

Review

# Is There an Association between Childhood Obesity and Pediatric Kidney Stone Disease? A Literature Review

Henry J. Paiste <sup>1</sup>, Luke Moradi <sup>1</sup> , Dean G. Assimos <sup>2</sup>, Kyle D. Wood <sup>2</sup> and Pankaj P. Dangle <sup>2,\*</sup>

<sup>1</sup> Medical School, University of Alabama Birmingham School of Medicine, Birmingham, AL 35233, USA; hpaiste@uab.edu (H.J.P.); lmoradi@uab.edu (L.M.)

<sup>2</sup> Department of Urology, University of Alabama Birmingham School of Medicine, Birmingham, AL 35233, USA; deanassimos@uabmc.edu (D.G.A.); kylewood@uabmc.edu (K.D.W.)

\* Correspondence: pankajdangle@gmail.com; Tel.: +1-205-996-8765

**Abstract:** Objectives: To examine the most recent literature and published science in determining any and all possible associations between pediatric obesity and pediatric urolithiasis. Methods: Retrospective literature review of pediatric stone formers with diagnosed stone disease and all associated risk factors. Peer-reviewed, published manuscripts from the past several decades were analyzed for risk factors associated with pediatric obesity such as diet, hypertension, and renal diseases. Comparing the pediatric obesity literature with the pediatric stone forming literature, any associations and correlations were derived and analyzed. Results: Despite the existing evidence that obesity is linked to stones in adults, the evidence remains unclear whether obesity plays a role in children. Nutritional discrepancies, in the setting of the obesity epidemic, have been shown to alter the risk profile of pediatric patients. Consistent with the published literature, and lack of consistent correlation with obesity and stone disease, is the knowledge that age, gender, geography, and climate may all play a role in the onset of pediatric obesity and may also be on the causal pathway toward pediatric urolithiasis. Conclusion: The manuscript demonstrates that there are a number of risk factors, congenital or acquired, that are associated with pediatric obesity. The mechanisms responsible for these associations may be on the causal pathway toward childhood urolithiasis. These mechanisms that underlie these associations need to be further investigated.

**Keywords:** kidney stones; pediatrics; obesity; diabetes; risk factors



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## 1. Introduction

The obesity epidemic in the United States and in many parts of the Western World continues to be an ongoing problem for both adults and children. In 1975, the childhood obesity prevalence was 4% and increased to 18% in 2016 [1]. There has been an increase in both the incidence and prevalence of pediatric nephrolithiasis [2]. The purpose of this review article is to examine whether any associations exist between obesity and kidney stones in children.

## 2. Materials and Methods

Our group utilized PubMed and Google Scholar and used the search terms “pediatric kidney stone disease” and “pediatric obesity” to search for articles predominantly from the past twenty years (2000–2020), with some landmark studies included from before 2000.

## 3. Epidemiology

Between 1984 and 2008, the incidence of pediatric nephrolithiasis increased 4% year over year. Dwyer et al. [2] reported that the proportion of patients with pediatric kidney stones in a freestanding hospital increased 10.6% in 2008 alone. Clayton et al. [3] have proposed many theories for these increases: changes in climate, dietary habits, and obesity incidence, among others. Routh et al. [4] found that the incidence of pediatric kidney

stones from 1997 to 2012 in South Carolina in teenagers increased 26% over five years, primarily in females and African Americans. Vicedo-Cabrera et al. [5] reviewed the same database of South Carolina patients and reported an increased prevalence of pediatric nephrolithiasis [6].

There is epidemiologic evidence demonstrating the association between obesity and incident kidney stones in adult cohorts, the leading hypothesis today thought to be insulin resistance, causing acidified urine and hypocitraturia, thus predisposing to stone formation [7–9]. This association of obesity and incident kidney stones is not as clearly defined in children. In a multivariate analysis of the Kids' Inpatient Database, Schaeffer et al. found that kidney stone risk was not affected by obesity in any age group, instead finding that age is the most significant predictor of kidney stone risk [10]. In contrast, Kokorowski et al., in a multivariable conditional logistic regression analysis of the Pediatric Health Information System Database, made up of 40 free-standing children's hospitals in the United States, found a significantly higher odds ratio for stones in obese subjects. Both groups also reported positive correlations with kidney stones and an existing diagnosis of hypertension, a condition associated with kidney stone risk.

