Epidemiology of pediatric urinary tract stones in Assiut Urology and Nephrology Hospital and its management

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Introduction
Renal stone disease remains a significant health problem in pediatric urology because of its higher morbidity and risk of end-stage renal failure.
Patients and methods
We reviewed the hospital records for all patients presented to the Assiut Urology and Nephrology Hospital between December 2014 and December 2017. Data was analyzed and compared to each other to detect the incidence and prevalence of urolithiasis in each group.
Results and conclusion
Of the patients, 85.7% were adults in comparison to 14.3% who were pediatric. Urolithiasis is more prevalent among the pediatric population than adults. Urolithiasis is the second most common urological disease after congenital anomalies. Urolithiasis is much more common in boys than in girls. According to the site of stone formation, the kidney, followed by ureter, then bladder and urethra are, respectively, the most common sites. Hematuria and gastrointestinal tract symptoms are the most common clinical presentation of pediatric urolithiasis. Majority of pediatric patients with urolithiasis (62.3%) presented with obstruction in the urinary tract. Radiopaque stones formed majority of pediatric stones (64%) rather than radiolucent stones (36%). Endoscopic management is considered the main line of treatment for renal stones (36.4%) followed by extracorporeal shockwave lithotripsy (32%), medical treatment (20.6%), and then surgical management (11%). Extracorporeal shockwave lithotripsy is more common among adult population than in the pediatric. Radiolucent ureteric stones are managed mainly endoscopically. Radiopaque ureteric stones are managed according to the site.
Conclusion
Urolithiasis is a severe problem and more detailed epidemiological studies are needed to enlighten the pathogenetic factors of stone formation and its geographical variations.

Keywords:
epidemiology, incidence, pediatric, urolithiasis

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Introduction

Pediatric urolithiasis remains endemic in low-resource countries affecting children less than 1–14 years. Urolithiasis in children should not be underestimated because of the associated significant morbidity and higher recurrence rate as compared with adults. The prevalence of calculi ranges from 4 to 20%.

The strong male predominance seen in the adult population is less clear in children, with more recent studies suggesting a roughly equal sex distribution in some countries [1].

It was found that abdominal pain is most common presentation followed by gross hematuria. Urinary tract infection (UTI) is also a common presentation (this is according to the former literature while in our study we found that hematuria and gastrointestinal tract symptoms are the most common clinical presentation) [2].

Stone composition:

Stones are classified into calcium stones and noncalcium stones.

Calcium stones

Calcium oxalate or calcium phosphate is considered the main constituent in calcium stones. There are two main causes for calcium oxalate stone formation which

are urine supersaturated by calcium (hypercalciuria) and oxalate (hyperoxaluria) or that the urine concentration of stone inhibitors decrease, including mainly citrate (hypocitraturia) and magnesium (hypomagnesemia).

Noncalcium stones

Uric acid stones

Uric acid stones contribute to 4–8% in pediatric urolithiasis. During metabolism of purine, uric acid is formed as an end product of metabolism. Uric acid stones formed in children are usually associated with increased uric acid secretion in urine (hyperuricosuria). Normal uric acid excretion is up to 10 mg/kg/day. Above this limit it is considered hyperuricosuria.

Cystine stones

In all, 2–6% of all pediatric urinary stones are formed of cystine stones. Cystinuria is an incompletely recessive autosomal disorder characterized by failure of renal tubules to reabsorb four basic amino acids: cystine, ornithine, lysine, and arginine. In kidney, ureter, and bladder (KUB) films, cystine stones are faintly radiopaque and may be difficult to visualize on regular radiograph studies. Cystine stones are hard stones and not easily disintegrated by shockwave lithotripsy (SWL) [3].

Infection stones (struvite stones)

Of the pediatric urinary tract stones, 5% are infection-related stones, though incidence increases over 10% in younger ages and in nonendemic regions.

Urease-producing bacteria (*Proteus*, *Klebsiella*, and *Pseudomonas*) are responsible for the formation of infective stones [4].

