Chapter 15 Obesity and Pediatric Nephrolithiasis



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Introduction

There is an ongoing obesity epidemic in the United States and in many other parts of the Western World. This involves not only adults, but it extends to children. In 1975, the childhood obesity prevalence was 4%. In 2016, this same statistic was 18% [1]. In parallel, there has been an increase in both the incidence and prevalence of pediatric nephrolithiasis. [2]. The purpose of this book chapter is to examine the current association between obesity and kidney stones in children.

Epidemiology

Once considered relatively rare, pediatric nephrolithiasis has become exceedingly more common. Between 1984 and 2008, the incidence of pediatric nephrolithiasis increased 4% per year [2]. Similarly, the proportion of patients with pediatric kidney stones in a freestanding hospital increased 10.6% in 2008 alone [3]. There have been many proposed theories for these increases including climate change, dietary habits, and obesity [4]. For example, when looking at the incidence of pediatric

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kidney stones from 1997 to 2012 in South Carolina in 15–19-year-olds, there was a 26% increase over 5 years (incidence rate ratio, 1.26; 95% confidence interval, 1.22–1.29). These increases in incidence were most prominent in females (relative to males) and in blacks (relative to whites) [5]. Other studies have looked at the same database of South Carolina patients and reported an increased prevalence of pediatric nephrolithiasis [6]. However, they did not report the same trends with race and gender.

Interestingly, female adolescents have a higher rate of stone formation compared to male adolescents, inverse to what is seen in the adult population [7]. Even in the adult population, trends from 1997 to 2002 showed the ratio of prevalence of kidney stones between genders has shifted from 1.7:1 to 1.3:1 male-to-female [8]. In addition, a study from 2002–2007 showed that adolescent females were 1.5 times more likely to be hospitalized for kidney stones [9]. In that same study, 88% of pediatric patients hospitalized for kidney stones were white and hospitalizations were more common in the North Central region compared to the Southern United States. These trends suggest that perhaps other factors, outside of obesity, may contribute to kidney stone risk in children as compared to adults.

There is compelling epidemiologic evidence demonstrating the association between obesity and incident kidney stones in adult cohorts [10–12]. However, this association is not as clearly demonstrated in children. In a multivariate analysis of the Kid's Inpatient Database ("KID"), Schaeffer and associates found that obesity did not influence the need for inpatient hospitalization for kidney stones [13]. In contrast, Kokorowski and colleagues, in a multivariable conditional logistic regression analysis of the Pediatric Health Information System Database, found a significantly higher odds ratio for kidney stones in obese subjects. Both groups also reported positive correlations with kidney stones and hypertension, a condition associated with kidney stone risk.

With the rise in both obesity and kidney stones in children, one might expect a tangible relationship [14]. However, when examining trends from 1999–2010 in pediatric obesity, there was an increase in BMI among boys age 12–19 (p = 0.04), but no such increase in any other age group or in girls [15]. In contrast, the increase in pediatric kidney stones seems to be predominantly adolescent girls [16]. Another study found no significant relationship between BMI and urolithiasis, but did find a significant decrease in the odds of urolithiasis in black race and Medicaid payer status [17]. While the aforementioned studies collectively do not identify a relationship between obesity and kidney stones in children, pediatric kidney stone formers may just be in a prodrome state marching towards obesity. Thus, longitudinal studies of this cohort are warranted [2, 18–22].

Diet and Nutrition

If we hypothesize that kidney stone formers are in a march towards obesity, nutritional habits of children in general need to be taken into consideration. Two dietary habits in children, low fluid intake and increased sodium consumption, can both lead to an increase in the supersaturation of stone forming salts, a surrogate for kidney stone risk [23, 24]. Children, on average, spend more time exercising and playing outdoors than adults, and therefore require more water on average per body weight. To compound this, children often do not meet their daily water intake requirements [25, 26]. A univariate and multivariate analysis demonstrated that overweight and obese children have lower urinary volumes than their normal-weight counterparts [27].

