# INTRODUCTION

In recent decades, the incidence of pediatric stone disease has increased markedly. The disease incidence has risen 6–10 % annually over the last two decades also Population-based observational studies have estimated contemporary incidence to range from 36 to 145 per 100,000 children ***(David et al., 2016).*** Also the increase in incidence in both sexes, incidence in girls has shown a greater increase more than boys ***(Paul et al., 2015).***

In pediatric patients a predisposing factors for stones can be found in more than 75% of children. The majority of cases have a metabolic disorder ***(Paul et al., 2015).***

Children are regarded as high-risk recurrent stone formers rates range from 19 to 34 % at a mean follow-up of 2–3 years ***(David et al., 2016).***

The three main treatment options available for pediatric stones treatment are Extracorporeal shock wave lithotripsy (ESWL), ureteroscopy (rigid and flexible), Percutaneous nephrolithotomy (PCNL) and open surgery has been reserved for complex stones associated with abnormal anatomy ***(Paul, 2015).***

ESWL was used in pediatric stones in 1986, which showed safety, efficacy and complications equivalent to adult and its efficacy for upper tract stones has been reported as ranging from 68% to 84% ***(Paul, 2015).*** Due to technical

problems that arise with localization and focusing of ureteric stones in children, success rates with ESWL are lower for distal ureteric stones ***(Mehmet et al., 2017).***

Extracorporeal shock wave lithotripsy in the pediatric population has higher success rate due to number of reasons including smaller body volumes and increased ureteral compliance allowing passage of stone fragments. Also Dimercaptosuccinic acid (DMSA) scanning post-ESWL did not identify any evidence of renal scarring ***(Paul et al., 2015).***

Ureteroscopy (URS) for stone disintegration was first documented by ***Ritchey et al. (1980)***. The advantage of flexible ureteroscopy in children includes high stone-free condition rates, low complication rates, minimal radiation exposure and short hospitalization periods ***(Mehmet et al., 2017)***.

The indication of flexible ureteroscopy has been extending, including intrarenal stones, ESWL failure, morbid obesity, musculoskeletal deformities and bleeding diathesis ***(ErdalAlkan et al., 2014).***

Initial concerns were raised regarding the traumatic sequelae to the pediatric ureter like Perforation, ischemia, stricture and reflux were expected following URS in children ***(Ezekiel et al., 2015).***

URS was found to be superior to ESWL in a prospective randomized study, rendering 94% stone free after one session compared with 43% stone free following SWL ***(Ezekiel, 2015).***

# AIM OF THE WORK

To assess the safety, efficacy and outcome of flexible ureteroscopy using holmium Yttrium aluminium garne (YAG) laser lithotripsy and compare its results with that of Extracorporeal shock wave lithotripsy EWSL in management of ureteric stones in pediatric age group.

# INCIDENCE AND EPIDEMIOLOGY OF PEDIATRIC UROLITHIASIS

Pediatric stone disease is one of the most common urological issues in pediatric urology practice. The incidence of urinary stone disease is increasing in children in last decades ***(Sas et al., 2010).***

Dietary alterations such as high sodium and carbohydrate consumption may be one of the reasons of this shift. Apart from environmental effects also some metabolic anomalies may be responsible for stone formation in children ***(Doganca and Onal, 2016).***

Stone formation in children is almost equal in male and female gender, in contrast to male gender dominancy in adults also most of Urinary stones are mostly located at the upper urinary tract ***(Milliner et al., 2009).***

Renal stone formation is a complex process that depends on several factors, including the urinary concentration of stone-forming ions, urinary pH and flow rate, various metabolic factors of crystallization and anatomic factors that encourage urinary stasis ***(Alpay et al., 2009).***

Studies over the past few decades have identified metabolic disorders in 33–95% of pediatric patients with urolithiasis, whereas structural urinary abnormalities and

infection were found in 8–32% of cases ***(Acar et al., 2008).*** Additionally, genetic abnormalities, drug use, nutritional and environmental factors were reported in a minority of cases ***(Dursun et al., 2008).***

The etiological paradigm for urolithiasis in children has shifted from predominantly infectious to metabolic causes ***(Nicoletta and Lande, 2006).***

## Stone composition

Calcium oxalate is the most common stone worldwide, and accounts for 60-90% of pediatric urolithiasis. Sturvite constitutes 1-18% of the stones in developed countries ***(Alpay et al., 2009).*** Calcium phosphate accounts for 10-20% stones. Uric acid constitutes 5-10%, cystine 1-5% (1 in 15000 live births). Cystine stones have a higher prevalence in endemic areas and in communities with high consanguinity ***(Kit et al., 2008).***

## Risk factors for urolithiasis in pediatric divided to:

I. Metabolic factors

II. Non metabolic factors

- Urinary tract infection
- Structure abnormality

III. Other causes

(Medication, Nutriational, Ethnicity, Climate and season).

