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Effect of age, BMI, and gender on urinary risk factors in pediatric idiopathic stone formers

Andrew M. Fang[a], **Elena Gibson**[a,b], **Robert A. Oster**[a], **Pankaj P. Dangle**[a,c,*]

[a]University of Alabama at Birmingham, AL, USA

[b]University of Utah, UT, USA

[c]Children's of Alabama, Birmingham, AL, USA

Summary

Introduction—The incidence of pediatric urolithiasis has been increasing over the years; however, the etiology of this increase is not well understood. Age, body mass index, and gender have been examined as possible risk factors for stone disease, but with inconsistent and variable associations.

Objective—We aim to investigate the urine chemistry factors, as assessed by 24-hour urinary parameters, in pediatric stone formers at a large volume tertiary referral center in the highest areas in the United States, the Southeast, based on age, body mass index, and gender.

Study design—We retrospectively reviewed all pediatric stone formers who completed a 24-hour study between 2005 and 2016. Patients were stratified by age (3–10 versus 11–18 years of age), overweight status (above versus below the 85th percentile for body mass index), and gender (male versus female). (Summary Figure). Statistical analysis included analysis of variance and logistic regression.

Results—243 patients were included in our analysis. Patients in the first decade of life were found to have greater numbers of urinary risk factors than those in the second decade. Non-overweight patients were more likely to have hyperoxaluria and hyperuricosuria, while overweight patients were more likely to have hypocitraturia. Female patients were more likely to have higher hyperoxaluria, while male patients were more likely to have hypercalciuria.

Discussion: In contrast to prior publications, obesity is not linked to increased risk of urolithiasis with non-overweight individuals having a greater number of risk factors than the overweight cohort. Despite stone disease being more prevalent in adolescents, the greatest number

*Correspondence to: Pankaj P. Dangle, Department of Urology, University of Alabama at Birmingham, 1600 7th Ave South, Suite 318, Birmingham, AL 35233, Phone: 205-638-9840, Pankaj.dangle@childrensal.org.

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Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (include name of committee + reference number) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards

Informed Consent: Informed consent was obtained from all individual participants included in the study.

of risk factors were present in the first decade of life. Lastly, female children had more urinary risk factors than males. Further understanding of the underlying causes of stone disease in various pediatric populations is warranted.

Conclusion—While more urinary risk factors were identified in younger, non-overweight, and female patients, there remains no consensus on the urinary risk factors for pediatric urolithiasis. Further study is needed to elucidate the risk factors and pathophysiology of pediatric stone disease.

Keywords

pediatric; urolithiasis; gender; age; nephrolithiasis; BMI

Objective:

Over the last 20 years, the incidence of pediatric urolithiasis has rapidly increased with an estimated adjusted annual increase of 10.6% [1]. While obesity, diet, and climate have been established risk factors in adult urolithiasis, the associations in pediatric stone disease is not well understood [2, 3]. Hypotheses ranging from the increased use and sensitivity of radiological imaging to the increased prevalence of childhood obesity have been suggested [4].

The traditional 3:1 ratio of the male predominant sex distribution of urolithiasis has also decreased in the adult population, despite the increase in the prevalence of stone disease [5]. Interestingly, the sex distribution of pediatric urolithiasis appears to vary with age, with higher male prevalence of urolithiasis in the first decade of life and a higher female prevalence in the second decade [6–8]. Furthermore, the greatest increase in urolithiasis has been observed in the adolescent population [4, 9, 10]. However, the pathophysiology behind the temporal and gender differences in pediatric stone disease remains unknown.

In adults, the relationship between obesity and urolithiasis is well established with 24-hour urine chemistry assessments demonstrating associations between obesity and differences in urine pH, oxalate, calcium, and uric acid levels [11, 12]. However, multiples studies have presented variable associations between obesity and these parameters in children [13–18]. The association of obesity and nephrolithiasis in the pediatric population is less clear.

The inconsistencies in the urinary risk factors across different centers may suggest an underlying geographic difference in pediatric stone disease. Therefore, our study aims to characterize 24-hour parameters in pediatric patients living in one of the highest risk areas in the United States, the Southeast. This region is part of the “stone belt”, a stretch of the nation with a particularly high stone burden[19]. Risk factors for patients living in this area include a higher prevalence of pediatric obesity, a Southern diet generally low in fruits and vegetables, and higher annual temperatures than the rest of the United States [20–22]. Therefore, we hypothesize that there are underlying differences in urine chemistry in overweight, adolescent females that could account for their increased risk for stone disease.