Two-thirds of water intake in the pediatric population occurs at mealtimes, perhaps indicating that during non-mealtimes many children are not adequately hydrating. Additionally, the same study found all age groups had a mean water intake that was less than the suggested adequate water intake. The aforementioned fluid consumption patterns may serve as a major contributing factor to stone disease [28]. In addition, water intake has been shown to be inversely associated with the consumption of energy dense foods, suggesting the unhealthier a child's diet, the less water intake they will have. It is well established that obese children eat a poorly energy dense diet, thus suggesting this cohort may be more susceptible to stone formation based on dietary and water intake factors.

In regard to sodium, an analysis of NHANES data has demonstrated that the average sodium consumption for the pediatric population was close to 3400 mg/day, when the recommended daily allowance is less than 2300 mg/day [29]. Sodium intake is positively correlated to urinary calcium excretion and the latter is correlated to kidney stone risk (Table 15.1).

It is well described that high sodium diets predispose to stone formation. These same high salt diets typically go hand-in-hand with high fat, high carbohydrate diets, potentially resulting in obesity [20]. BMI directly correlated with increases in urinary sodium, calcium, uric acid, magnesium, and oxalate, while also decreasing the urinary pH. In addition to higher urinary volumes and low dietary sodium, weight reduction would be useful when counseling stone formers [30].

In a mouse model, feeding mice a diet rich in both sodium and fructose yielded both an increase in uric acid in the urine and a decrease in "stone inhibitors," such as magnesium and citrate [31]. Not only did increasing intake of sodium result in more sodium in the urine, effectively concentrating the urine output, but the decrease in protective factors such as magnesium and citrate further increase the risk of stone formation. It is important to note that adolescents, aged 12–18, have the greatest consumption of fructose (73 g/day) than any other age group [32].

The association between sugar-sweetened beverages and obesity and Type II diabetes in children and adolescents has been demonstrated by several epidemiological

Note
<3 L/day
>2300 mg/day
Hypercalciuria, hypocitraturia
Temperature, relative humidity
Topiramate, calcitriol, steroids

 Table 15.1 Risk factors for pediatric stone forming patients [7]

trials [33]. The intake of sugar-sweetened beverages, such as soda and juice, has been on the climb in the United States [34]. Providing children and adolescents with proper knowledge of nutrition may be a necessary primary preventative measure, thereby reducing obesity and any downstream disease, such as pediatric kidney stone disease [35].

Obesity may lead to a plethora of other acute and chronic renal conditions, including an increased risk of urinary tract infections (UTIs). UTIs can increase risk of certain types of kidney stones. At all data stratifications, obese patients were significantly more likely to be diagnosed with a UTI or pyelonephritis than non-obese patients. The data remains inadequate to draw such conclusions in children, thus necessitating the requirement for more studies to be conducted analyzing obesity, UTIs, and infection-related stones [36].

24-Hour Urine

24-hour urine has widely been considered the gold standard in the workup of pediatric urolithiasis. Normal values can vary based on a child's age, gender, growth status, and race. Given the wide range of a child's diet, environment, and genetics, two 24-hour urine collections are now becoming a common component of clinical workup. While there are no studies yet suggesting how many 24-hour urine samples are adequate for children, adult studies support two collections on initial presentation [37–39]. Spot 24-hour urine testing has been utilized to assess stone risk but due to its shortcomings is mainly used in situations where accurate 24-hour urine specimens cannot be collected.

One study retrospectively analyzed 110 stone forming pediatric patients and sorted these patients into two groups: BMI below 85th percentile and BMI above 85th percentile. When analyzing the 24-h urine parameters of these patients, the study found that overweight and obese patients (BMI >85th percentile) had lower body surface area adjusted citrate (p = 0.03), lower urine phosphate (p = 0.04), lower urine magnesium (p = 0.01), and an increased incidence of hypercalciuria (p = 0.02). While this study did not find an association between BMI and urine pH, it may help describe the causal pathway of obesity, to changes in 24-h urinary parameters, to eventual stone formation in obese pediatric patients [40]. Despite some studies showing 24-h urine differences, other studies have determined that BMI itself could not be considered a separate and definite risk factor for urolithiasis in pediatric patients [41]. The lack of consistent findings further warrant larger studies to investigate pediatric BMI and its effects on 24-h urinary parameters.