## I. Metabolic risk factors:

Metabolic risk factors increase the risk of stone recurrence. The prevalence of metabolic risk factors ranged from less than 20% to greater than 50% in different studies ***(Alpay et al., 2009).***

Hypercalciuria and hypocitraturia are the common metabolic abnormalities, detected in one-third of the stone-formers ***(VanDervoort et al., 2007).*** The prevalence of hyperuricosuria and hyperoxaluria has been reported to be approximately 20% ***(Alpay et al., 2009).***

### 1. Hypercalciuria

Hypercalciuria, or excessive urinary calcium excretion, occurs in about 5-10% of the population and is the most common identifiable cause of calcium kidney stone disease. Indeed, about 80% of all kidney stones contain calcium, and at least one third of all calcium stone formers are found to have hypercalciuria when tested ***(Vezzoli et al., 2008).***

Hypercalciuria may be in idiopathic (primary) or secondary form. Idiopathic hypercalciuria is diagnosed when clinical, laboratory, and radiographic investigations fail to delineate an underlying cause of the condition ***(Acar et al., 2008).***

Secondary hypercalciuria occurs when a known process produces excessive urinary calcium may be result of increased

bone resorption (hyperparathyroidism, hyperthyroidism, immobilization, acidosis, metastatic disease) or gastrointestinal hyperabsorbtion (hypervitaminosis D), Renal tubular acidosis, Sarcoidosis and other granulomatous diseases, Glucocorticoid excess and Paget disease ***(Parks et al., 2009).***

The following are the most common types of clinically significant hypercalciuria ***(Madani et al., 2012):***

- Absorptive hypercalciuria
- Renal phosphate leak hypercalciuria (also known as absorptive hypercalciuria type III)
- Renal leak hypercalciuria
- Resorptive hypercalciuria - This is almost always caused by hyperparathyroidism

**2. Hyperoxaluria**

Approximately 2–36% of patients with pediatric urolithiasis have hyperoxaluria, which is defined as a urinary oxalate excretion >0.5 mmol/1.73 m2 per day ***(Dursun et al., 2008).***

**The 4 main types of hyperoxaluria are the following:**

Primary hyperoxaluria (types, I, II and III) primary hyperoxaluria have been described, with the increased

endogenous oxalate caused by different hepatic enzyme deficiencies in each type ***(Cohen-Solal et al., 2001).***

- Enteric hyperoxaluria It is due to a gastrointestinal problem usually associated with chronic diarrhea. Malabsorption from any cause can result in enteric hyperoxaluria. Such causes include intestinal bacterial over growth syndrome, fat malabsorption, chronic biliary or pancreatic disease, various intestinal bypass surgical procedures, inflammatory bowel disease, or any medical condition that causes chronic diarrhea ***(Brändle et al., 1998).***

- Dietary hyperoxaluria A high intake of oxalate-rich foods (eg, chocolate, nuts, spinach) and a diet rich in animal protein can result in hyperoxaluria. Low dietary calcium intake can also result in hyperoxaluria via decreased intestinal binding of oxalate and the resulting increased absorption. Ascorbic acid can be converted in oxalate, resulting in increased urinary oxalate levels ***(Whitson et al., 2010).***

- Idiopathic or mild hyperoxaluria This is by far the most common variety of hyperoxaluria observed in patients with calcium oxalate stones. It may be due to a simple dietary excess of high-oxalate food sources or to increased endogenous oxalate production ***(Hoppe et al., 2009).***

**Types of primary hyperoxaluria:**

- Type I primary hyperoxaluria is a rare autosomal recessive genetic disorder that results from deficient alanine-glyoxylate aminotransferase and is characterized by excessive synthesis of oxalate and urinary excretion of both oxalate and glycolate ***(Alpay et al., 2009).***

- Type II primary hyper oxaluria is caused by a deficiency of glyoxylate reductase/hydroxypyruvate reductase and has a milder clinical course.47 Primary hyperoxaluria type III is caused by defects of HOGA1, the gene that encodes 4-hydroxy-2- oxoglutarate aldolase, which is involved in the metabolic pathway of hydroxyproline ***(Belostotsky et al., 2010).***

**3. Hyperuricosuria**

Uric acid stones are responsible for urinary calculi in 4% to 8% of children. Uric acid is the end product of purine metabolism. Daily output of uric acid more than 10 mg/kg/d is considered to be hyperuricosuria ***(Poyrazog˘lu et al., 2009).***

**Causes of hyperuricosuria**

- Idiopathic renal hyperuricosuria is often inherited and can be asymptomatic. Such patients have normal serum levels of uric acid ***(Doganca and Onal, 2016).***

- Secondary hyperuricosuria can result from a high-protein or ketogenic (high-fat and low-carbohydrate) diet, or the use of certain medications, including ascorbic acid, probenecid, salicylates and phenylbutazon ***(La Manna et al., 2001).***