Diagnostic evaluation

The aim of diagnostic evaluation includes:

(1) To detect the stone:
   (a) First presentation and symptomatology:
   Presentation tends to be age dependent, with symptoms such as flank pain and hematuria being more common in older children. Nonspecific symptoms (e.g. irritability, vomiting) are common in very young children [5].
   (b) Diagnostic imaging:
      (1) Ultrasound (US).
      US should be used as the primary diagnostic imaging tool. US is safe (no risk of radiation), reproducible, and inexpensive. It can identify stones located in the calyces, pelvis, and pyeloureteral and vesicoureteric junctions, as well as in patients with upper urinary tract dilatation. US has a sensitivity of 45% and specificity of 94% for ureteric stones and a sensitivity of 45% and specificity of 88% for renal stones.
      (2) KUB film
      The sensitivity and specificity of KUB radiography is 44–77 and 80–87%, respectively. KUB is helpful in differentiating between radiolucent and radiopaque stones and for comparison of site of stone during follow-up [6].
      Non-contrast-enhanced computed topography (NCCT):

      In addition to stone site detection, NCCT can determine stone diameter and density. It images other peritoneal and retroperitoneal structures and help when the diagnosis is uncertain. Low-dose CT scan in children is used nowadays to reduce radiation dose exposure and subsequently reducing risk malignancy occurrence [7].
      (3) MRI
      A major advantage of MRI is the ability to provide three-dimensional imaging without radiation. The sensitivity of MRI is 82%, which is higher than that of US and KUB radiography but less than that of CT, as stones are less easily visible when using MRI than they are when using CT.
(4) To detect the cause of stone formation:
   (a) Basic laboratory analysis in nonemergency urolithiasis patients:
   (1) Urine analysis:
   To detect red blood cells, pus cells, nitrite, and urine PH.
      (1) Serum analysis: Serum creatinine to detect renal function. Serum uric acid: in a trial to detect the cause of stone formation.
      (2) Serum sodium and potassium and serum calcium.
      (3) Metabolic evaluation.
      (4) Due to the high incidence of predisposing factors for urolithiasis in children and high stone recurrence rates, every child with a urinary stone should be given a complete metabolic evaluation.

Metabolic evaluation includes:

(1) Family and patient history of metabolic problems and dietary habits.
(2) Analysis of stone composition (following stone analysis, metabolic evaluation can be modified according to the specific stone type).
(3) Electrolytes, blood/urea/nitrogen, creatinine, calcium, phosphorus, alkaline phosphatase, uric acid, total protein, carbonate, albumin, and parathyroid hormone (if there is hypercalcemia).

(4) Spot urinalysis and culture, including ratio of calcium to creatinine.
(5) Urine tests, including a 24-h urine collection for calcium, phosphorus, magnesium, oxalate, uric acid citrate, protein, and creatinine clearance.
(6) 24-h cystine analysis if cystinuria is suspected (positive sodium nitroprusside test, cystine stone, cystine hexagonal crystals in urine).

Management of urolithiasis

(1) Medical management of pediatric calculi:
  (a) Prevention of stone formation:
  All patients (and their parents) are counseled to improve fluid intake. It is important to emphasize that dietary calcium is not to be avoided in this age group.
  (b) Medical treatment of stones:
    (1) Pain relief:
    In cases of acute renal colic, NSAIDs and paracetamol are highly effective in such patients and have better analgesic efficacy than opioids.
    (2) Medical expulsive therapy:
    Medically expulsive therapy (MET) is only used in cases with urinary tract stones not indicated for active stone removal. Treatment should be discontinued if complications develop (infection, refractory pain, deterioration of renal function). Several drug classes are used for MET.
    The primary outcome of most trials assessing MET was stone passage, or follow-up, up to 4 weeks.

    MET is mainly applied for cases with ureteric stones especially lower third stones. Best results occur in cases with ureteric stones of less than 5 mm.
    Tamsulosin is one of the most commonly used alpha blockers. Tamsulosin dose was adjusted to the age of the patients (>4 years, 0.4 mg and <4 years, 0.2 mg). However, one small study has suggested that tamsulosin, terazosin, and doxazosin are equally effective, indicating a possible class effect [8].
    (3) Chemolysis:

Oral chemolysis

Uric acid stones, but not sodium or ammonium urate stones, can be dissolved by oral chemolysis. Stone composition could be detected by urine analysis through urinary pH measurement and type of crystals present in urine. Also KUB findings can give us more information about the stone type (radiolucent or radiopaque stone). Oral chemolysis is based on alkalization of urine by the application of potassium citrate or sodium bicarbonate. The pH should be adjusted to 7.0–7.2.

