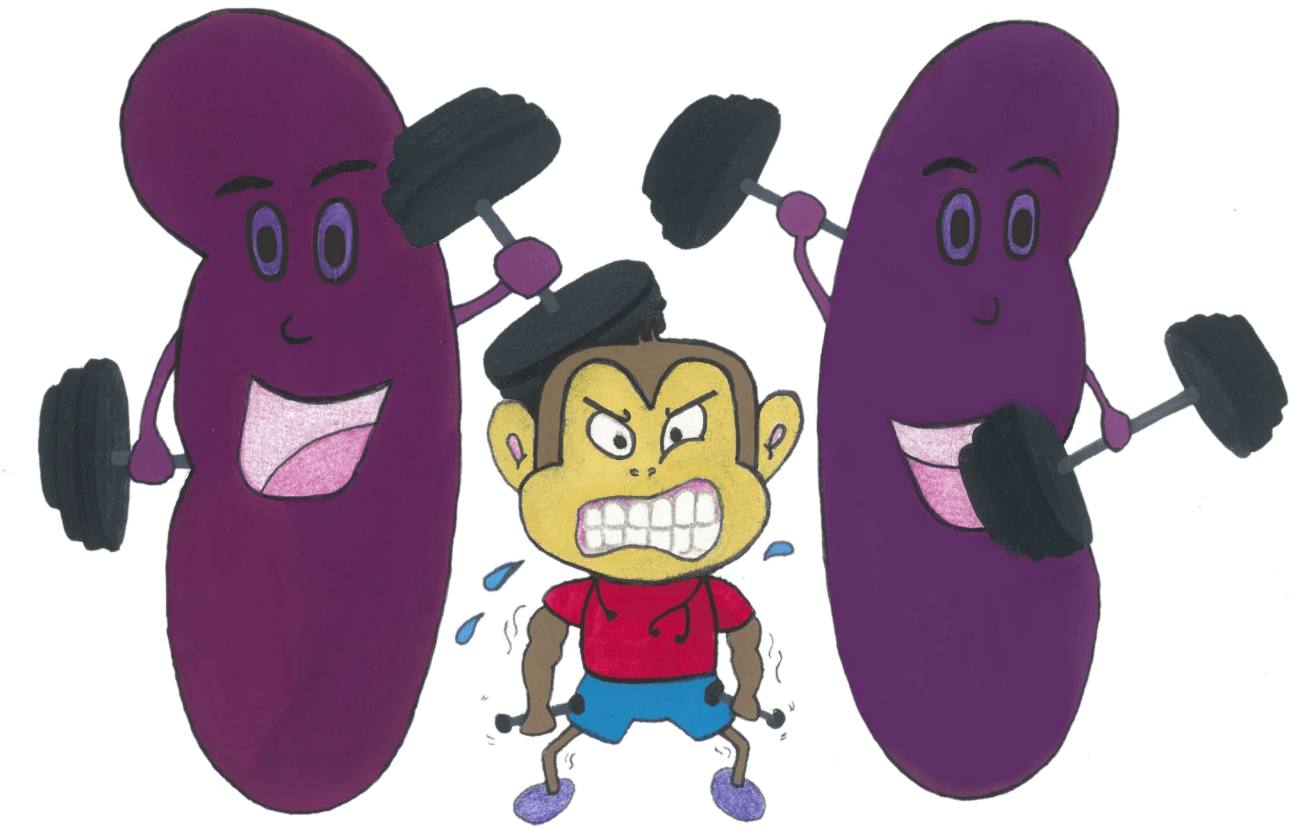
Chapter 17:

RENAL DISORDERS

Student Authors: Gauta Kgomo, Ismatou Balde and Neo Mahlatsi

Specialist Advisor: Dr Ashton Coetzee



This chapter covers the following topics:

- Renal anatomy and physiology
- Urinary tract infections (UTIs)
- Nephritic syndrome
- Nephrotic syndrome
- Acute kidney injury (AKI)
- Haemolytic uraemic syndrome (HUS)
- Urinary tract obstruction
- Nephrolithiasis (renal stones)
- Hypospadias
- Chronic kidney disease (CKD)
- Paediatric hypertension (HPT)

RENAL ANATOMY AND PHYSIOLOGY

The kidneys are paired organs located between the T12 and L3 vertebrae. They are both retroperitoneal with the left kidney situated more superiorly than the right.

