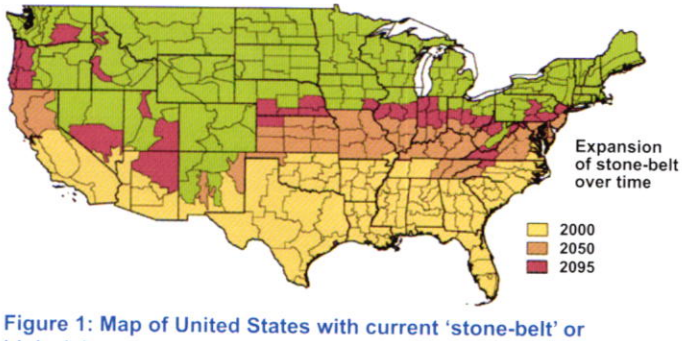

Figure 1: Map of United States with current 'stone-belt' or high-risk stone area (risk ratio >1.2) in yellow. Computer model predicts 56 percent of the population will be in a high-risk zone by 2050 and 70 percent by 2095. Currently, 41 pecent of the population is within a high-risk zone. *Reproduced from Fakheri and Goldfarb with permission from Nature Publishing Group.*

Etiology and Types of Kidney Stones

The main kidney stone types encountered in children are calcium, struvite, uric acid and cystine stones. Of these, the most common are calcium stones, including calcium oxalate, calcium phosphate and calcium urate stones (Fig. 2). The formation of kidney stones is linked to the increased supersaturation of stone-forming solutes in the urine, the increased urinary concentration of stone-promoting compounds in the face of inadequate amounts of stone-inhibiting compounds. Urine pH and urine flow rates are also key players in the complex process of stone formation. In more than 75 percent of children, an underlying predisposing factor for kidney stone formation is identified, the majority being metabolic disorders (Table 1). Therefore, metabolic evaluation is recommended in all children who present with kidney stones. Identification of a causative factor is necessary for the development of an appropriate therapeutic regimen. Other risk factors associated with kidney stone formation in

children include structural urinary tract abnormalities, infection, genetic abnormalities, nutritional and environmental factors as well as drug use. Of all metabolic risk factors, idiopathic hypercalciuria is the most commonly identified disorder in children with kidney stones. Struvite stones form in the context of chronic urinary tract infection with urease-producing organisms such as Proteus, Klebsiella and Pseudomonas. Uric acid, a byproduct of purine metabolism, may precipitate when urinary pH is low, to form stones. Uric acid stones are rare in children. Cystine stones form as a result of an intrinsic metabolic defect resulting in failure of renal tubular reabsorption of cystine, ornithine, lysine and arginine. Urine becomes supersaturated with cystine, with resultant crystal deposition.

Genetics

The genetic basis of kidney stone formation has been well characterized in some rare diseases such as cystinuria, primary hyperoxaluria and renal tubular acidosis, all of which probably account for less than 2 percent of kidney stone formers. There are, however, kidney stone formers who have a predisposition to forming stones without a discrete underlying genetic abnormality. This hereditability of kidney stone disease has long been recognized. Approximately 25 percent to 40 percent of patients with kidney stone disease are known to have a first-degree family member with kidney stones. Research is ongoing to more clearly define this familial risk.

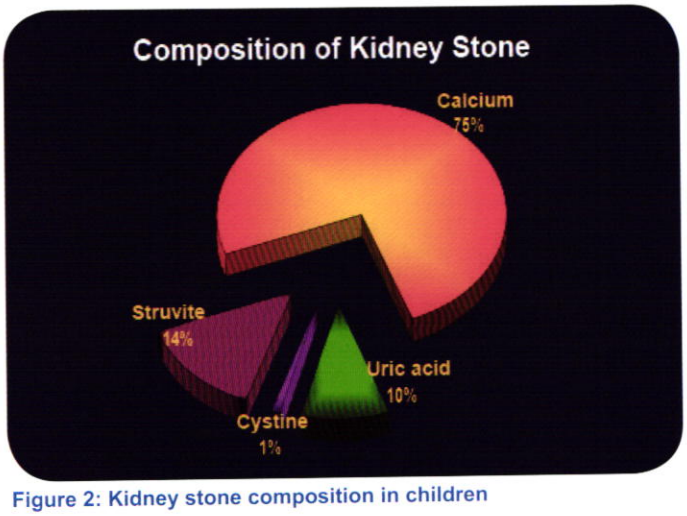

Figure 2: Kidney stone composition in children

Clinical Presentations and Diagnosis

The majority of children with kidney stones will present with non-specific symptoms that might be difficult to interpret. These include agitation, abdominal or flank pain, nausea and vomiting, especially in young children. Gross hematuria, dysuria, urgency and frequency, when present, may lead to the suspicion of a urinary tract infection. Indeed, some children may present with a urinary tract infection that leads to the finding of a kidney stone on imaging. A significant number of children are asymptomatic, with kidney stones incidentally discovered during the course of evaluation for other medical conditions. Evaluation of a