Stone removal

(1) Extracorporeal SWL
  The power of the shockwave should be started from the lowest level (14 kV) and may be escalated to the maximum level (20 kV) until fragmentation is observed in fluoroscopy and/or US. The number of shock waves should be limited to either the fragmentation observed or a maximum of 1000 waves per session for children younger than 5 years and to fragmentation or a maximum of 2500 waves per session for older children. Pulse frequency may be 70 pulses per minute.
  The site of stone and its localization is a very important factor for the success of stone disintegration.
  Most complications arising from SWL in children are self-limiting and transient [9].
  In our study, we used a Dornier MPL 9000 lithotripter for disintegration of stones.
(2) Endoscopic treatment:
  (a) Percutaneous nephrolithotomy (PCNL):
  PCNL is increasingly being used as monotherapy and in combination with SWL (sandwich therapy) in children and adults, with stone-free rates ranging from 68 to 100%. Although debatable, indications for PCNL as primary therapy in children include large upper tract stone burden greater than 1.5 cm, lower pole calculi more than 1 cm, concurrent anatomical abnormality impairing urinary drainage and stone clearance, or known cystine or struvite composition.
  With the availability of smaller size instruments, miniaturized PCNL 'mini-perc' through a 13 F or 14 F sheath has become possible, with decreased transfusion rates. This miniaturization has been further developed into the technique of 'micro-perc' using a 4.85 F 'all-seeing needle.' This technique enables the stone to be fragmented by a laser in situ and left for spontaneous passage [10].
  (b) Ureteroscopy:
  Ureteroscopy using a Holmium : YAG laser or pneumatic lithotripsy was used to fragment ureteric stones of up to 1.5 cm, preferably in the lower and midureter.
  (c) Cystolithotripsy:
  Transurethral cystolithotripsy was performed in urinary bladder stones of up to 2.5 cm using pneumatic lithotripsy or Holmium : YAG laser.

Recently percutaneous suprapubic cystolitholapaxy or percutaneous suprapubic stone extraction is used to treat children to avoid damaging their urethra. Percutaneous cystolithotomy is indicated in children or patients with large stone burdens [11].

(3) Open or laparoscopic stone surgery:
Nowadays, the role of open surgery in the management of pediatric renal stones is restricted.

Patients and method

This is a retrospective study. This research was performed at the Department of General Surgery, Assiut University Hospitals. Ethical Committee approval and written, informed consent were obtained from all participants.

We identified patients in our electronic medical record with International Classification of Diseases (pediatric urolithiasis) between the ages of 0 and 14 years (which according to our institution included pediatric patients of up to the age of 14 years).

We reviewed the hospital records for all patients presented to the Assiut Urology and Nephrology Hospital between December 2014 and December 2017.

Data was collected and analyzed using SPSS (Statistical Package for the Social Sciences, version 20; IBM, Armonk, New York, USA). Continuous data was expressed in the form of mean±SD or median (range), while nominal data was expressed in the form of frequency (percentage).

Aim of the work: to examine the prevalence, presenting features, and treatment strategies in children with stones in Assiut Urology and Nephrology Hospital from October 2014 to October 2017.

Results

Tables 1–5 denote demographic criteria of pediatricurolithiasis, Tables 6–9 denote stone criteria, and Tables 10–14 explain different treatment modalities for pediatric urolithiasis.

Table 1 Total number of patients that attended the outpatient clinics

	N=83 364
During 2014	30 183 (36.2)
During 2015	24 644 (29.6)
During 2016	28 537 (34.2)

Data expressed as *n* (%).

Table 2 Frequency of pediatric to adult patients during the study period

	Total	Adult	Pediatric
During 2014	30 183	25 863 (85.7)	4320 (14.3)
During 2015	24 644	22 591 (91.7)	2053 (8.3)
During 2016	28 537	26 237 (92)	2300 (8)
Total	83 364	74 691 (89.6)	8673 (10.4)

Data expressed as *n* (%).

Table 3 Frequency of urolithiasis among pediatric and adult populations in the period of study

	Adult	Pediatric
During 2014	5690 (22)	1080 (25)
During 2015	4518 (20)	472 (23)
During 2016	4970 (18.9)	594 (25.8)
Total	15 613 (20.3)	2146 (24.5)

Data expressed as *n* (%). χ^2 test was used.

Table 4 Causes of attendance among pediatric patients during the study period

Year	Urolithiasis	Congenital anomalies	Nocturnal enuresis	Other problems
2014	1080 (25)	1944 (45)	821 (19)	475 (11)
2015	472 (23)	883 (43)	410 (20)	288 (14)
2016	594 (25.8)	1020 (44.3)	495 (21.5)	191 (8.3)
Total	2146 (24.2)	3847 (44)	1726 (19.9)	954 (10.9)

Data expressed as *n* (%).