Gross Anatomy of the Kidney

The functional unit of the kidney is the nephron. The nephron is comprised of:

- Glomeruli – filter blood as it travels through the afferent and efferent arterioles
- Proximal convoluted tubule (PCTs) and Loops of Henle (LoHs) – play important roles in absorption
- Distal convoluted tubules (DCT) – play important roles in dilution
- Collecting tubules – fine-tune the pH of the urine

The functions of the kidney are to maintain homeostasis, which includes:

- Fluid balance (via the renin-angiotensin-aldosterone-system; RAAS)
- Electrolyte balance
- Waste excretion e.g. nitrogen, urea, ammonia, creatinine
- Acid-base balance
- Endocrine functions:
    - Erythropoietin production by the interstitial cells of the renal medulla in response to decreased O_2 delivery
    - Renin production by the juxtaglomerular apparatus
    - Metabolism of vitamin D and its constituents

Pathology

Renal pathology can either be primary or secondary. Primary disease refers to an intrinsic structural or functional kidney abnormality that is symptomatic e.g. minimal change nephrotic syndrome, polycystic kidney disease, renal tumour. Secondary disease refers to a systemic condition that affects the kidney function e.g. HPT, post-infectious glomerulonephritis, Wegener's granulomatosis, use of nephrotoxic drugs.

URINARY TRACT INFECTIONS (UTIs)

UTIs are quite common in children and occur more in females (30% of girls) than in boys (1%), except in the <1 year age group. They range from lower urinary tract disease (e.g. urethritis, cystitis) to more severe and complicated upper UTIs (e.g. pyelonephritis, renal abscesses).
The UTI may be uncomplicated (lower UTI in a generally well child) or complicated (upper UTI or a systemically unwell child).

Aetiology

Urine is normally sterile but there is sometimes colonisation of urine and proliferation of disease-causing organisms. 90% of the bacteria which cause UTI form normal flora of the GIT. Common causative organisms include:

- *E. coli* sp.
- Enterococcus sp.
- Klebsiella sp.
- Pseudomonas sp.
- Proteus sp.

Risk Factors

Children at greater risk of developing a UTI are:

- Females (as they have shorter urethra)
- Uncircumcised males (at risk of recurrent UTIs)
- Those with anatomical urogenital anomalies
- Chronically constipated children
- Those with poor hygiene or ablution habits

Clinical Features

They include:

- Lethargy
- Dehydration
- Pyrexia
- Abdominal tenderness

- Renal angle tenderness
- In neonates and infants:
    - FTT
    - Irritability
    - Vomiting
    - Diarrhoea
- In older children (classical symptoms):
    - Dysuria
    - Frequency
    - Urgency
    - Abdominal/flank pain or mass

Investigations

The following investigations should be done:

- Urinalysis:
    - The urine may be collected by suprapubic aspiration or catheterisation for younger, ill and uncooperative children, or a midstream sample may be collected in older children.
    - Urine dipsticks:
        - They are done to look for leucocytes and nitrites – diagnostic of a UTI.
        - The test is more sensitive if both leucocytes and nitrites are detected.
    - Urine MC&S (UMCS):
        - It is done to identify pyuria and grow colony forming units.
        - The antibiotic choice is adjusted based on UMCS results.
- Serum urea and electrolyte levels (U&E; if the child is systemically unwell, dehydrated or has recurrent UTI)
- Abdominal USS (all children with UTIs must have an initial USS to rule out anatomical causes)
- Voiding cystourethrogram or MAG3 scan (if ultrasound is abnormal)