Methods

After approval from our Institutional Review Board, we retrospectively identified pediatric urolithiasis patients with a 24-hour urinary studies recorded in a database of stone patients treated at a single institution between July 2005 and August 2016. The 24-hour urine studies were obtained per individual provider's practice patterns after the passage or treatment of the patients' stones, and all patients were stone free at the time of urine analysis. However, due to the heterogeneity of the practice patterns of the providers, the timing of urine analysis was not standardized and therefore not reported. The dataset included only idiopathic stone formers and patients with cystinuria, inborn errors of metabolism, anatomic urologic abnormalities, and other established medical conditions that raise the risk of urolithiasis were excluded. We also excluded patients with inadequate urine collection, defined by creatinine (Cr) excretion of <12 mg/kg.

Each patient completed a single 24-hour urine collection via Litholink™ (Itasca, Illinois, USA). Kits contained a combination of gentamicin and potassium chloride to serve as an antibiotic and preservative, respectively. Urine samples were then sent to Litholink™ for further analysis. Pediatric stone risk factors obtained from the Litholink™ report included urine volume, supersaturation of calcium oxalate (SSCaOx), calcium, oxalate, citrate, supersaturation of calcium phosphate (SSCaP), urine pH, and supersaturation of uric acid (SSUa) were analyzed. Dietary risk factors obtained from the report included sodium, potassium, magnesium, phosphorus, chloride, sulfate, and urine urea nitrogen. Urinary parameters were recorded in total amounts per 24-hour period and subsequently normalized for body surface area (BSA) using the Mosteller formula for BSA (√height (cm) x weight (kg)/3600) and creatinine (Cr). SSCaP, SSCaOx and SSUa were unadjusted. Hypercalciuria was defined as ≥ 4mg/kg/day, hyperoxaluria was defined as ≥ 40mg/BSA, hypocitraturia was defined as < 310 mg/BSA for females and <365 mg/BSA for males, and hyperuricosuria was defined as ≥ 0.815 mg/BSA [23, 24]. Due to the large variances in body composition at different ages in children, patient BMI was classified into two groups of above the 85^{th} percentile or below the 85^{th} percentile for age according to the Center for Disease Control (CDC). Overweight was defined by the CDC as a BMI at or above the 85^{th} percentile.

Patients were then stratified by age (3–10 versus 11–18 years old [yo]), BMI (non-overweight versus overweight), and gender (male versus female). Eight models were utilized in our analyses, as demonstrated in Figure 1. Descriptive statistics, such as means and standard deviations (for continuous variables) and frequencies and proportions (for categorical variables), were obtained for the 24-hour urinary parameters and the urinary pathology analytes. Continuous outcome measures were analyzed using analysis of variance (ANOVA). The ANOVA models included terms for age group, gender group, and BMI group. Categorical outcome measures (all were dichotomous) were analyzed using logistic regression analysis; the Firth method was used due to small frequencies in some of the sub-groups. Odds ratios and their corresponding 95% confidence intervals were obtained. Statistical tests were two-sided and were performed using a significance level of 5%. Statistical analyses were performed using SAS (version 9.4; SAS Institute, Cary, NC).

Results

A total of 266 patients were identified and 23 patients were excluded due to a history of cystinuria, missing weight data, and inadequate urine volume, defined as a Cr excretion of <12mg/kg. Of the remaining 243 idiopathic stone formers, 95 (39%) were between 3 and 10 years of age, 99 (40.6%) were considered overweight (BMI ≥85th percentile for their age group), and 97 (39.9%) were of the male gender. As race was reported in approximately two-thirds of our cohort and the vast majority was of the Caucasian race (93%), it was not examined in our study. Full descriptive statistics of each model are summarized in Table 1, Table 2, and Supplemental Table 1.

Several statistically significant associations were found for the continuous outcome measures through use of ANOVA, as demonstrated in Table 3. Patients between 3 and 10 yo had higher oxalate/BSA, citrate/BSA, potassium/BSA, magnesium/BSA, phosphorus/BSA, sulfate/BSA, calcium/Cr, oxalate/Cr, citrate/Cr, and uric acid/Cr than those between 11 and 18 yo. Overweight patients had more creatinine, calcium, oxalate, citrate, uric acid, sulfate, and sodium than non-overweight patients, and a higher supersaturation (SS) of uric acid. However, the only difference in urinary analytes found when corrected for BSA and Cr between overweight and non-overweight patients was for uric acid/Cr, where overweight patients had more. Males had less citrate/BSA, calcium/Cr, citrate/Cr, and uric acid/Cr than females.