Table 5 Sex distribution among the pediatric patients

Sex	*N*
Boys	1071 (63.9)
Girls	603 (36.1)
Total	1674

Data expressed as *n* (%).

Table 6 Site of stones among pediatric patients

Site of stones	*N*=2146[a]
Kidney	1437 (67)
Ureter	537 (25)
Bladder	156 (7.2)
Urethra	17 (0.8)

Data expressed as *n* (%). [a]472 patients out of 1674 patients in this study had bilateral urolithiasis so we have 2146 cases.

Table 7 Laterality of renal and ureteric stones (*P*=0.07)

Side	*N*=1501[a]
RT	493 (32.8)
LT	536 (35.7)
Bilateral	472 (33.8)

Data expressed as *n* (%). χ^2 test was used. [a]After exclusion of patients with bladder and urethral stones from the total number of patients.

The number of pediatric patients with urolithiasis in this study is 1674.

No data could be found about patients who had both renal and ureteric stones at the same time.

Table 8 Main clinical presentation of pediatric urolithiasis

Symptoms	*N*=1674
Hematuria	599 (35.8)
GIT symptoms	526 (31.4)
Vague abdominal symptoms	328 (19.6)
Irritative bladder symptoms	262 (15.7)
Anuria	167 (10)
Febrile UTI	37 (2.2)
Acute retention	17 (1)

Data expressed as *n* (%). GIT, gastrointestinal tract; UTI, urinary tract infection.

Table 9 Opacity of stones among pediatric patients

Opacity	*N*=2146
Opaque	1373 (64)
Radiolucent	773 (36)

Data expressed as *n* (%). χ^2 test was used.

Table 10 Type of management among pediatric patients with renal stones

Type of management	*N*=2146
Medical therapy	443 (20.6)
SWL	687 (32)
Endoscopic management	780 (36.4)
Surgical management	236 (11)

Data expressed as *n* (%). SWL, shockwave lithotripsy.

Table 11 Outcome of medical therapy among pediatric patients

	N=609
Success	443 (72.7)
Failure	166 (27.3)

Data expressed as *n* (%). χ^2 test was used.

Table 12 Frequency of extracorporeal shockwave lithotripsy in adult and pediatric patients with urolithiasis

Type of management	Adult (*N*=15 613)	Pediatric (*N*=2146)
ESWL	6557 (41.9)	687 (32)

Data expressed as *n* (%). ESWL, extracorporeal shockwave lithotripsy.

Table 13 Modalities of treatment for radiolucent ureteric stone according to site

Site		Endoscopy	Open surgery
Upper third	4 (2.4)	4	–
Middle third	3 (1.8)	3	–
Lower third	157 (95.7)	157	–
Total (*N*)	164 (30.5)	164	–

Data expressed as *n* (%).

Modalities of treatment for radiolucent ureteric stone according to site

Table 14 Modalities of treatment for radiopaque ureteric stone according to site

Site		Endoscopy	Open surgery
Upper third	52 (13.9)	4	48
Middle third	13 (3.4)	–	13
Lower third	307 (82.5)	307	–
Total (*N*)	372 (69.4)	311 (83.6)	61 (16.3)

Data expressed as *n* (%).

Management of pediatric bladder and urethral stones

Out of the enrolled cases, 17 (0.8%) had urethral stones and all of them were endoscopically treated through pushback of the stone and its disintegration using a pneumatic disintegrator. There were 156 (7.3%) bladder stones; 19/156 (12.2%) stones were managed with open surgery while 137/156 (92.7%) were endoscopically managed (17 patients underwent suprapubic puncture using a laparoscopic port and the rest (120 patient) underwent cystolithotripsy by a pneumatic disintegrator.

Discussion

Milliner [12] reported a five-fold increase in the incidence and prevalence of stone disease in the last decade, where in our study there is frequency of urolithiasis among pediatric and adult patients in the period of study by 22, 20, and 18.9% among adults and 25, 23, and 25.8% in 2014, 2015, and 2016, respectively.

In our study, the incidence of stone disease in the pediatric (24.5%) population is slightly more than in adults (20.3%).

In our study, the incidence of urolithiasis is more common in pediatric patients (age above 2 years) (86.1%) more than that in infants (age under 2 years) (13.9%), with an annual rate of incidence about 7% in both age groups, which agrees with what was reported by Tasian *et al.* (2014) about the annual rate of incidence which ranges from 6 to 10% [13].

In our study, the number of male patients with pediatric urolithiasis (63.9%) outweigh female patients (36.1%), which agrees with Elmacı *et al.* (2014), who also reported male predominance in pediatric urolithiasis (58% were males and 42% were females) [14].

