RENAL INFUNDIBULAR STENOSIS WITH UROLITHIASIS: A LITERATURE REVIEW

Rama Firmanto, Nur Rasyid.

Department of Urology, Faculty of Medicine/Universitas Indonesia, Cipto Mangunkusumo General Hospital Jakarta.

ABSTRACT

Objective: This literature review was performed to improve the insight in renal infundibular stenosis with urolithiasis. Material & Methods: We searched several literatures about infundibular stenosis and its association with urolithiasis. Pubmed and ScienceDirect databases were used to identify relevant studies. Results: Infundibulopelvic stenosis (IFPS) is rarely found. It is not always a congenital condition. IFPS is caused by extrinsic factor, such as carcinoma or retroperitoneal fibrosis, or intrinsic factor, such as inflammation, infection, calculus, Fraley's syndrome, or surgery performed on kidney. Urinary stasis in the pelvicalyceal system that happened in IFPS increases the chance of stone formation. Its anatomical abnormality plays important role to stone formation. The clear treatment algorithm has not been found. The management for kidney stones depends on stone characteristic, location, and symptoms of the patient, as recommended by Koopman et al. Bayne et al. recommend methods of nephrotomy and calicocalicostomy. While Balbo et al. recommend holmium-based therapy. Conclusion: Infundibulopelvic stenosis is a risk factor of urolithiasis. It is a rare condition, but the treatment algorithm has not been found. There are several recommendations for kidney stone management in infundibulopelvic stenosis.

Keywords: Renal infundibular stenosis, urolithiasis.

INTRODUCTION

Renal infundibular stenosis is narrowing of the infundibular lumen, with or without dilated calyx. This condition can be focal, diffuse, and/or bilateral. If diffuse and/or bilateral stenosis is found, other kidney and urinary tract abnormalities may appear as a comorbid thus some syndromes, such as Beckwith-Wiedemann syndrome and Bardet-Biedl syndrome, must be considered. In some cases, severe obstruction or stenosis in renal infundibular may cause secondary urinary retention which leads to nephrolithiasis or urolithiasis. Renal infundibular stenosis is rarely found and usually found in children.
Urolithiasis, also called urinary calculus, is stone, or calculi, formation in the urinary tract. It can happen in the renal pyelocalyceal system, ureter, bladder, or urethra. Following urinary tract infections and prostatic abnormalities, urolithiasis make up as the third most common urinary tract diseases. The prevalence rate for urolithiasis vary from 1% to 20% depends on several factors such as ethnic, dietary food, geographical, and genetic factors.

**OBJECTIVE**

We performed a literature review to improve the insight in renal infundibular stenosis with urolithiasis.

**MATERIAL & METHODS**

We performed computer-aided search of the Pubmed dan ScienceDirect database. Studies in English language with the keywords 'infundibular stenosis' and 'urolithiasis' were identified. Literature selection was made according to the major topic of the article. Finally, the reference lists of relevant articles were reviewed, which also identified studies for inclusion. The author reviewed all studies that were considered for inclusion. After inclusion, the following variables were extracted from each study: epidemiology and etiology of infundibular stenosis, infundibular stenosis as risk factor for urolithiasis, pathogenesis, clinical findings, and management of urolithiasis.

**RESULTS**

Infundibulopelvic stenosis (IFPS) is a rare condition. Husman et al. reported 21 cases of IFPS within 33 years. This report marked as the biggest IFPS finding that is reported in literature. Lucaya et al. reported only three cases out of 11,500 patients who underwent intravenous pyelogram (IVP) within 17 years in Spain. Dally et al. found unilateral IFPS in 2.5% patients with multicystic contralateral dysplastic kidney (MCDK).

Kobayashi et al. attempted to examine three generation family with IFPS and managed to identify haplotype chromosome between type 1 polycystic kidney disease (PKD) and tuberous sclerosis in chromosome 16p. This chromosomal haplotype is inherited by autosomal dominant inheritance pattern. Bayne et al. reported IFPS findings in 17 years old man after getting a right flank baseball injury. This finding suggest that IFPS is not always a congenital condition. Thus, the etiology of IFPS divided into two, extrinsic, such as carcinoma or retroperitoneal fibrosis, and intrinsic, such as inflammation, renal tuberculosis, obstructive calculus, Fraley's syndrome, or surgery performed on kidney.