Management

It includes:

- Excluding and managing risk factors
- Prescribing analgesia (give paracetamol and avoid NSAIDs)

For the child with an uncomplicated UTI:

- Prescribe 5-7 days of amoxicillin/clavulanic acid (adjust antibiotic based on urine culture)
- Encourage feeding and hydration
- Review in a week with urine culture, if necessary

For the child with a complicated UTI:

- Admit the child to hospital
- If there is severe disease, start ceftriaxone or amoxicillin/clavulanic acid. The enteral route (oral or via NGT) is preferred over the parenteral route
- Maintain fluids, feeds and electrolytes
- Review the child's response to treatment in 24-48 hours. If responsive, switch to oral antibiotics and continue treatment for 7 days (10-14 days in neonates) and adjust antibiotic choice according to culture results. If unresponsive, add gentamicin with trough level monitoring and review again.
- Follow up in 1-2 weeks with a urine culture. More frequent follow-up is required if the child has recurrent episodes.

NEPHRITIC SYNDROME

It is caused by glomerular damage and is characterised by a triad of symptoms – macro-/microscopic haematuria**,** oligo-/anuric renal failure and HPT.

Pathophysiology and Aetiology

Nephritic syndrome is caused by damage to the glomerulus of any cause:

- Bacteria
- Toxins
- Stones
- Trauma
- Tumours

- Immunological responses that cause inflammation
- Cell proliferation and glomerular dysfunction

Nephritic syndrome is most commonly due to post-streptococcal glomerulonephritis i.e. there is a group A streptococcus throat infection 5-21 days prior to the nephritis (more common than after impetigo). Glomerular damage is due to deposition of circulating immune complexes or as a result of bacterial protein deposition within the basement membrane, leading to in-situ immune activation.

Clinical Features

The child may present with:

- Haematuria (usually the reason for presentation at a healthcare facility)
- Oliguria/anuria
- HPT (examine target organs e.g. eyes and heart)
- Proteinuria
- Oedema
- Inflamed throat, impetigo or history of recent throat or skin infection (with associated fever, lethargy or rash)
- Palpable purpura (vasculitis of the skin)
- Family history of sickle cell, renal stones or haematuria
- Abdominal or flank pain/tenderness
- Dysuria and urinary frequency
- History of trauma
- Arthritis

Complications

Nephritic syndrome may be complicated by:

- Hypertensive crisis
- Seizures
- Encephalopathy
- Pulmonary oedema
- Heart failure

Investigations

They should include:

- Urinalysis:
    - Urine dipstick (will show haematuria and may show proteinuria)
    - UMCS (will contain casts and crystals, and show microscopic haematuria and proteinuria)
- Blood tests:
    - Creatinine and U&E
    - Calcium
    - Protein (albumin)
    - FBC
    - C3 and C4
    - Anti-DNAse B, ASOT and ANA (only request if there are other features of autoimmune disease or low C3 and C4)
- Throat or skin swab (for culture; not routinely performed)
- Imaging:
    - Renal USS
    - CXR
    - ECG (if indicated)
- Biopsy (often unnecessary)

Management

One must:

- Identify the cause and remove or treat it e.g. treat underlying streptococcal infection with IM benzyl benzathine penicillin or oral phenoxymethylpenicillin
- Restrict fluids (give diuretics if the child is fluid overloaded), sodium and potassium
- Perform daily weight, dipsticks and BP checks
- Start antihypertensives:
    - Furosemide is usually given as the HPT is due to fluid overload.
    - Amlodipine may be given if the BP remains uncontrolled.
    - Labetalol may be used in hypertensive urgencies or emergencies.
- Monitor and manage complications

Table 17.1: Approach to Coloured Urine

Approach to Coloured Urine

Urine may be coloured because of:

- Haematuria:
  - Patients with glomerular haematuria will have positive dipsticks and abnormal RBCs or RBC casts on urinalysis. Causes include:
    - Post strep GN
    - IgA nephropathy
    - Infections
    - Toxins
    - Trauma
  - Patients with non-glomerular haematuria will have positive dipsticks and normal RBC on urinalysis. Causes include:
    - Urolithiasis
    - Pyelonephritis
    - Obstruction
    - Cystitis
    - Menstruation
    - Strenuous exercise
    - Tumours
    - Iatrogenic
- Haemoglobinuria; causes include:
  - DIC
  - Intravascular haemolysis (e.g. sickle cell)
- Myoglobinuria; causes include:
  - Rhabdomyolysis
  - Trauma
  - Burns
  - Myositis
- Pigmenturia; causes include:
  - Porphyria
  - Urate
  - Beets
  - Drugs e.g. rifampicin

NEPHROTIC SYNDROME

It is characterised by proteinuria, oedema, hypoalbuminaemia and hypercholesterolaemia.

Pathophysiology

Nephrotic syndrome is due to glomerular or tubular disruption which impairs the basement membrane proteins and effects of their negative charge, making the basement membrane more permeable to serum proteins. This leads to a decrease in serum protein, decreased oncotic pressure and the shift of fluid into the interstitium. The effective decrease in plasma volume results in the activation of RAAS, which retains more fluid and leads to the shifting of even more fluid into the interstitium. Lastly, hepatic lipoprotein synthesis is activated and there is a resultant increase in triglycerides and cholesterol.

Aetiology

Nephrotic syndrome may be:

- Primary (idiopathic nephrotic syndrome):
    - Minimal change nephrotic syndrome
    - Focal segmental glomerulosclerosis
    - Membranoproliferative glomerulonephritis
- Secondary:
    - SLE
    - Granulomatosis with polyangiitis
    - Infection
    - DM

Clinical Features

The child may present with:

- Sudden-onset pitting oedema or ascites
- Pleural effusion
- Anorexia
- Malaise
- Abdominal pain
- Diarrhoea (because of the oedematous bowel)
- Respiratory distress
- Heart failure

Investigations

The following investigations should be performed:

- Urinalysis:
    - It will show proteinuria and an elevated spot urine protein:creatinine ratio (UPCR >0.2 g/mmol).
- Blood tests:
    - U&E
    - Cholesterol
    - Albumin and total protein
- Renal USS
- Renal biopsy (if a secondary cause is suspected)

Other tests which may be performed to diagnose a secondary cause:

- ASOT and anti-DNAseB
- HBV and HCV antibodies
- HIV, syphilis, CMV
- Anti-dsDNA

Management

General Measures

The child should be put on a diet with restricted sodium and saturated fat restriction. However, fluids should not be restricted. The diet must maintain nutrition and contain sufficient multivitamins, calcium and folic acid. Daily weights, BP, dipsticks and UPCRs should be done.

Prophylaxis against secondary infections should be given. If the child has anasarca, phenoxymethylpenicillin should be administered, as these patients are at risk of pneumococcal peritonitis. The child should also be given the routine vaccinations against pneumococcus, VZV and HBV according to the EPI, once s/he is in remission and not on steroids or immunosuppressive therapy.

Specific Management

The child with idiopathic nephrotic syndrome should be started on empiric steroid therapy (prednisone 2 mg/kg up to maximum of 60 mg) for a minimum of 4-6 weeks. In secondary nephrotic syndrome, the underlying illness needs to be treated.

Mild oedema will improve with conservative management and steroids (if the nephrosis is steroid-responsive). Resistant oedema may be cautiously treated with diuretics and severe anasarca may require an albumin infusion. Enalapril, chronic diuretics and statin therapy are only indicated in steroid-resistant cases and should be given under specialist supervision.