Huang *et al.* [15] also reported male predominance in the prevalence of urolithiasis in China (study was done on 186 patients, 69.9% were males and 30.1% were females).

In our study, stone disease in the pediatric patients is considered as a main pediatric health problem accounting for 24.2% of total pediatric urological problem. It is worth noting that pediatric stone disease is considered one of the most common causes for acute renal failure in children (30.13%).

The clinical presentation of pediatric urolithiasis revealed reasonable difference in symptomatology than adults; 1674 patients presented by 1936 different symptoms where 51% of patients presented with gastrointestinal tract symptoms (31.4%) and vague

abdominal symptoms (19.6%). This is followed by hematuria which forms 35.8%, and then irritative bladder symptoms as pinching of penis forms 15.7%. Obstructive anuria was present in 167 patients, which constitute about 10% of patients. Febrile UTI and acute retention of urine constitutes about 3.2%. However, at the same time the results agree with what was reported in Egypt by Zakaria *et al* (2012), that the main clinical presentations in pediatric urolithiasis were 50% pain; hematuria was found in 23% of patients; and vague symptoms were present in about 12% of population. However, 15% of the study cases were diagnosed during routine checkups [16].

Also our results agree with Alaya *et al.* (2014), who reported the clinical presentation in pediatric urolithiasis in Tunisia was pain in 28.7% of patients, hematuria in 24.2% of patients, UTI in 9.4%, anuria in 7.4%, and accidental finding in 3.2% of patients.

In our study, 33.8% of cases had bilateral stone disease; 30.5% had right side lesion; and 35.7% were left which is unlike what was reported by Zakaria *et al.* (2012) that 25% patients had bilateral stone disease and 75% patients had unilateral stone disease [17].

We concluded that upper urinary tract stones (renal 67% and ureteric 25%) are much more common in than the lower urinary tract stones (bladder 12.2% and urethral 0.8%) in the pediatric population. This result agrees with what was reported by Huang and colleagues as regards the site of stone that 83.3% were renal stones, 6% were ureteric, 10% were bladder, and 0.8% were urethral stones.

In our study, all patients investigated by US and KUB film as a routine. KUB film was done to discriminate between radiolucent and radiopaque stones. NCCT was done for most patients in our study. This agrees with what Strohmaier (2015) recommended, as he used US as a primary imaging technique to diagnose pediatric urolithiasis. Although the sensitivity of CT is highest, he favored conventional radiology with respect to radiation doses [18].

Gupta and Castellan reported a combination of KUB and US should be more routinely considered in pediatric patients with renal colic or suspicious of nephrolithiasis with high sensitivity (79%) for direct detection of stones [19].

In our study, we reported that radiopaque stones (calcium-containing stones) (64%) are much more common in children than radiolucent stones (36%), which also agrees with previous literature that detected that 67% of cases had calcium-containing stones and about 30% had noncalcium-containing stones. These confirm that calcium-containing stones are more common among pediatric population than noncalcium-containing stones.

In our study, PNL became first line of treatment for radiopaque renal stones by 57%, followed by SWL (26.7%), and lastly open surgery (16.3%). No role for medical treatment in radiopaque renal stones.

Also in our study, radiolucent renal stones, most of them responded for medical treatment (82.6%). The rest of the cases (17.4%) are either noncompliant or not responding to medical treatment. These cases are treated by PNL (65%), followed by SWL (18.7%), then open surgery (16.3%). Elderwy *et al.* (2014) reported that the success rate for dissolution therapy for radiolucent renal stones in children is about 73%.

In our study, radiopaque ureteric stones form about 69.5% of all ureteric stones and 30.5% for radiolucent stones. Also in our study, lower third ureteric stones form the majority of ureteric stones either in radiolucent (95.77%) or radiopaque stones (82.5%) [20].

In our study, all radiolucent ureteric stones were managed successfully by endoscopy. Also in our study, endoscopy became the main line of treatment for all lower third ureteric stones. MET has no significant role in the treatment of ureteric stones in children.

In our study, the role of open surgery as a line of treatment for ureteric stones is restricted only for middle third and most of upper third ureteric radiopaque stones.

We concluded that we should try medical treatment as the first line of treatment in cases of radiolucent renal stones as there is a success rate of about 72.7%.

In our study, all bladder and urethral stones were treated successfully endoscopically (including both transurethral cystolitholapaxy and suprapubic cystolitholapaxy) with minimal complications.

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Conflicts of interest
No conflict of interest.

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