Looking strictly at changes in body mass index (BMI), utilizing a representative sample of the healthy United States (US) child and adolescent population, Ogden et al. examined trends from 1999 to 2010 in pediatric obesity and found an increase in BMI among boys aged 12–19, but no such increases in any other age group or in girls [11]. Looking strictly at kidney stones, Novak et al. found an increase in pediatric kidney stones predominantly in first decade boys and second decade adolescent girls [12]. 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 [13]. While the aforementioned studies collectively do not identify a definitive relationship between obesity and kidney stones in children, longitudinal studies may be warranted [2,14–18].

As evidenced by the aforementioned, occasionally contradictory literature, there are a number of variables which can influence pediatric urolithiasis. Underlying renal metabolic abnormalities may be seen, such as absorptive hypercalciuria, renal hypercalciuria, and/or uric acid hyperexcretion [19]. An underlying metabolic abnormality was not discovered in 14% of patients [19]. Another study found the most common stone to be idiopathic (26%) in their pediatric patients [20]. In both of these studies approximately 30% of stones were related to a UTI, but these were predominantly in Middle Eastern countries. Other factors and etiologies may also play an independent or synergistic role in stone formation, such as genetic abnormalities, sporadic mutations, diet, nutrition, exercise, and lifestyle choices [21] (Table 1).

**Table 1.** Risk factors for pediatric stone forming patients.

Risk Factors in Pediatric Stone Formers	Note
Decreased fluid intake	<3 L/day
Increased salt intake	>2300 mg/day
Metabolic Abnormalities	Hypercalciuria, hypocitraturia
Environmental	Temperature, relative humidity
Medications	Topiramate, calcitriol, steroids

#### 4. Diet, Nutrition, Obesity

A. Diet, Nutrition, and Obesity—The relationship between diet, obesity, sugar-sweetened beverages, and diabetes in children has been demonstrated by several epidemiological trials [22]. The intake of sugar-sweetened beverages, such as soda and juice, have continued to increase in the United States [23]. Providing children and adolescents with proper knowledge of nutrition is a necessary primary preventative measure, to reduce obesity and subsequent downstream sequelae, such as kidney stone disease [24]. Additionally, the makeup of our food continues to change, with

- increased processing and chemical use, which must be considered as the diet of pediatric patients continues to change [25].
- B. Low Fluid Intake—Decreased fluid intake led to an increase in the supersaturation of stone-forming salts, a surrogate for kidney stone risk [26,27]. Children spend more time exercising and playing outdoors than adults, thus requiring more water on average per body pound. Additionally, children do not meet their daily water intake requirements. Cambareri et al. [28,29] demonstrated that overweight and obese children have lower urinary volumes than their normal weight counterparts [30]. The first study to document significant increases in juice intake was Dennison et al. in 1996, who then reported preschooler juice intake had increased in recent years from 3.2 fluid ounces per day to 5.5 [31]. They also noted a decrease in milk intake but did not look at changes in water intake.
  - C. High Sodium Intake—High-sodium diets predispose to stone formation by way of decreasing the renin–angiotensin–aldosterone axis and thus decreasing proximal tubule calcium reabsorption [16]. BMI directly correlates with increases in urinary sodium, calcium, uric acid, magnesium, and calcium oxalate, while also with decreased urinary pH [32]. In addition to higher void volumes and low dietary sodium, weight reduction may be useful when counseling stone formers [33]. National Health and Nutrition Examination Survey (NHANES) data have demonstrated that the average sodium consumption for the pediatric population is 3387 mg/day, nearly 1100 mg/day over the recommended daily limit of 2300 mg/day [34]. Adult studies have demonstrated that a dietary intake of greater than 10 g/day of salt correlates to an increased prevalence of hypercalciuria [35].
  - D. High Protein Intake—Proteins are an essential component of the human diet, yet are known to have a negative effect on the tubules of chronic kidney stone formers [36]. Excess protein is known to cause a negative calcium balance, decrease urine pH, and decrease urinary excretion of citrate, potassium, and magnesium, which are well-described stone inhibitors [37,38]. Additionally, animal proteins breakdown into purines, thus also contributing to hyperuricosuria in both uric acid and calcium stones [39].
  - E. High Sugar Intake—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 [40]. Of all demographics, adolescents, aged 12–18, have the greatest consumption of fructose (73 g/day), more than any other age group [41]. Johnson et al., in an adult randomized controlled study, found that with increased fructose intake came increased serum uric acid, decreased urinary pH, increased urine oxalate, and decreased urinary magnesium. With an increase in stone-forming risk factors (increased uric acid, increased urine oxalate, and decreased urine pH) and a decrease in stone inhibitors (urinary magnesium), fructose may very well play a contributing role in stone formation [42].
  - F. Other Factors—Factors such as low magnesium intake, low citrate intake, and high oxalate intake must all be considered as contributing factors to stone disease as well. Fruits and vegetables are a primary source of magnesium, which inhibits calcium oxalate formation by binding up free oxalate and increasing its solubility [43]. Citrate plays a well described role in alkalinizing the urine and inhibiting the crystallization of calcium crystals [44]. Lastly, oxalate-rich foods, such as spinach and chocolate, increase oxalate intake, subsequently requiring the kidneys to filter more oxalate, which supersaturates with calcium, resulting in calcium oxalate crystallization [45]. An ideal, daily diet should consist of fruits and vegetables for magnesium, low calorie orange juice for citrate, and to be mindful of oxalate-rich food intake [46].