Statistically significant associations for the categorical outcome measures were found through the use of logistic regression analysis. Patients in the first decade of life were more likely to have hypercalciuria, hyperoxaluria, hyperuricosuria, elevated urinary sodium, elevated urinary magnesium, elevated urinary phosphorus and lower urinary volume. On the other hand, patients in the second decade of life and were more likely to have elevated Ca/Cr ratio, and hypocitraturia compared to the younger cohort, as demonstrated in Figure 2. Non-overweight patients were more likely to have dietary risk factors of elevated urine sodium, elevated urine phosphate, and elevated urine chloride, as demonstrated in Figure 3. They were also more likely to have stone risk factors of hyperoxaluria, hyperuricosuria, and lower urine volume. On the other hand, overweight patients were more likely to have hypocitraturia. Males were more likely to have hypercalciuria and hypocitraturia, while females were more likely to have hyperoxaluria and elevated urine urea nitrogen, as demonstrated in Figure 4.

Discussion

Despite the growing evidence that the epidemiology of urolithiasis in the pediatric population has been changing over the last couple of decades, the pathophysiology and risk factors for stone formation is not well understood. In this study, we provide a comprehensive analysis on urine chemistries for idiopathic pediatric stone former in the Southeast United States. Patients in their first decade of life had more urinary risk factors for stone disease than those in the second decade. Older patients were only more likely to have hypocitraturia. While there were differences in urinary analytes between between non-overweight and overweight patients, these trends did not continue when corrected

for BSA and Cr. Overweight patients were more likely to have hypocitraturia, while non-overweight patients were more likely to have hyperoxaluria, hyperuricosuria, and lower urine volume. Females were more likely to have higher calcium/Cr, citrate/Cr, uric acid/Cr, and hyperoxaluria, while males were more likely to have hypercalciuria. Our findings at a single institution in the Southeast United States are surprisingly not consistent with current epidemiologic trends regarding age and obesity. Younger patients were found to have more risk factors for stone disease and non-overweight patients were more likely to have hyperoxaluria, hyperuricosuria, and hypercalciuria. However, our findings do support the increasing prevalence in female pediatric urolithiasis as females had more urinary and dietary risk factors on 24-urine urine samples than males. Nevertheless, pediatric urinary risk factors are heterogenous and likely reflect the differing cultural, dietary, geographic, or potentially hormonal differences. Our population's urinary risk factors could reflect a metabolic reaction to the hot and humid environment of the South compounded with the high protein and high fat diets seen in this region. However, separate studies that controlled for climate and diet are needed to further elucidate these geographic differences.

The association between age and stone formation in the pediatric population has been noted in several studies. Utilizing the Kids' Inpatient Database, Schaeffer et al examined 6,115,443 children from 2003 and 2006 and determined that age was the strongest predictor of stone risk ($p<0.001$) with a >30-fold increase in risk between their youngest and oldest age groups [25]. A more recent analysis of the Kids' Inpatient Database and Healthcare Costs and Utilization Project National ED Sample continued to show that the frequency of urolithiasis, particularly in adolescent females, continued to rise [9]. Further corroborating this trend, Dwyer et al's examination of 207 children across a 25-year period found that the adolescent years of 12 to 17 years was the predominant time period for stone formers in their cohort [4]. However there remains no definitive data that elucidates this apparent association.

While the relationship between obesity and urolithiasis is well established in the adult population, multiple studies have in turn hypothesized that the rise in childhood obesity is linked to the rise in pediatric urolithiasis. When compared to normal weight children, obese children have been found to have less fluid intake and decreased hydration status, which may be a potential risk factor for stone disease [26]. However, geographic and cultural differences may also play a role in the pathogenesis of pediatric urolithiasis. Cambareri et al performed a multi-center retrospective study comparing overweight/obese patients to a group of normal-weight urolithiasis patients from multiple regions of the U.S. including the Pacific West (California), South (Tennessee, Virginia) and Midwest (Michigan). They found lower urine volumes and higher urinary uric acid levels in children with a BMI ≥ the 85^{th} percentile, but differences across geographic regions were not identified [27]. Another U.S. study in the Pacific West (California), stratified patients into quartiles based on BMI and found that weight was associated with increased SSCaP and decreased urine oxalate. [28] Bandari et al observed increased rates of hypercalciuria and decreased urine citrate, phosphorus, and magnesium in a population of overweight pediatric patients living in the Northeast U.S.[13]. Among children in a Midwest state (Wisconsin), a BMI >95^{th} percentile was associated with decreased urine volume and no significant differences in metabolic parameters [29]. Internationally, a study in Turkey stratified patients by BMI and reported decreased urine oxalate and uric acid levels among overweight children [14].