- Uric acid overproduction might result from errors in purine metabolism, such as complete (as in Lesch–Nyhan syndrome) or partial hypoxanthine phospho ribosyltransferase 1 enzyme deficiency ***(Polito et al., 2009).***

- Aside from causes, tumor lysis syndrome, lymphoproliferative or myeloproliferative disorders can lead to the overproduction and excessive excretion of uric acid ***(Belostotsky et al., 2010).***

**4. Cystinuria**

Cystinuria is the underlying cause of metabolic stones in 2–8% of children, Cystinuria is a disorder of the renal tubular transport of cystine, ornithine, arginine and lysine. An auto somal recessive inherited disorder, cystinuria is caused by defects in either SLC3A1 (type A) or SLC7A9 (type B). Type AB cystinuria—which is caused by the mutation in both genes—is found in 2% of patients with cystinuria ***(Goodyer et al., 1998).***

**5. Hypocitraturia**

Hypocitraturia, a low amount of citrate in the urine, is an important risk factor for kidney stone formation. Citrate in the

urine has long been recognized as an inhibitor of calcium salt crystallization. The mean urinary citrate excretion is 640 mg/d in healthy individuals ***(Hoppe et al., 2009).***

The following are causes of hypocitraturic calcium nephrolithiasis:

- Distal renal tubular acidosis (RTA)
- Chronic diarrheal syndrome
- Thiazide diuretic or acetazolamide administration
- Diet high in animal protein
- Strenuous physical exercise
- High sodium intake
- Gout or gouty diathesis

***(Karsli et al., 2013)***

Hypocitraturia enhances urine calcium salt supersaturation and reduces calcium crystallization inhibition, increasing the risk of calcium nephrolithiasis. It also may play a role in uric acid solubility and uric acid stone formation ***(Vega et al., 2007).***

**6. Other solute excesses**

Xanthinuria is a rare autosomal recessive disorder of purine metabolism that leads to urolithiasis. A deficiency of xanthine oxidoreductase or xanthine dehydrogenase results in the production of high levels of xanthine or hypoxanthine, which are both associated with decreased production of uric acid ***(Cochat et al., 2010).***

## Non metabolic risk factors:

- ***Structural abnormalities of the urinary tract:***

Functional or anatomical obstructions of the urinary tract such as ureteropelvic junction obstruction, ureterocele, horseshoe kidney, autosomal dominant polycystic kidney disease and tubular ectasia (medullary spongy kidney) increase the potential for stone formation by promoting urinary stasis and infection. Indeed, anatomical abnormalities of the urinary tract are found in 8–32% of children and adolescents with urolithiasis ***(Spivacow et al., 2010).*** Also hyperoxaluria, hypercalciuria or hypocitraturia have been identified in a considerable proportion (66–80%) of patients with urolithiasis and structural abnormalities (of the kidney or ureter) who underwent metabolic evaluation ***(Cameron et al., 2005).***

- ***Urinary tract infections:***

Children with a history of recurrent UTI have an increased risk of developing urolithiasis. Bacteria with urease

activity such as Proteus spp., Klebsiella spp. and Staphylococcus aureus can increase the risk of urolithiasis because urease increases urinary pH, which promotes the supersaturation of urine with magnesium ammonium phosphate (as in struvite stones) and calcium phosphate (as in apatite stones). Struvite stones account for ~2.1–24% of all urolithiasis cases in children ***(Bastug and Düsünsel, 2012).***

## Other causes of urolithiasis

### *Medication-induced urolithiasis*

A number of medications are known to induce nephrolithiasis, and an estimated 1–2% of all kidney stones might be drug-related. Renal excretion of drugs (or drug metabolites) can exceed urine solubility, which can lead to stone formation ***(Bastug and Düsünsel, 2012).***

### *Drugs*

- Loop diuretics
- Vitamin D
- Sulfadiazine
- Theophylline
- Triamterene
- Carbonic anhydrase inhibitors
- Ceftriaxone
- Ampicillin
- Topiramate

## *Nutritional causes*

High-protein intake predisposes patients to an increased urinary uric acid concentration, calcium and oxalate excretion, as well as lower urinary citrate concentrations and urinary pH, all of which promote calcium oxalate stone formation. Excessive dietary sodium or calcium might also induce hypercalciuria ***(Grases et al., 2006).***

Oxalate-rich foods such as turnip greens, rhubarb, strawberries, star fruit, sweet potatoes, wheat bran, cocoa,beets, spinach, dill, nuts and citrus juices can cause hyperoxaluria, particularly if the diet is low in calcium ***(Nicoletta and Lande, 2006).***

## *Ethnicity*

Idiopathic stone disease has been reported to be more frequent in white Caucasians than in African-Americans from both adult and pediatric studies ***(Michaels et al., 1994).***

## *Climate and season*

The relationship between urolithiasis and high ambient temperature can be explained by intravascular volume contraction resulting from a combination of dehydration and inadequate fluid intake. Volume contraction increases urine concentration and promotes stone formation ***(Nicoletta and Lande, 2006).***