

# **URINARY (RENAL) STONE (NEPHROLITHOISIS) – An Overview**

**UNIVERSITY OF PNG  
SCHOOL OF MEDICINE AND HEALTH SCIENCES  
DIVISION OF BASIC MEDICAL SCIENCES  
DISCIPLINE OF BIOCHEMISTRY AND MOLECULAR BIOLOGY  
PLB MBBS II SEMINAR**

**VJ Temple**

## What are Urinary (Renal) Stones (Nephrolithoisis or Renal Calculi)?

- Accumulation of minerals in the urinary system;
- Occur when salts or mineral crystals accumulate on inner surfaces of Kidney or Urinary Tract;
- Renal calculi are often jagged and sharp crystals that may accumulate anywhere in the urinary tract;
- Crystals may break off causing severe pain as they move through the urinary tract, especially along the Ureter;
- Renal Stones are common causes of Pain, Obstruction and Secondary infection in the urinary system;
- Pieces of stones may pass without pain, others too large to pass, thus embed in wall of ureter causing pain;

## What are urinary stones made of?

- Most urinary stones consist of one or more compounds:
  - **Calcium Oxalate, Calcium Phosphate, Uric Acid, Cystine or Xanthine;**
- Struvite or “Infection” stone is a mixture of these compounds with Magnesium Ammonium Phosphate;
- General characteristic of these compounds:
  - Most are poorly soluble in aqueous medium,
  - For others solubility is influenced to a major degree by urinary pH
  - They crystallize within an Organic Matrix, forming stone;

## What mechanism is involved in formation of urinary stones?

- Exact mechanism(s) not fully know;
- Most common suggested mechanism for stone formation is:
  - **“Super-Saturation Crystallization”**
  - **Dehydration causes Calcium Phosphates, Oxalates, Urea, Uric Acid, and/or other compounds to combine and crystallize;**

## What are some factors that influence formation of urinary stones?

- Some related factors for urinary stone formation are:
  - Age, Sex, and Family history of Stones,
  - Water Consumption, Climate,
  - Associated Medical Problems,
  - Dietary Patterns
- Example of dietary effect:
  - Intake of high doses of Vit C supplements on a regular basis (500mg or more) increase risk of urinary stone formation in some individuals;
  - Eating foods High in Oxalate may trigger urinary stone formation;

- Examples of foods with high Oxalate levels: Spinach, Rhubarb, Beets, Nuts, Chocolate, Wheat Bran, Tea, Strawberries;
- Usually males suffer from urinary stones more often than females;
- Abnormal and Excessive Accumulation of Stone forming substances in urine,
  - Examples: Calcium, Oxalate, Uric Acid, Cystine,
    - They are usually soluble in presence of Citrate and Pyrophosphates, that inhibits formation of stones;
  - **Stone formation occurs when concentration of stone forming substances are very high and inhibitors are low;**
- Imbalance of factors affecting solubility of components in the urine;

- Some inherited metabolic disorders may or may not result in stone formation,
  - Examples of disorders: Hypercalciuria, Hyperoxaluria, Cystinuria
- Low intake of fluids,
  - People living and working in hot conditions are liable to become dehydrated, and show greater tendency to form renal stones, as the urine become more concentrated;
- Urinary infection, because debris of Bacteria promotes crystal formation;

- Urine pH (altered by bacterial activity and metabolic factors),
  - Alkaline urine due to infection with Urea Splitting bacteria
  - Example: Proteus predisposes to formation of Magnesium Ammonium Phosphate stones (insoluble in alkali),
- Mucoproteins in urine provide Organic Nidus on which crystal deposition occurs;
- Congenital Anomalies of Urinary Tract Obstruction;
- Hyperparathyroidism,
- Renal Tubular Acidosis (RTA) can cause stone formation;

## Why do some individuals have multiple recurrences of urinary stones?

- Exact reasons and mechanisms for multiple recurrences of urinary stones in some individuals are not completely understood, but may involve multitude of factors including the following:
  - Low urine flow (low fluid intake),
  - Factors increasing Super-saturation of urine with stone-forming salts,
    - Example: Over excretion states and conditions that lead to low urine flow rate;

- Absence of substance or substances in the urine that inhibit formation of crystal;
  - Example: Absence of abnormal crystal growth inhibitors, such as Citrate;
- Occupation of the individual – as possible cause of dehydration;
- Nature of the diet of the individual;
- Medical conditions such as:
  - Recurrent urinary infections,
  - Gout,
  - Cystinuria,
  - Family history of gout or urinary calculi;