Pediatric patients with kidney stones present with abdominal and/or flank pain, gross hematuria, and dysuria [47]. The patient's history may reveal a history of previous stones, family history of stones, history of underlying metabolic disease, and current medications.

Obese pediatric patients will likely not present much differently than their normal-weight pediatric equivalents.

Per the American Urological Association (AUA), laboratory evaluation should include: urinalysis, urine culture, renal panel, Vitamin D, Parathyroid Hormone, Urine Calcium/Creatinine ratio, and CBC [48]. Imaging evaluation should include: non-contrast CT and/or ultrasonography and/or plain abdominal radiograph. Ultrasonography is preferred due to its high sensitivity and lack of radiation exposure [49]. The 24 h urine studies will be discussed in the following section.

## 5. The 24 h Urine Collection

The 24 h urine collection is widely considered the gold standard in the work up of kidney stone disease. Normal values can vary based on a child's age, sex, growth status, and race. Given the wide range of a child's diet, environment, and genetics, two 24 h urine collections are now becoming the mainstay of clinical workup. Adult studies support two collections on initial presentation [50–52]. While there is agreement on the significance of obtaining a 24 h urine study, guidelines allow for variability when deciding whether one sample or multiple samples are indicated [48]. However, 24 h urine collections are particularly challenging in the pediatric population. The efficacy of spot urine collection for normalized urine creatinine and overnight spot urine collections has been studied as a potential test for determining urinary abnormalities in these pediatric patients.

- A. **Urinary Risk Factors**—Certain disease states, such as hypocitraturia or metabolic syndrome, affect urinary parameters, thereby theoretically increasing the risk of pediatric stone formation [53]. For example, pediatric patients diagnosed with metabolic syndrome have specific urine findings: decreased urinary pH and increased relative saturation ratio of calcium oxalate [54]. The 24 h urine studies have also demonstrated that pediatric kidney stone formers have lower urine volume, higher calcium excretion and increased in the relative supersaturation of calcium phosphate and calcium oxalate. Murphy et al. [55] demonstrated that obese pediatric patients do have lower levels of citrate, potassium, and urine pH compared to their normal-weight counterparts [18].
- B. **Dietary Risk Factors**—Updated nutritional guidelines have been published that suggest increasing fluid intake to 3 liters, maintaining 2 liters of daily urine output to prevent supersaturation of calcium, and increasing urinary citrate with lemon and orange juices [56]. 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 [57]. Other guidelines broadly suggest low-protein (<20 g daily) and low-salt (<2 g daily) intake, and adequate hydration (3 L daily) [58] (Table 2).

**Table 2.** Dietary risk factors and recommendations dependent on stone type.

Type of Stone	Dietary Risk Factors	Dietary Recommendation
Calcium Oxalate	↑ oxalate, ↑ sodium	↓ oxalate, ↓ sodium, limit animal protein
Calcium Phosphate	↑ sodium	↓ sodium, limit animal protein
Uric Acid	↑ animal proteins	↓ animal proteins
Cystine	↓ water intake	↑ water intake

- C. **Regional variations in the United States**—24 h urine studies are not unanimous in their variation. When examining studies on a regional basis in the United States, there were few risk factors that were clearly established. Internationally, some studies were contradictory in their findings: Eisner et al., in California, finding decreased oxalate in stone formers and Sarica et al., in Turkey, finding increased oxalate in stone formers [32,59]. Based on the variation seen in these studies, the etiology underlying

these stones may not be solely from obesity, but rather multifactorial, unidentified risk factors, such as environmental, geographical, and familial (Table 3).