There have been attempts to associate pediatric stone formation with metabolic disorders, such as hypocitraturia [42]. These disease states, including metabolic syndrome, affect urinary parameters, thereby theoretically increasing the risk of pediatric stone formation. When measuring BMI, urinary pH, and other parameters in obese adolescents, it appears those diagnosed with metabolic syndrome have specific urine findings: decreased urinary pH and increased relative saturation ratio

	Abnormal Values	
Calcium	>4.0 mg/kg/day	
Uric acid	>10.7 mg/kg/day	
Oxalate	>40 mg/1.73 m²/day	
Citrate	<320 mg/1.73m ² /day	
Magnesium	<1.2 mg/kg/day	
Calcium/citrate	>0.33 mg/mg	

Table 15.2 Abnormal 24-h urinary findings in pediatric stone formers [68, 69].

of calcium oxalate [43]. 24-h urine studies have also demonstrated that pediatric kidney stone formers have lower urine volume, higher calcium excretion, and increases in the relative supersaturation of calcium phosphate and calcium oxalate [44] (Table 15.2). One single-institution study looked closer at the urinary mineral profile and showed that obese pediatric patients do have lower levels of citrate, potassium, and urine pH compared to their normal-weight counterparts [22].

While poor nutrition may lead to obesity and predispose to pediatric stone disease, proper nutrition may be the key to stone prevention for the patient. Newer nutritional guidelines have been published that suggest increasing fluid intake to 3 L, trying to maintain 2 L of daily urine output to prevent supersaturation of calcium, and increasing urinary citrate with lemon and orange juices [45]. Additionally, limiting sodium intake per child age group (to less than <2 g of sodium per day) and increasing intake of fruits and vegetables to alkalinize the urine all help prevent stone formation in pediatric patients [46]. Other guidelines broadly suggest low-protein (<20 g daily), low-salt (<2 g daily), and adequate hydration (3 L daily) [47].

Stone Composition

In children, most stones are a composition consisting of calcium oxalate and/or calcium phosphate, with mixed uric acid stones having a relatively higher prevalence compared to the adult population [48]. This differs slightly from adults where mixed uric acid stones are much less common. A study showed that as pediatric BMI increased, urine oxalate excretion decreased, and supersaturation of calcium phosphate increased [49]. Another study hypothesized is that the pediatric population may have different renal handling of solutes compared to adults and may have more pronounced effects of diet on the renal handling of uric acid.

The western diet, rich in animal protein, refined carbohydrates, processed foods, and added sugar, act as an acid load on the body, which may explain the uric acid found in pediatric kidney stones. It is possible that obesity may not directly lead to stone formation, instead that the dietary indiscretions seen in obese children may predispose to increased calcium phosphate, calcium oxalate, and/or uric acid in the renal tubules. The complexity of stone composition changes in the pediatric population over time makes it difficult to determine any one cause for the changes [50, 51].

A composition analysis of 5245 pediatric urinary stones between the years of 2000 and 2009 determined that calcium was seen in 89% of all stones and that ammonium-containing stones decreased with age [52]. Additionally, a 24-h urine analysis in the pediatric stone population showed that calcium oxalate stones have a stronger association with calciuria and a moderate association with oxaluria, magnesuria, and acidification of urine, whereas calcium phosphate stones had lower associations with urinary risk factors, suggesting calcium oxalate stones may be more closely linked to traditional risk factors [53].

Medical Management

Should a pediatric patient, obese or not, experience severe or recurrent stone disease, treatment may progress from dietary to medical.