In most cases, IFPS may progress to calyceal diverticula or nephrolithiasis. These happen due to urinary stasis in pelviocalyceal system thus increasing the chance of mineral deposition in urine. Eshghi et al. reported that deposited stones in calyceal diverticula cause chronic or recurrent pain, pyonephrosis, local and progressive kidney disease, and renal stones deposition in 9.5-39% patients.

The stone formation comprises complex cascade of events that occurs in the glomeruli. This process initiated with supersaturation of urine with stone-forming salts which will precipitate out of solution and form crystals. Formed crystals will develop more crystal deposition, the process called crystal growth and aggregation, which will lead to stone formation. Some factors, which will be discussed later, prevent these process from occurring hence crystals flow out with the urine.

A solution considered saturated if the dissolved component concentration is the same or higher than the solubility product constant (Ksp) value. Addition more dissolved component when the solution is already saturated will cause precipitation. In urine, when the stone-forming salt concentration exceed the Ksp, crystallization does not automatically happen because other molecules, such as citrate acid, act as inhibitor to prevent the precipitation of stone-forming salt out of solution. Increasing salt concentration causes the molecules cannot be retained any longer in the solution, hence the molecule will form crystal out of the solution. At this state, dissolved molecules concentration is called formation product (Kf). State of salt saturation showed in picture 1.

The first process of crystallization is called nucleation. Nucleation happens by the de novo precipitation or spontaneously if the stone-forming concentration is higher than Kf. Homogenous nucleation is nuclei formation process or early-formed crystals that are not dissolved in solution. If the saturation level and nuclei stability are adequate, and time to form the nuclei fast enough than urine transit time in nephron, the nuclei will remain in the nephron. The presence of
Phenomena

Nucleation will occur
Inhibitor not generally effective

Crystal growth will occur
Crystal aggregation will occur
Inhibitor will impede or prevent crystalization
De novo nucleation is very slow
Heterogeneous nucleation may occur
Matrix may be involved

Crystals will not form
Exciting stones may dissolve

Formation product

Concentration product

Solubility product

Figure 1. State of saturation within the dissolved molecule. In general, there are 3 stages; (1) concentration below the Ksp, hence the stones are not formed, (2) metastable concentration and de novo precipitation. In this state, stones may formed in several conditions, and lastly (3) concentration above the Kf, hence the stones are formed.

Crystal formation also affected by the presence of inhibitor or promoters to stones in general or specific stones forming. Citrate acts as an inhibitor to prevent calcium oxalate and calcium phosphate stones. Magnesium prevents the formation of oxalate stones. Nephrocalcin inhibits nucleation and aggregation of calcium oxalate stones. Tamm-Horsfall protein, the most abundant protein found in urine, inhibits aggregation, and uropontin, inhibits crystal growth. Osteopontin also found to prevent nucleation, growth, and aggregation of calcium oxalate crystal and suppress the binding of crystal with the epithelial cells.

Figure 2. Intravenous Pyelogram (IVP) of the patient with IFPS. (a) 16-year-old girl showing dilatation on right lower pole calyces and delayed filling of the upper pole calyces. No pelvic dilatation was seen (b) 17-year-old man showing severe right calyces dilatation, no right renal pelvic dilatation, and small contralateral renal pelvis. The pelvic of left renal is slightly atrophic, a variation of infundibulopelvic stenosis.
Patients with abnormality in anatomical structure that cause urinary obstruction show higher incidence in stone formation. Some of those conditions are ureteropelvic junction obstruction (UPJO), horseshoe kidney, calyceal diverticula, medullary sponge kidney (MSK), and some other conditions. Morphology of pelviocalyceal system is also anatomical factors contributing to renal stone forming. The study by Balawender et al. showed that several factors measured, such as infundibulopelvic angle (IPA), infundibular width (IW), infundibular length (IL), and calyceopelvic height (CPH), only able to conclude that IPA presents as the risk factors of kidney stones in lower pole of the kidney. Other study, by Wadekar et al. showed that there is a significant difference between IL of normal kidney compared to IL of the kidney with stones. Mean of IW also lower in kidney with stones, even though is not statistically significant.