Table 1

RISK FACTORS ASSOCIATED WITH KIDNEY STONE DISEASE IN CHILDREN

RISK FACTOR	CONDITIONS ASSOCIATED WITH RISK
Hypercalciuria	Idiopathic hypercalciuria, primary hyperparathyroidism, hypercalcemic hypercalciuria, distal renal tubular acidosis, diuretics, normocalcemic hypercalciuria, hypervitaminosis A and D, metastatic bone disease, immobilization, Cushing syndrome, hypo/hyperthyroidism, adrenal insufficiency and adrenocorticosteroid excess, medullary sponge kidney, long-term parenteral nutrition, long-term assisted ventilation
Hyperoxaluria	Primary hyperoxaluria (I-III), dietary oxalate excess, secondary oxaluria of childhood (Crohn's disease, celiac disease, cystic fibrosis, A-beta-lipoproteinemia), absence of intestinal oxalate-degrading bacteria (oxalobacter formigenes)
Hyperuricosuria	Disorders of purine overproduction, high dietary purine, hereditary renal hyperuricemia, glycogen storage disease type 1, hyperuricosuric drugs
Cystinuria	Renal tubule immaturity in infants, hereditary cystinuria
Hypocitraturia	Distal renal tubular acidosis, malabsorption syndromes, hypokalemia, idiopathic hypocitraturia, infection
Hypomagnesuria	
Structural renal abnormalities	Vesicoureteral reflux, ureteropelvic junction obstruction, medullary sponge kidney, polycystic kidney disease
Infection	Urea-splitting organisms (Proteus, Klebsiella, Pseudomonas, Staphilococcus)
Drugs	Loop diuretics, Vitamin A and D, ethylene glycol, excessive calcium administration, carbonic anhydrase inhibitors, topiramate, ceftriaxone, ampicillin, indinavir, ascobic acid, probenecid, corticosteroids, triamterene, sulfadiazine, melamine
Diet	High salt, oxalate and protein intake, ketogenic diet
Environmental	Climate, global warming

child with suspected kidney stones should be prompt and must begin with a thorough history. Information about any previous kidney stones, recurrent urinary tract infections, underlying malabsorption syndromes/inflammatory bowel disease, diet, use of drugs associated with kidney stones must be obtained. In premature infants, a history of furosemide use is particularly helpful in determining the cause of kidney stones. Determination of the presence of a family history of kidney stone disease should be made. Physical examination should include assessment of vital signs, growth parameters, a thorough abdominal and flank examination, as well as examination of the musculoskeletal system to uncover any skeletal deformities that might suggest an underlying metabolic disorder such as renal tubular acidosis.

Laboratory evaluation should include a urinalysis, looking for the presence of red blood cells and crystals. A urine culture should also be sent. Other laboratory studies to be obtained include a comprehensive metabolic panel (including a uric acid level), to assess renal function and evaluate for the presence of metabolic risk factors. Further metabolic work-up is better performed when patients are on their usual diet, fluid intake and activity level. This includes a 24-hour urine collection for metabolic and urinary risk factor analysis. In younger children, this may be difficult, and a spot urine sample for urinary solute concentrations may be adequate. Chemical stone analysis for

stone composition is the best diagnostic evaluation, but should go along with evaluation for metabolic risk factors as earlier discussed. Patients and their caregivers should be encouraged to retrieve any stones that are passed for chemical analysis. Other tests to consider include parathyroid hormone, vitamin D and A levels (for patients with hypercalciuria), and plasma oxalate. Genetic testing is reserved for patients with suspected underlying genetic disorders such as primary hyperoxaluria.

Imaging

There are currently three most commonly-used imaging modalities in the diagnosis of kidney stones: ultrasonography, plain abdominal radiography and non-contrast enhanced spiral computed tomography. Of these, CT is the most sensitive for the detection of renal stones (97 percent sensitivity and 96 percent specificity), followed by ultrasonography and plain radiography (radiopaque stones). The advantage of CT over other modalities include its ability to detect small stones (1mm), which may not be detected by ultrasonography or plain radiography; ureteral stones, which may not be detected by ultrasonography; and radiolucent stones, which may not be detected by plain radiographs. In small children, there are concerns about radiation exposure from CT, and so it is recommended to obtain an ultrasonography first. If no stones are found but symptoms persist, a non-contrast enhanced helical CT can then be obtained. In institutions where radiation doses can be adjusted to the size and weight of the child to reduce the radiation exposure while at the same time maintaining adequate image quality, CT is recommended as the initial imaging modality.