ACUTE KIDNEY INJURY (AKI)

Pathophysiology

AKI is characterised by an abrupt decline in the glomerular filtration rate (GFR) and tubular function, resulting in decreased excretion of creatinine, urea, nitrogen, phosphate and fluid. This child will, therefore, be azotaemic and fluid overloaded with normal, decreased or increased urine output.

Aetiology

AKI may have a pre-, intra- or post-renal cause.

Table 17.2: Pre-, Intra- and Postrenal Causes of AKI

Pre-Renal AKI	Intrarenal AKI	Post-Renal AKI
● Dehydration ● Septic shock ● Heart failure ● Haemorrhage ● Burns ● Renal artery or vein issues	● Acute tubular necrosis ● Nephrotoxins ● Glomerulonephritis ● Acute cortical necrosis ● Interstitial nephritis ● Infection	● Urethral obstruction ● Ureteral obstruction ● Extrinsic compression of outlet e.g. tumour ● Neurogenic bladder

Clinical Features

The child may present with:

- History of any cause of hypoperfusion e.g. vomiting, diarrhoea, bleeding
- History of use of a nephrotoxic drug
- Family history of coagulopathy or tumours
- Anuria or polyuria

- Flank or abdominal mass/pain
- Haematuria
- Proteinuria
- Hypotension or other signs of dehydration (examine the eyes, oedema, skin)
- Bleeding
- Signs of heart failure
- Distended bladder

One must examine the child for features of genetic syndromes associated with renal disease e.g. Down syndrome, FASD

Investigations

They should include:

- Urinalysis:
    - Dipsticks to screen for infection (proteinuria, haematuria, leukocytes and nitrites).
    - UMCS to assess RBC dysmorphology, attempt to grow bacteria and look for RBC/WBC/protein casts.
    - Fractional excretion sodium percentage to distinguish between pre-renal AKI (<1%) and intrarenal failure (>1%).
    - Blood urea nitrogen:creatinine ratio >20:1 suggests pre-renal failure.
    - Spot UPCR to assess for proteinuria.
- Blood tests:
    - Creatinine and U&E
    - Creatinine clearance and GFR
- Imaging:
    - Perform an USS and, if abnormal, further imaging e.g. voiding cystourethrogram (VCUG), CT scan, MRI.
- Renal biopsy (if indicated)

Management

General Measures

One must identify and manage the cause(s) e.g. relieve obstruction in post-renal AKI, treat active infection. Adequate perfusion and fluid balance must be maintained

(replace fluid losses and restrict fluid intake as needed). Feeding must be maintained and the child placed on sodium-, potassium- and phosphate-restricted, high-protein diet. Daily weights, BP and dipstick checks should be done.

Specific Management

One must manage:

- Fluid balance:
    - Restrict fluids if the patient is fluid overloaded.
    - Replace fluids if the patient is fluid depleted.
    - Consider furosemide if the patient remains anuric despite fluid administration.
- Electrolytes:
    - If the patient is hyperkalaemic, shift according to emergency guidelines and restrict potassium.
    - If the patient has metabolic acidosis, correct the acidosis with sodium bicarbonate.
    - If the patient has symptomatic hypocalcaemia or hyperphosphataemia, administer 10% calcium carbonate if the patient.
    - If the patient has severe anaemia, give a slow transfusion of packed RBCs (administer with caution and only if necessary as it can lead to fluid overload, HPT and hyperkalaemia).
- Seizures:
    - Causes may include HPT, uraemia, hypocalcaemia and hyponatraemia.
    - Treat with diazepam and investigate for the cause (may be due to ARF or an unrelated cause).
- Pulmonary oedema:
    - Treat with furosemide, morphine and oxygen.

Dialysis (peritoneal dialysis or haemodialysis) is indicated when the above-mentioned issues become refractory or the child has been poisoned with a dialysable agent.