## What are the characteristics of Calcium Oxalate stones?

- **Calcium Oxalate Stones:**
- Most common urinary stones encountered;
- Usually associated with:
  - Low urine output resulting in concentrated urine,
  - Increased excretion of urinary Calcium or Oxalate,
  - Contains mainly Calcium Oxalate with small quantities of Calcium Phosphate and Uric Acid;
- Test for calcium and oxalate output in urine of must be assessed to ascertain that mechanism of urinary acidification is normal,

- High fluid intake is beneficial, it is effective in diluting Calcium and Oxalate preventing **Hypercalciuria**;
- To prevent Hypercalciuria, patients need to pass at least 1.5L of urine per 24-hour;
- Simple guide: Ensure urine is as colorless as possible;
- **As a rule**: Dark urine indicate high concentration, hence greater tendency for stone formation;
- Diuretic drugs used to increase urine flow rate, thus preventing the super-saturation of urine with Calcium Oxalate,
- **NB**: Chronic Negative Calcium Balance may occur if patient consumes low Calcium diet for prolonged period as a method for preventing stone formation;

## What is Hypercalciuria?

- Hypercalciuria (High Calcium in Urine):
- Defined as urinary excretion rate of Calcium of:
  - 300 mg/day (for men),
  - 250 mg/day (for women) or
  - 4 mg/kg for both male and female;

## What is Hyper-oxaluria?

- Hyper-oxaluria (High Oxalate in urine): May be due to
  - Enteric disease;
  - Excess Ingestion of Oxalate-containing foods
    - Examples: Spinach, Cocoa, Nuts, Pepper, Tea
- Amount of Oxalate in urine and Clinical history can be used to identify the causes of Hyper-oxaluria;
- Usually suggested that Stone-formers with Mild Hyper-oxaluria should consume diet high in Calcium

### Why?

- Because Calcium binds Free Oxalate in GIT and prevents its absorption and subsequent excretion in urine;

- Idea that stone-formers should eat more foods rich in Fiber content and hence Phytic Acid with the aim of binding Calcium in GIT is not a good suggestion; **Why?**
  - Because the fiber binds Calcium, thus less amount of Calcium is available to bind Oxalate;
  - Best strategy is to consume diet low in Oxalate;

## What is Hyper-uricosuria?

- Hyper-uricosuria is High Uric Acid in urine;
  - Occurs when Uric Acid in urine is greater than
    - **750 mg/24hrs in Female,**
    - **800 mg/24hrs in Male,**
- Uric acid crystals provide Nidus on which Calcium Oxalate crystals can orient themselves and grow;
- Hyper-uricosuria is due to excess consumption of Purine,
- **What are the sources of Purines in diets in PNG?**

## What are the characteristics of Uric Acid Stones?

- Uric acid stones **can occur** in patients with normal serum and urinary levels of Uric Acid;
- Some patients with uric acid stones may either have been diagnosed as having Gout or be shown to have Gout during investigation;
- Myeloproliferative disorders and Chemotherapy can cause Uric Acid stone,
- Majority of patients with Uric Acid stones can be treated medically;

- Treatment involves:
  - High fluid intake to maintain an output of at least 2.0L of urine a day;
  - Adjustment of Urinary pH to 6.5 – 7.0;
  - Important to monitor urine pH with test strips and adjust medication accordingly;
  - If patient is not responding;
  - Allopurinol can be used to reduce the excretion of Uric Acid by blocking Xanthine Oxidase;

## What causes Uric acid stone formation?

- **Uric acid stones** may occur because of increased urine acidity in which Uric Acid crystallizes,
- **Urate is more soluble than Uric Acid,**
- Example:
  - Urine at **pH 7.0** dissolves between 150 - 200 mg/dl of Urate, whereas
  - Urine at **pH 5.0** dissolves only one-tenth as much Urate (between 15 - 20 mg/dl),
  - Normal urine usually has pH below 5.8,
  - Urine Acidification occurs in Distal Tubules and Collecting Ducts;

- **Sodium Urate** is formed at sites Proximal to the site of urine acidification;
- **Uric Acid Crystals are formed at Distal sites;**
- Most stones in the urinary collecting system are composed of Uric Acid, thus stone formation can be reduced by Alkalinization of the Urine;
- This can be achieved by using Sodium Bicarbonate tablets, or Sodium or Potassium Citrate;