Several studies have also noted a more balanced gender ratio in pediatric urolithiasis in recent years. Novak et al's examined the 2003 Kids' Inpatient Database and found the sex distribution of patients discharged for stone disease was not uniform across all ages with stone disease being more prevalent in boys in the first decade and girls in the second decade. In fact, they too found a positive association between age and stone disease ($p<0.001$) [6]. These findings were further corroborated with Kusumi et al's population study with females accounting for 60% (standard error [SE] 0.85) of children from 1997 to 2012 [9]. Our findings further corroborate these gender differences with 60% of stone formers were female in the first decade of life and 60.1% of stone formers were female in the second decade. Hormonal changes during the pubertal years have been postulated as a possible explanation of the age related associated. Heller et al found that estrogen treatment in postmenopausal women altered their urine chemistries by decreasing urinary calcium excretion and calcium oxalate when compared to women who did not receive estrogen replacement [30]. However, whether hormonal changes in the pubertal period influence urine chemistries and stone formation remains to be elucidated. Nevertheless, it is possible that estrogen levels in females has the potential to be a risk factor in stone disease.

There are several limitations to our results. The first is the retrospective nature of the study, with clinical data limited to what was recorded in the medical record. Therefore, some factors including family history were not readily available in the record and not analyzed. Second, the analyzed data stems from a single tertiary pediatrics hospital in the Southeast United States, which may limit its generalizability to other healthcare institutions. Furthermore, the normalized reference ranges provided by Litholink as a comparative set may not be applicable across the range of patients seen in a pediatric population. Additionally, only one 24-urine collection was obtained per patient. As with other cohort studies, single 24-hour urine collections may be insufficient to full evaluate a patient before metabolic treatment for stone prevention, as significant variation may exist between urine collections [31, 32]. Ideally, future, prospective, and matched cohort studies comparing pediatric stone formers and non-stone formers that account for the children's environment and dietary intake are needed to determine the metabolic risk factors associated with urolithiasis. Lastly, studies are also needed to determine the normalized reference ranges of 24-hour urine parameters in pediatric populations to provide clinicians a comparison to guide medical stone prevention and management.

Conclusions

There is an increasing incidence of pediatric urolithiasis especially in the adolescent and female populations with pediatric obesity being examined as an underlying factor. However, we found that patients in the first decade of life had more metabolic deviations in their 24-hour urine collection than patients in their second decade. Non-overweight patients were more likely to have hyperoxaluria, hyperuricosuria, and low urine volume. Lastly, hyperoxaluria and higher calcium/Cr, citrate/Cr, and uric acid/Cr were identified ask risk factors that potentially account for the rise in stone disease in female children. While these risk factors support the increasing prevalence of stone disease in female children, there remains no consensus on the association between childhood obesity and urolithiasis. Further study is needed to elucidate the risk factors and pathophysiology of pediatric stone disease.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

BMI	body mass index
SSCaP	supersaturation of calcium phosphate
SSCaOx	supersaturation of calcium oxalate
SSUa	supersaturation of uric acid
BSA	body surface area
CDC	Centers for Disease Control
yo	years old
Cr	creatinine
CT	computed tomography

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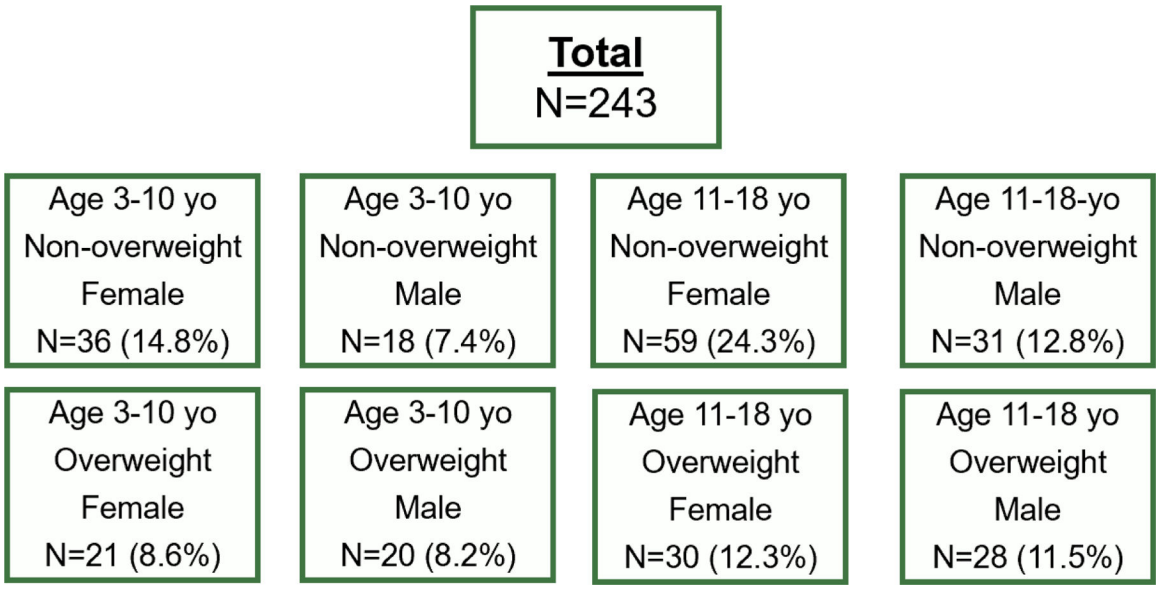