**Table 3.** The 24 h urine findings in obese patients by USA regions and country.

Author	Region	# of Patients	Prospective vs. Retrospective	% of Study Patients Who Are Overweight/Obese	Risk Factors
Bandari	Northeast (Pennsylvania)	110	Retrospective	26%	↑ urine Ca <sup>2+</sup> ↓ citrate ↓ urine PO <sub>4</sub> ↓ urine Mg <sup>2+</sup>
Murphy	South (Kentucky)	111	Retrospective	37%	↓ citrate ↓ potassium ↓ urine pH
Roddy	Midwest (Wisconsin)	117	Retrospective	100%	no differences ( <i>vs. National Survey of Children's Health 2007</i> )
Eisner	West Coast (California)	43	Retrospective	33%	↑ urine CaPO <sub>4</sub> ↓ oxaluria
Cambareri	“four institutions”	206	Retrospective	35%	↑ uricosuria ↓ urine volume
Sarica	Turkey	94	Prospective	46%	↑ oxaluria ↑ urinary Ca <sup>2+</sup> ↓ citraturia

## 6. Stone Composition

In pediatric patients, the majority of stones are composed of calcium oxalate and/or calcium phosphate. However, there appears to be an age at which stones occur—calcium phosphate stones occur more commonly in the first decade of life and calcium oxalate in the second decade [60]. Mixed uric acid stones have a relatively lower prevalence in the adult population. Eisner et al. [61] showed that as pediatric BMI increased, urine oxalate excretion decreased, and the supersaturation of calcium phosphate increased [32]. Another study hypothesized is that the pediatric population may have different renal handling and may have more pronounced effects of diet on the renal handling of uric acid [62]. The complexity of stone composition changes in the pediatric population over time makes it difficult to determine any one cause for the changes [60].

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 [63]. 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 [64]. Calcium phosphate stones had lower associations with urinary risk factors, thus suggesting that calcium oxalate stones may be more closely linked to traditional risk factors [64].

## 7. Treatment

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 together [65]. For example, Straub et al. found that 85% of patients could significantly decrease their risk of stone recurrence by taking primary precautions such as adjusting lifestyle and dietary habits [66]. In the remaining patients refractory to these changes, in whom stones continue to recur, the combination therapy of thiazides and citrate therapy were sufficient as medical treatment [66].

AUA guidelines recommend following a tiered approach in pediatric kidney stone disease [67]. Uncomplicated ureteral stones less than 10 mm should be observed, with or with-



out medical expulsion therapy (MET) [67]. Should observation or MET fail, ureteroscopy (URS) or shockwave lithotripsy (SWL) are the next steps. Should a stone be too large, typically greater than 20 mm, a non-contrast CT should be obtained before undergoing percutaneous nephrolithotomy (PCNL) [67] (Table 4).

**Table 4.** Comparison of international governing bodies of urology for pediatric kidney stones.

Governing Body	First-Line Workup	MET	Surgical	Diet/Fluids	Other Recommendations
AUA	<ul style="list-style-type: none"> <li>Metabolic assessment and active ultrasound surveillance</li> </ul>	<ul style="list-style-type: none"> <li>If stone <math>\leq</math> 10 mm, offer observation +/- alpha blockers</li> </ul>	<ul style="list-style-type: none"> <li>URS or SWL if <math>\leq</math> 20 mm</li> <li>If <math>&gt;</math>20 mm, obtain CT, proceed with PCNL</li> </ul>	<ul style="list-style-type: none"> <li>No suggestions or conclusions.</li> </ul>	<ul style="list-style-type: none"> <li>Do not routinely pre-stent patients</li> </ul>
EAU	<ul style="list-style-type: none"> <li>Metabolic assessment</li> </ul>	<ul style="list-style-type: none"> <li>No suggestions or conclusions</li> </ul>	<ul style="list-style-type: none"> <li><math>&lt;</math>20 mm SWL (URS feasible alternative)</li> <li><math>&gt;</math>20 mm PCNL</li> </ul>	<ul style="list-style-type: none"> <li>2.5–3.0 L/day fluid</li> <li>Diet rich in vegetables and fiber</li> <li>1.0–1.2 g of <math>\text{Ca}^{2+}</math>/day</li> <li>Limit NaCl to 4–5 g/day</li> <li>Limit animal protein 0.8–1.0 g/kg/day</li> </ul>	<ul style="list-style-type: none"> <li>Retain a normal BMI level</li> <li>Neutral-pH beverages</li> </ul>
BAUS	<ul style="list-style-type: none"> <li>Metabolic assessment +/- ultrasound</li> <li>CT if ultrasound indeterminate</li> </ul>	<ul style="list-style-type: none"> <li>If stone <math>\leq</math> 10 mm, consider alpha blockers</li> <li>Manage pain with NSAIDs +/- paracetamol</li> </ul>	<ul style="list-style-type: none"> <li><math>&lt;</math>10 mm URS or SWL</li> <li>10–20 mm URS, SWL, PCNL</li> <li><math>&gt;</math>20 mm: URS, SWL, or PCNL</li> </ul>	<ul style="list-style-type: none"> <li>1–2 L/day water</li> <li>Add fresh lemon juice to water</li> <li>350 to 1000 mg of <math>\text{Ca}^{2+}</math>/day</li> </ul>	<ul style="list-style-type: none"> <li>Consider pre-stent for renal staghorn calculi</li> </ul>