## How can Uric acid stone formation be reduced?

- Consumption of large amounts of foodstuffs rich in Purines, can increase Plasma Urate levels over 7.0 mg/dl (0.4 mmol/L) **Why?**
  - Because dietary Purines are converted to Uric Acid by Intestinal Xanthine Oxidase that converts:
    - **Hypoxanthine to Xanthine,**
    - **Xanthine to Uric acid;**
- Foods with low Purine lowers Plasma Urate level;
  - Examples of Foods with high Purines: Sweet breads, Liver, Yeast, Kidneys, Sardines, Tea, Coffee, Cacao;

- Diet adequate but not high in protein should be eaten;
- Obesity causes high Uric Acid level because of high intake of food;
- Avoid dehydration,
- Reduce intake of Alcohol (**Why**):
  - It causes diuresis leading to dehydration,
  - High rate of alcohol metabolism results in Lactic Acidosis, which suppresses Tubular Secretion of Uric Acid,

## What are some of the characteristics of Struvite stones?

- Struvite stones consist of Magnesium Ammonium Phosphate;
- Struvite stones occur twice as commonly in women than men; **Why?**
  - Struvite stones are associated with infection, although it is still unclear whether it is the stone that causes the infection or vice versa,
  - Organisms associated with Struvite produce Urease, which splits Urea, thus raising Urinary pH and causes formation of Struvite stone,
    - Examples of organisms: Proteus, Pseudomonas and Klebsiella, Staphylococcus;

- Urease inhibitors, such as Acetohydroxamic acid or Hydroxyurea, have been used to prevent Alkalization of urine and precipitation of Struvite;
- To minimized the risk of recurrence, complete removal of the stone should be done and high fluid intake should be encouraged;

## What are the characteristics of Cystine stones?

- Cystine stones do not occur regularly, but correct diagnosis is often delayed;
- May be caused by Inherent Error in metabolism, due to increased excretion of:
  - **Cystine, Ornithine, Arginine and Lysine;**
- Family history is important;
- Stones are composed mainly of **Cystine**, which is less soluble in urine than other amino acids;
- Cystine stones should be suspected in patient that presents with family history of stones at an early age, and has not responded to common forms of treatment;

- Diagnosis can be confirmed by either rapid screening using the **Nitroprusside test** or high 24-hour Cystine excretion or Stone analysis;
- Prevention of stone formation is adequate hydration,
- Patient needs to produce **more than 3.0L of urine per 24 hours**, which usually means drinking at least two glasses of water at night,
- Alkalization of urine with high Bicarbonate tabs;
- Most patients find it difficult to maintain regimen long-term, thus there is usually high recurrence rate;

## What biochemical Investigations are done on Patients with Renal Stones?

- Chemical analysis of urinary stones is important in investigation of their composition and why they formed;
- Stones may have characteristic Colors or Appearance, but Crystallographic Analysis is used to determine the composition of stones;
- Some Biochemical tests helpful in reaching a diagnosis:
  - Plasma Calcium, Phosphate, Total CO<sub>2</sub>,
  - Plasma Albumin,
  - Urate concentrations,
  - Alkaline Phosphatase activity in plasma,
  - Full acid-base assessment,

- Complete Urinalysis;
- 24-hour excretion of Calcium, Phosphate and Urate;
- Urinary excretion of Oxalate, Cystine or Xanthine;
- Urinary Acidification Tests,
- Renal Function Tests,
- Plasma Creatinine,
- Plasma Urea,
- Plasma Electrolytes,
- Microbiological examination of Urine;

## REFERENCES

- Textbook of Biochemistry, with clinical correlations, Ed. By T. M. Devlin, 4th Ed.
- Harper's Illustrated Biochemistry 26<sup>th</sup> Edition; 2003; Ed. By R. K. Murray et. al.
- Biochemistry, By V. L. Davidson & D. B. Sittman. 3rd Edition.
- Hames BD, Hooper NM, JD Houghton; Instant Notes in Biochemistry, Bios Scientific Pub, Springer; UK.
- VJ Temple Biochemistry 1001: Review and Viva Voce Questions and Answers Approach; Sterling Publishers Private Limited, 2012, New Delhi-110 – 020.