Figure 1:
Subdivision of the study models based on age, overweight status, and gender

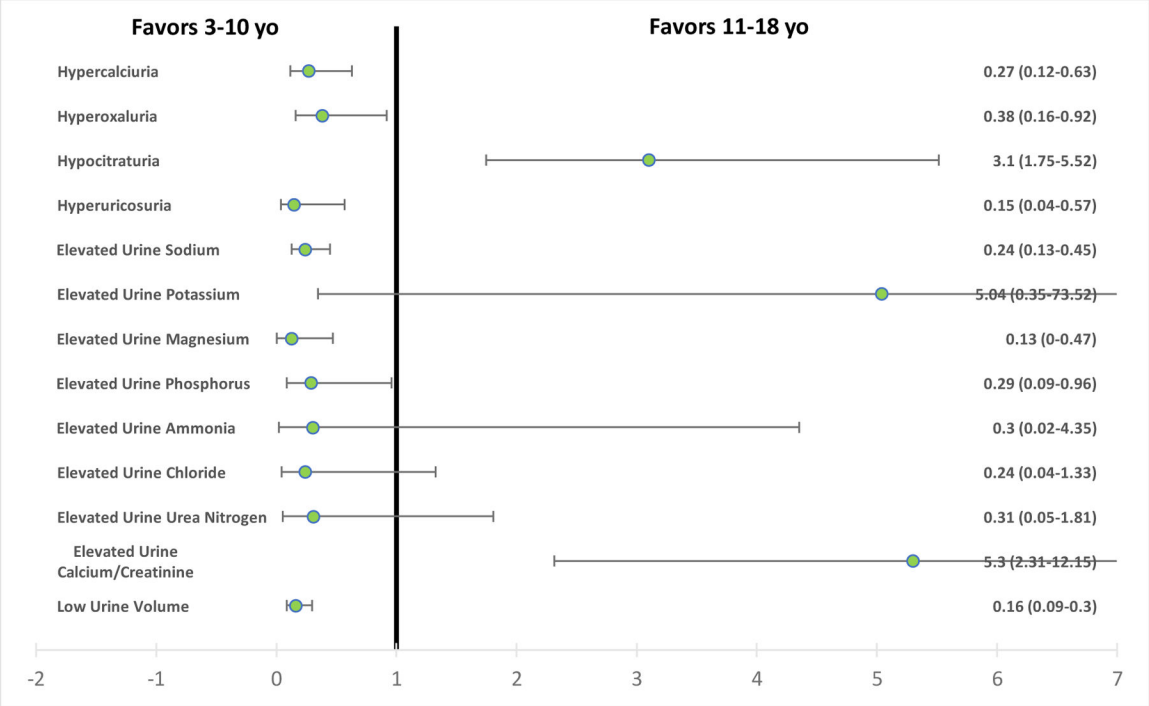

Figure 2:
Odds ratios of urinary pathology for patients between patients 3 to 10 yo versus 11 to 18 yo