The stone formation process, as already explained, shows how IFPS, which cause a stasis within the pelviocalyceal system may present as a risk factor of urolithiasis. Renal calculi formed due to deposition and crystallization of mineral within the urine during the transit time in pelviocalyceal system. Normally, urine transit time in the pelviocalyceal system is 5 to 7 minutes. If IFPS presents, the flow of urine in pelviocalyceal will be slower because the dilated calyx, with greater diameter, cause decreased resistance of the system. With the end of the calyx, also called infundibula, having stenosis, the resistance within calyx outflow will increase thus calyceal flow to pelvic is hampered. Increasing flow towards calyx and decreasing flow to pelvic cause increase in urine transit time in pelviocalyceal system, thus called stasis. The stasis that keeps occurring will promote mineral deposition and crystallization and eventually, stones formed.

According to Bayne et al, IFPS is a part of congenital obstructive dysmorphism entity, referred to as the infundibulopelvic dysgenesis. This condition may lead to a variety of congenital anomalies, such as calyx diverticulum, obstruction of the urethral-pelvic junction, and multicystic dysplasia depends on the location and severity of the disease. The major findings of IFPS are infundibulum stenosis and renal pelvic atrophy. In some cases, the calix is found to be dilated. However, calyx stenosis is also sometimes found, thus the infundibulum stenosis/IFPS is theorized as a resultant of calyx stenosis. However, in congenital IFPS, patients are often found to have hydrocalycosis, a condition with one or more dilated cycles. Thus, for congenital IFPS, differential diagnosis with non-obstructive calix widening, such as megacalycoses, should be ruled out. Ideal diagnostic methods for IFPS are IVP and endoscopy. In establishing the diagnosis of IFPS, some clinical hallmark such as creatinine serum elevation (in early phase), hypertension and proteinuria (late phase) should be examined.

Management for kidney stones depends on several aspects such as stone composition, stone size, and also the symptoms experienced by the patient. Symptoms commonly experienced by patients are renal colic that could be treated with non-steroidal anti-inflammatory drugs (NSAIDs) such as metamizole. Administration of NSAIDs, as a pain reliever, have to be given in patients with acute

Figure 3. (a) IVP showing an upper pole calyx diverticulum with stones inside. (b) Non-contrast CT-scan stones inside the upper pole calyx diverticulum.
stone episodes as the first line therapy. Other symptoms that may be experienced are the occurrence of sepsis and/or anuria due to kidney obstruction. Both of these are urban emergencies. Decompression is the main thing to prevent further complications in stones-induced secondary hydronephrosis infections, either unilateral or bilateral kidney obstruction.

The management of kidney stones, especially on the calix, depends on the characteristics of the stones. Some indications for removal of stones include the growing stone, the occurrence of stone obstruction, the presence of infection and symptoms (pain or haematuria), stone size > 15 mm, et cetera. Kidney stone therapy could be divided into therapy for stone in the renal pelvis or upper/middle calyx and inferior renal stone therapy at the poles. Some modalities for stone therapy in the renal pelvis or upper/middle calyx are extracorporeal shockwave lithotripsy (ESWL), percutaneous nephrolithotomy (PNL), and retrograde renal surgery (RIRS). The efficacy of the PNL procedure is not affected by rock size, while the stone-free rate (SFR) is inversely related to the stone size in ESWL and ureterorenoscopy (URS). ESWL achieved fairly good SFR results on rock sizes up to 20 mm, except in the inferior pole regions. Stones with size > 20 mm should be treated with PNL as ESWL generally requires continued therapy and the presence of the risk of ureteral obstruction so that follow-up procedures are needed. RIRS is a second-line procedure in patients with PNL contraindications.