Treatment and Prevention of Kidney Stones

The goals of acute management of kidney stones in children are to relieve pain, ensure adequate hydration and facilitate passage or removal of the stone. Pain control is achieved with the use of non-steroidal anti-inflammatory agents, narcotic agents or a combination of both. Although medical therapies (with calcium channel blockers, corticosteroids and β-blockers) to facilitate the passage of stones have been reported in children and adults, they are rarely used. Urologic intervention in the form of shock wave lithotripsy, ureteroscopy or percutaneous nephrolithotomy may be required for stone removal in the case of obstructing stones. Patients with infection-related stones require sterilization of the urinary tract, removal of the stones and correction of any obstructive lesions.

Chronic management of kidney stones in children hinges on treatment of any specific underlying metabolic disorder and prevention of stone recurrence. Reduction of solute concentration in the urine is key to preventing stone formation. A high fluid intake of >1.5-2L/1.73m^2 per day is recommended in all treatment regimens, to maintain high urine flow and help lower urinary solute concentration. Dietary recommendations generally include maintenance of normal calcium intake, low sodium and oxalate intake and correction of low urinary citrate levels. Urinary citrate binds to calcium, forms a soluble complex reducing the precipitation of calcium with other substances, thus leading to a decreased urinary saturation index. Severe hypercalciuria is treated with thiazide diuretics that reduce urinary calcium excretion by increasing calcium uptake in the distal tubule and promoting calcium reabsorption in the proximal tubule.

Prognosis and Follow-up

The prognosis of children with kidney stone disease is generally good, and most patients do not develop long-term kidney problems. However, children with underlying metabolic defects may suffer significant morbidity from recurrent stone disease. Serial ultrasonography is helpful in identifying children with recurrent disease. Patients with kidney stone disease require close follow-up and should be managed in specialized centers with experienced medical staff.

Summary

The incidence and prevalence of kidney stone disease has been rising in the last several decades. All children who present with kidney stones should be thoroughly evaluated for the presence of any underlying genetic or metabolic disorders so appropriate individualized treatment regimens can be developed. High fluid intake is an important part of any treatment regimen, regardless of underlying disorder. The best treatment of kidney stone disease is prevention.

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Rehab Center receives CARF reaccreditation

The Commission on Accreditation of Rehabilitation Facilities (CARF) has granted Children's Hospital a reaccreditation to the hospital's Rehabilitation Program. Children's Hospital is the only freestanding pediatric hospital in Louisiana that has CARF accreditation.

"CARF has standards, values and quality control benchmarks that allow us to see how we compare against other institutions," said Ann Tilton, MD, director of the Gilda Trautman Newman Rehabilitation Center at Children's Hospital. "We are constantly striving to raise the bar when it comes to the quality of patient care the Rehab Center delivers to our patients."

CARF is an independent, non-profit accrediting body whose mission is to promote the quality, value and optimal outcomes of services through a consultative accreditation process and continuous improvement services that center on enhancing the lives of persons served.

An accreditation from CARF International is the highest level of accreditation that can be awarded to an inpatient rehabilitation organization and shows the organization's conformance to the CARF standards.

Children's Hospital's inpatient rehabilitation is comprised of a 12-bed center where children from throughout the Gulf South region come to participate in comprehensive, interdisciplinary, family-centered, team-oriented care to achieve their highest level of functioning after a life-changing event.

Children's Hospital opened 60 years ago as the 50-bed, $1.2 million Crippled Children's Hospital, a rehabilitation hospital for children recovering from polio. Today, Children's Hospital serves as the Gulf South's leading pediatric medical center and is dedicated to providing the very best healthcare possible.

The Rehabilitation Center was last accredited by CARF in November, 2011.

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1. Which of the following is (are) true of kidney stone disease in children?
   a. The incidence of kidney stones in children has decreased in the last several decades.
   b. There is an underlying predisposing factor in the majority of cases.
   c. The most common types of stones in children are calcium stones.
   d. b and c

2. Kidney stone formation is influenced by which of the following?
   a. Increased urinary supersaturation of stone-forming solutes
   b. Urinary pH
   c. Urine flow rate
   d. All of the above

3. Treatment and prevention of kidney stone disease in children includes which of the following?
   a. Increased oral fluid intake
   b. Maintenance of a low calcium diet
   c. Use of thiazide diuretics in patients with hypercalciuria
   d. a and c

4. Which of the following statements best describes the prognosis of children with kidney stone disease?
   a. Most children do well and do not develop kidney disease
   b. Children with kidney stone disease are at high risk for developing chronic kidney disease
   c. The prognosis of children with kidney stones remains unknown
   d. Children with kidney stone disease rarely suffer recurrence of symptoms

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