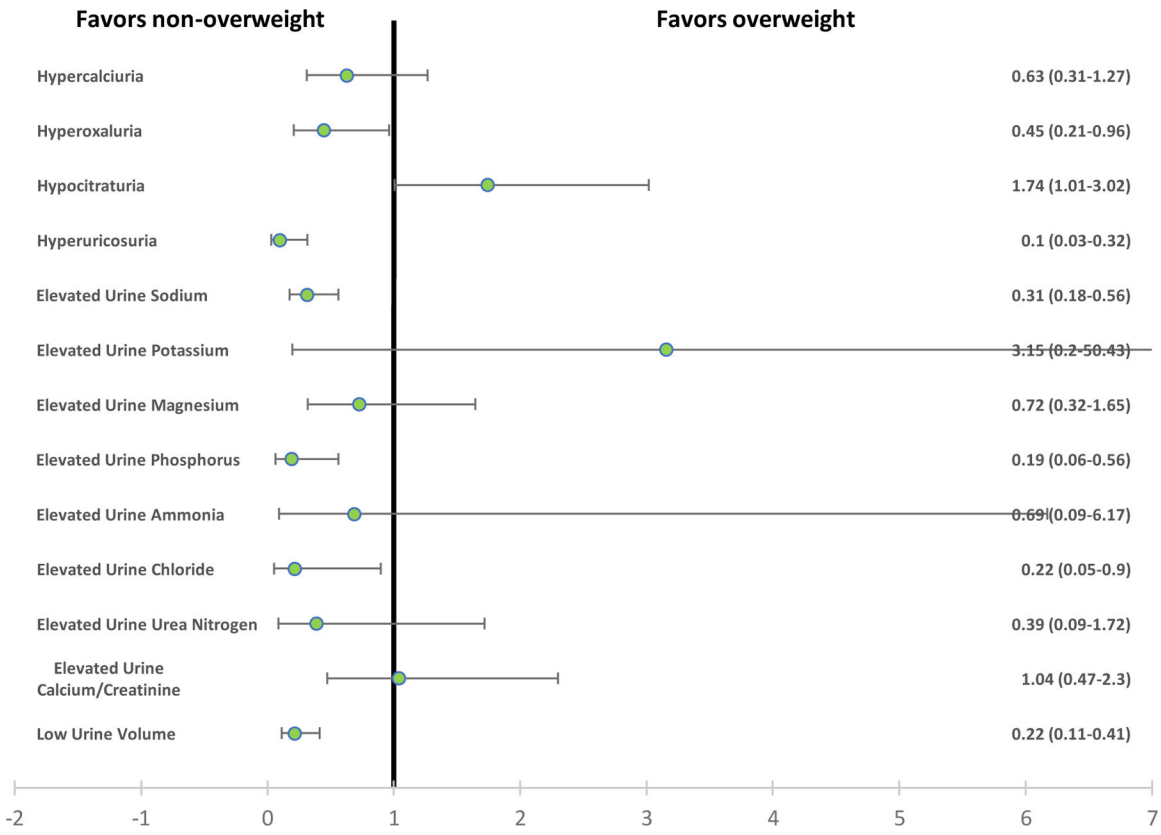

Figure 3:
Odds ratios of urinary pathology for non-overweight versus overweight patients