Kidney stone therapy on the inferior pole could be done by PNL or RIRS method for stones with a size of more than 1 cm. This consideration is based on limited ESWL efficacy as it is influenced by several factors, including IPA steepness, long calix, and low and narrow IW. In more complex cases, laparoscopic might be considered an alternative.

IFPS is a complicated urology problem yet the clear treatment algorithm has not been found. Bayne et al. recommend methods of nephrotomies and calicocalicostomy. The purpose of this surgical intervention is to provide an opportunity to reduce or stop the progressivity of renal insufficiency. This surgical approach utilizes three-dimensional preoperative modeling through magnetic resonance urography (MRU).

The purpose of surgery recommended by Bayne et al. is to prevent or delay further renal insufficiency. Unfortunately, there has been no clear indication for this intervention. Moreover, the factors that indicate progressive renal insufficiency have not been clearly defined in the literature. There are also other methods developed to manage IFPS patients. Balbo et al., based on the results of his experiment, recommended holmium-based therapy: yttrium-aluminum-garnet laser. Holmium:yttrium-aluminum-garnet (YAG) laser therapy is known to be efficacious in ureter narrowing therapy. Kim et al. performed ureteroscopy and holmium YAG laser to overcome the problem of infundibulum stenosis. The use of these two procedures could be applied with proper controls cutting depths. The ureteroscopic incision of infundibulum stenosis using a YAG holmium laser might be the first-line option in the treatment of infundibulum stenosis.

Figure 4. 10-years old girls with IFPS. (a) MRU showing bilateral severe calyceal dilatation without ureter or pelvic dilatation. (b) Reconstruction is performed before surgery to plan nephrotomies (red line) and calicocalicostomies (yellow lines with arrows). (c) Photograph showing nephrotomies and calicocalicostomy. (d) Photographs showing nephrotomy closure with nephrostomy tube (white) and ureterocalicostomy (red loops).
especially in anterior infundibular stenosis. Ene et al. recommend holmium laser therapy with RIRS (Retrograde Intrarenal Surgery). In all Ene et al. patients, a Ho laser incision was made to infundibular-calix stenosis and Ho laser lithotripsy was used to destroy the stone. All cases are stone free at the end of the procedure. Double J stents are placed through the stenosis area for 4 weeks. Intraoperative complications that occur include bleeding (in 2 cases, SWL series), perforation of the calyceal with minimal extravasation (1 case). Postoperative complications that occur are fever (3 cases), UTI (2 cases), double J displacement (1 case).

IFPS patients with complications of urolithiasis could be identified through IVP and CT-Scan. Regarding the management, Koopman et al. found and recommend patient urolithiasis with intrarenal stenosis or IFPS’ management algorithm. This algorithm is described in Figure 6.

**DISCUSSION**

In infundibular stenosis, urine transit time in pelviocalyceal system is increased. The calyx with the greater diameter and the infundibula having stenosis are causing higher flow towards calyx and lower flow to pelvic. The stasis that occurred is a risk

![Figure 5](image1.png)  
**Figure 5.** Endoscopy showing infundibulum stenotic at the middle right renal calyx. (a) Before procedure. (b) After procedure holmium: yttrium-aluminum-garnet laser.

![Figure 6](image2.png)  
**Figure 6.** IFPS patient with urolithiasis’ management algorithm. RIRS = retrograde intrarenal surgery; ESWL= extracorporeal shockwave lithotripsy; PCNL = percutaneous nephrolithotomy.
factor of stone formation. The presence of kidney stone could be identified through IVP and CT-scan. There are several recommendations for kidney stone management. Stone composition, size, location, and also the symptoms experienced by the patient can be taken into consideration for choosing management methods. Despite its strength, such as providing a thorough and comprehensive explanation of renal infundibular stenosis, this review also has its limitation. There are limited number of latest references available discussing renal infundibular stenosis with urolithiasis.

CONCLUSION

Infundibulopelvic stenosis is a risk factor of urolithiasis. It is a rare condition, but the treatment algorithm has not been found. There are several recommendations for kidney stone management in infundibulopelvic stenosis.

REFERENCES