- A. Medical Expulsion Therapy (MET)—Observation is the mainstay of treatment for first-time stone formers. For stones less than 5 mm, 62% passed merely with observation. For stones greater than 5 mm, the stone-free rate was 35% [68]. Randomized controlled trials have shown that alpha blocker therapy for distal ureteral stones provides significant benefit, with an overall odds ratio of being stone free of 4.0 (95% CI 1.1–14.8) [69]. Alpha blocker therapy is typically tried for up to four to six weeks until definitive therapy is indicated. The role of alpha blockers in proximal and middle ureteral stones remains poorly defined in pediatric patients [70].
- B. Surgical—The two surgical methods, as outlined below, would be non-invasive endourological or invasive, open procedures.
  - a. Non-invasive—Should a pediatric patient fail observation or MET, or the stone is larger than 10 mm, shockwave lithotripsy (SWL) is the preferred non-invasive modality. SWL is typically preferred in certain pediatric populations, such as very small children, in which ureteroscopy access may be limited or challenging [71].
  - b. Invasive—Once more, should the patient fail observation or MET, or the stone burden be too significant for SWL, ureteroscopy (URS) or percutaneous nephrolithotomy (PCNL) are two choices for invasive, definitive treatment [72]. URS is typically indicated for stones up to 20 mm and when patient anatomy is amenable to ureteroscopy access [73]. SWL and URS have similar stone-free rates. For stones greater than 20 mm, a non-contrast CT should be obtained, followed by PCNL. Children are particularly susceptible to ionizing radiation due to their rapidly developing tissues, thus exposure should be kept as low as reasonably achievable (“ALARA” principle) [74] (Table 5).

**Table 5.** Pros and cons of main surgical approaches in pediatric patients.

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 tech
Percutaneous Nephrolithotomy	High success rate	Invasive, increased surgical complications

Historically, extracorporeal shock-wave lithotripsy was considered the preferred management, particularly for stones <20 mm [71]. Recent analyses of surgical techniques at major institutions across the United States have shown ureteroscopy is quickly gaining popularity, particularly in children [73]. Advances in endoscopy, including scope size and micro-ureteroscopy, 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 stent will be placed following ureteral perforation or extravasation. Even less commonly, a ureteral stricture may occur, requiring ureteral reimplantation [72,75]. With advancements in both optics and in the size of the ureteroscopy scope, these complications are likely to decrease with time, cementing this as a safe and efficacious first-line surgical intervention in the pediatric population [76]. Should a stone burden exceed 20 mm, progression to percutaneous nephrolithomy is typically the next best indication [67].

## 8. Conclusions

Based on the available data, there is no consistent agreement between studies showing strong association between obesity and stone disease in pediatric patients. The presence of risk factors is variable in published literature; especially with 24 h urinary parameters. Unlike adults, the association between pediatric obesity and pediatric stone disease may be interfaced with other variables related to genetic predisposition, environmental, demographic characteristics, and dietary/fluid variation. Obesity may be on the causal pathway but is not the sole factor driving stone formation in obese pediatric patients. Further multicenter prospective longitudinal studies may be able to decipher the complex relationship between obesity and stone disease.

**Limitations:** There are many limitations to this review article. New studies examining the incidence and mechanisms underlying pediatric kidney stones are being released almost monthly. Our review article is a snapshot in time of the current literature as of 2021. Our literature search was limited by what was currently published, not works in progress nor articles under review. Additionally, our literature were from the United States.

**How to Apply This Knowledge:** We recommend continuing your diligent approach in working up this fragile population of stone formers—pediatric patients. We recommend the use of a multidisciplinary team in these obese patients: urologists, nephrologists, and nutritionists. As seen in adults, weight loss may be one of the single most helpful lifestyle changes, followed by dietary changes based on the stone type.

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