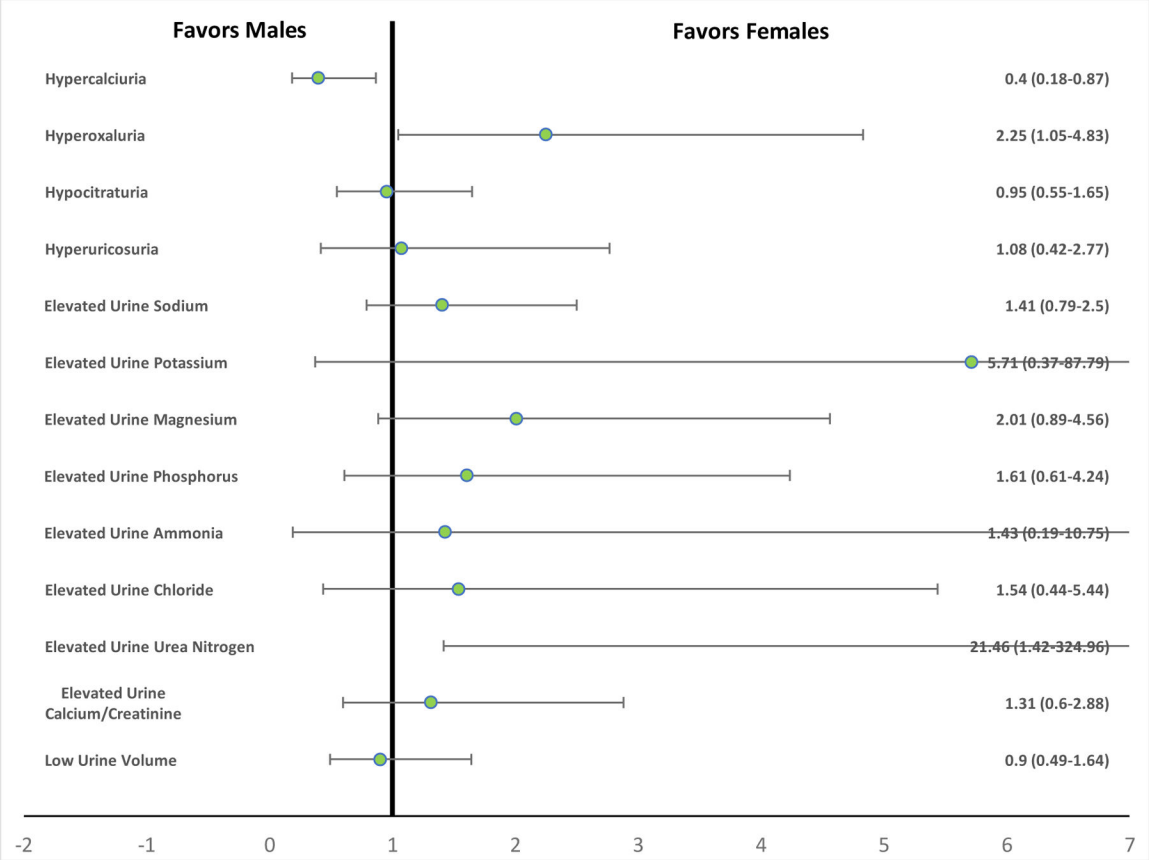

Figure 4:
Odds ratios of urinary pathology for male versus female patients

Table 1:

Descriptive statistics of 24-hour urinary parameters for each model normalized by body surface area (BSA) and creatinine (Cr)

	Age 3–10 - Nonoverweight – Female Mean (SD) N=36	Age 3–10 - Nonoverweight – Male Mean (SD) N=18	Age 3–10 - Overweight – Female Mean (SD) N=21	Age 3–10 - Overweight – Male Mean (SD) N=20	Age 11–18 - Nonoverweight – Female Mean (SD) N=59	Age 11–18 - Nonoverweight – Male Mean (SD) N=31	Age 11–18 - Overweight- Female Mean (SD) N=30	Age 11–18 - Overweight – Male Mean (SD) N=28
Analyte/BSA								
Calcium	137.8 (191.1)	98.2 (65.1)	118.1 (60.5)	110.6 (73.5)	103.5 (51.2)	98.7 (43.4)	96.1 (42.0)	89.2 (42.6)
Oxalate	31.6 (43.6)	21.5 (9.7)	25.1 (10.4)	23.9 (8.6)	17.9 (6.5)	21.8 (8.9)	18.3 (6.7)	17.7 (5.2)
Citrate	512.4 (841.0)	335.6 (223.5)	446.2 (173.5)	358.6 (178.2)	382.4 (212.6)	289.9 (162.2)	357.7 (131.2)	254.1 (105.2)
Uric Acid	0.4 (0.7)	0.3 (0.1)	0.4 (0.1)	0.4 (0.1)	0.3 (0.1)	0.3 (0.1)	0.4 (0.1)	0.4 (0.1)
Sodium	136.4 (254.3)	98.9 (45.6)	111.4 (38.1)	107.3 (30.5)	87.3 (34.5)	104.1 (44.5)	100.3 (39.1)	92.5 (39.0)
Potassium	36.4 (47.6)	35.5 (31.1)	31.4 (15.4)	25.9 (10.7)	23.2 (10.6)	25.7 (10.5)	25.4 (10.6)	21.8 (8.7)
Magnesium	83.2 (108.0)	64.4 (16.5)	70.6 (29.1)	58.2 (18.9)	54.1 (18.5)	63.0 (23.1)	48.6 (15.1)	50.9 (15.0)
Phosphorus	0.7 (1.0)	0.5 (0.2)	0.6 (0.2)	0.7 (0.2)	0.4 (0.2)	0.5 (0.2)	0.5 (0.2)	0.5 (0.2)
Sulfate	25.7 (44.1)	18.8 (8.0)	21.6 (9.6)	20.0 (8.5)	15.8 (6.1)	19.2 (7.3)	16.7 (4.6)	17.2 (6.1)
Urine Urea Nitrogen	6.3 (9.9)	4.8 (1.3)	5.2 (2.2)	5.4 (2.4)	4.2 (1.6)	5.0 (1.8)	4.4 (1.1)	4.8 (1.6)
Analyte/Cr								
Calcium	210.0 (83.9)	176.8 (109.0)	198.4 (99.4)	161.9 (103.7)	147.9 (66.9)	122.7 (59.4)	133.0 (60.3)	122.7 (52.6)
Oxalate	50.8 (36.8)	41.7 (31.2)	44.8 (29.9)	36.0 (14.0)	26.0 (10.1)	27.1 (10.5)	26.1 (12.2)	24.5 (8.3)
Citrate	743.0 (246.9)	627.1 (454.9)	761.7 (379.1)	537.5 (289.3)	538.1 (248.9)	368.1 (213.7)	500.0 (194.4)	362.5 (190.7)
Uric Acid	0.7 (0.2)	0.6 (0.1)	0.7 (0.2)	0.6 (0.1)	0.4 (0.1)	0.4 (0.1)	0.5 (0.1)	0.5 (0.1)

Table 2:

Frequencies of urinary pathology per Litholink™ report for each model

Analyte/24hr	Age 3–10 - Nonoverweight – Female (%) N=36	Age 3–10 - Nonoverweight – Male (%) N=18	Age 3–10 - Overweight – Female (%) N=21	Age 3–10 - Overweight – Male (%) N=20	Age 11–18 - Nonoverweight – Female (%) N=59	Age 11–18 - Nonoverweight – Male (%) N=31	Age 11–18 - Overweight- Female (%) N=30	Age 11–18 - Overweight – Male (%) N=28
Hypercalciuria	1 (2.8)	0 (0)	5 (23.8)	1 (5.0)	15 (25.4)	6 (19.4)	10 (33.3)	3 (10.7)
Hyperoxaluria	1 (2.8)	0 (0)	3 (14.3)	3 (15.0)	3 (5.1)	9 (29.0)	6 (20.0)	7 (25.0)
Hypocitraturia	33 (91.7)	14 (77.8)	14 (66.7)	11 (55.0)	30 (50.9)	17 (54.8)	13 (43.3)	15 (53.6)
Hyperuricosuria	0 (0)	0 (0)	2 (9.5)	0 (0)	1 (1.7)	2 (6.5)	8 (26.7)	8 (28.6)
Elevated Urine Sodium	3 (8.3)	2 (11.1)	6 (28.6)	8 (40)	19 (32.2)	15 (48.4)	20 (66.7)	17 (60.7)
Elevated Urine Potassium	0 (0)	1 (5.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Elevated Urine Magnesium	0 (0)	0 (0)	1 (4.8)	1 (5.0)	6 (10.2)	8 (25.8)	5 (16.7)	6 (21.4)
Elevated Urine Phosphorus	0 (0)	0 (0)	2 (9.5)	1 (5.0)	0 (0)	4 (12.9)	6 (20.0)	5 (17.9)
Elevated Urine Ammonia	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3.2)	1 (3.3)	0 (0)
Elevated Urine Chloride	0 (0)	0 (0)	1 (4.8)	0 (0)	1 (1.7)	1 (3.2)	2 (6.7)	4 (14.3)
Elevated Urine Sulfate	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Elevated Urine Urea Nitrogen	0 (0)	0 (0)	0 (0)	1 (5.0)	0 (0)	2 (6.5)	0 (0)	4 (14.3)
Elevated Urine Calcium/Creatinine	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Low Volume (cc/kg)	6 (16.7)	5 (27.8)	13 (61.9)	12 (60.0)	42 (71.2)	18 (58.1)	26 (86.7)	25 (89.3)

Table 3:

Results of Analysis of Variance Models for Urine Analytes

Analyte/24h	Age Group p-value	BMI Group p-value	Gender p-value	Model p-value
Volume	<0.001	0.600	0.068	<0.001
pH	0.104	0.126	0.317	0.098
Creatinine	<0.001	<0.001	0.002	<0.001
Calcium	<0.001	0.018	0.845	<0.001
Magnesium	<0.001	0.082	0.101	<0.001
Oxalate	<0.001	<0.001	0.110	<0.001
Citrate	<0.001	0.019	<0.001	<0.001
Uric Acid	<0.001	<0.001	0.147	<0.001
Sulfate	<0.001	<0.001	0.029	<0.001
Sodium	<0.001	<0.001	0.226	<0.001
Potassium	<0.001	0.026	0.468	<0.001
Phosphorus	<0.001	<0.001	0.015	<0.001
Urine Urea Nitrogen	<0.001	<0.001	0.004	<0.001
SS Calcium Oxalate	0.661	0.637	0.206	0.597
SS Calcium Phosphate	0.880	0.357	0.084	0.324
SS Uric Acid	0.183	0.002	0.781	0.009
Analyte/BSA				
Calcium	0.055	0.512	0.259	0.138
Oxalate	0.001	0.404	0.655	0.010
Citrate	0.037	0.537	0.020	0.015
Uric Acid	0.064	0.462	0.629	0.238
Sodium	0.090	0.827	0.733	0.384
Potassium	0.002	0.311	0.676	0.015
Magnesium	0.003	0.130	0.686	0.013
Phosphorus	0.021	0.293	0.995	0.084
Sulfate	0.025	0.686	0.867	0.158
Urine Urea Nitrogen	0.055	0.800	0.861	0.291
Analyte/Cr				
Calcium/Cr	<0.001	0.305	0.014	<0.001
Oxalate/Cr	<0.001	0.276	0.196	<0.001
Citrate/Cr	<0.001	0.478	<0.001	<0.001
Uric Acid/Cr	<0.001	0.037	0.019	<0.001