Interestingly, medications alone are typically not the most beneficial treatment. Following general guidelines, such as increasing or decreasing certain dietary parameters, adding or removing specific food groups, or adjusting fluid intake, play an additive or synergistic role with the aforementioned medications [54]. Eighty five percent of patients could significantly decrease their risk of stone recurrence by taking primary precautions such as adjusting their lifestyle and dietary habits. In the remaining 15% in which stones continued to recur, the combination therapy of thiazides and citrate therapy were sufficient as medical treatment [55] (Table 15.3).

Surgical Management and Techniques

Should non-surgical management of acute pediatric stone disease fail, there are more immediate and invasive approaches to treating the stone [48]. If medical expulsion therapy or other non-invasive treatments fail, surgical interventions such as extracorporeal shockwave lithotripsy, ureteroscopy (URS), and percutaneous nephrolithotomy may be indicated [56] (Table 15.4).

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Suggested medical	
treatment(s)	Suggested dietary treatment(s)
Thiazide diuretics	Decreased salt intake
Potassium citrate	Increased fruit and veggies
Allopurinol	Decreased protein intake
None	Decreased salt intake
Pyridoxine	Reduction of oxalate-rich foods (e.g.,
	spinach)
Alkalinization therapy	Decreased protein intake
	treatment(s) Thiazide diuretics Potassium citrate Allopurinol None Pyridoxine

 Table 15.3
 Associated urinary findings with possible medical management [70]

Type of Surgical		
Approach	Pros	Cons
Shockwave lithotripsy	Non-invasive	Lower success rate, post-operative HTN
Ureteroscopy	Better stone clearance, advancing technology	Ureteral stenting, dependent on available technology
Percutaneous nephrolithotomy	High success rate	Invasive, increased surgical complications

 Table 15.4
 Pros and cons of main surgical approaches in pediatric patients [7]

Historically, extracorporeal shockwave lithotripsy was considered the preferred management, particularly for stones <20 mm [57]. Recent analyses of surgical techniques at major institutions across the United States have shown ureteroscopy is quickly gaining traction as arguably a better surgical approach, particularly in children [58]. Advances in endoscopy, including scope size and improved optics, has allowed for the adoption of ureteroscopy in the pediatric population, particularly in obese patients that present with more challenging anatomy.

While ureteroscopy is gaining traction and may overtake shockwave lithotripsy as the first-line surgical intervention in pediatric patients, it is important to note the challenges and limitations with this modality. A child's ureters are still developing and are both fragile and smaller than adult ureters, occasionally necessitating pre-stenting. Rarely, a ureteral stricture may occur, requiring ureteral reimplantation [59, 60]. With advancements in both optics and in the size of the ureteroscope, these complications are likely to decrease with time, cementing this as a safe and efficacious first-line surgical intervention in the pediatric population [61].

In terms of relative outcomes, ureteroscopy complications are not significantly different from shockwave lithotripsy. The success rates of the two types of operations were around 90% and not significantly different [62]. The challenging component of applying adult ureteroscopy techniques towards a pediatric population are surgeon training, ability, experience, and available technology [63]. It may be in the urologist's best interest to consider utilizing the latest ureteroscopy technology, with semi-rigid or flexible scopes, given a pediatric patient's fragile anatomy [64]. Should a stone's burden exceed 20 mm, progression to percutaneous nephrolithomy is typically the next best indication [65].

In the case of failure of progression from nephrolithiasis to urolithiasis, retrograde intrarenal surgery (RIRS) may be the next step. The RIRS approach has risen to the first rank in the preference of pediatric urologists, partly due to the method's reliability and efficacy. It may serve as a replacement for shockwave lithotripsy in small renal calculi and percutaneous nephrolithotomy in larger renal calculi [66]. The RIRS approach has been shown to be similar in overweight or obese pediatric patients when compared to normal weight, making it a useful surgical technique in this population as well [67].

Conclusion

Despite the existing evidence that obesity is linked to stones in adults, the evidence remains unclear if obesity plays a role in children. Further research into this area is needed.

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