URINARY (RENAL) STONE (NEPHROLITHOISIS) – An Overview

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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

  o 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 Alkalization of the Urine;

• This can be achieve by using Sodium Bicarbonate tables, 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$_2$,
  • 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;
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