HAEMOLYTIC URAEMIC SYNDROME (HUS)

Pathophysiology and Aetiology

There are many types of HUS but the most common type is associated with a prodromal diarrhoeal phase. HUS typically occurs 7-10 days after a diarrhoeal illness caused by bacteria which secrete Shiga or verotoxins e.g. Shigella sp. or *E. coli*, respectively. The toxin binds to and damages glomerular endothelial cells, resulting in coagulation.

If severe, glomerular and interstitial thrombosis and haemolysis result (RBCs are squeezed through the narrowed vessel lumens). Thus, HUS presents with the triad of microangiopathic haemolytic anaemia, thrombocytopenia and acute renal injury (haematuria or renal failure).

Clinical Features

The child may present with:

- Haemorrhagic diarrhoea (dysentery)
- Lethargy and irritability
- Fever
- Dehydration
- Features of renal failure e.g. haematuria, proteinuria, HPT, oedema
- Petechiae
- Hepatosplenomegaly (occasionally)

Investigations

They should include:

- Urinalysis:
    - A dipstick is done to identify haematuria and proteinuria.
    - The UMCS is used to assess for casts and organisms.
- Blood tests:
    - U&E
    - The FBC will show elevated reticulocytes, decreased haptoglobin and, possibly, leucocytosis.
    - LDH will be elevated.

    - INR/PTT will be normal (done to exclude sepsis-related DIC).
    - A PBS is done to look for evidence of intravascular haemolysis (e.g. schistocytes, helmet and burr cells, fragmented erythrocytes).
- Stool tests:
    - A stool culture may show vero- or Shiga toxin-producing strains of *E. coli* or *Shigella.*

Management

It is supportive and includes:

- Managing fluid status and electrolyte levels
- Maintaining BP control with anti-hypertensives
- Performing a RBC transfusion (as needed)
- Platelet transfusion (if still actively bleeding)
- Maintaining nutrition
- Managing complications e.g. pulmonary oedema, seizures, hypertensive crisis

URINARY TRACT OBSTRUCTION

It is a common condition which can occur at any anatomical level of the genitourinary tract.

Aetiology and Pathophysiology

Common congenital causes of urinary tract obstruction are:

- Pelvi-ureteric junction (PUJ) obstruction
- Posterior urethral valves (PUVs)
    - PUVs are the most common cause of bladder outlet obstruction in males.
    - The valves are present because of persistence of the urogenital membrane or abnormal integration/involution of embryonic structures.
- Vesico-ureteric junction (VUJ) obstruction (much less common)

The obstruction may be:

- Intraluminal e.g. stones, clots, stenosis
- Intramural e.g. tumours, uterocoeles

- Extramural e.g. tumours, other masses

Clinical Features

The child may present with:

- Fever
- Irritability
- Poor stream strength
- Dribbling
- Straining
- Recurrent UTIs
- Lower abdominal pain/mass
- Flank mass/pain
- Stunted growth
- Renal scarring
- Urinary reflux hydronephrosis
- Chronic renal impairment
- History of intrauterine concerns
    - Oligohydramnios
    - Facial distortion
    - Lung hypoplasia
    - Rupture of the ureter leading to urine ascites in the neonate
- Congenital syndromes/facies
- Anaemia
- Features of renal impairment e.g. oedema, haematuria, proteinuria, HPT
- Features of UTI e.g. dysuria, fever, frequency, irritability

Investigations

They should include:

- Urinalysis
    - Urine dipsticks
    - UMCS
- Blood tests:
    - U&E

    - FBC
- Imaging:
    - Kidney, ureter and bladder (KUB) USS (useful for identifying anomalies).
    - VCUG (can show elements of reflux or obstruction).
    - MAG3 (can assess PUJ severity and for renal scars).
    - MRI/CT scan (if indicated).

Management

The obstruction must be relieved as soon as possible with a catheter. One must exclude or manage dysfunctional voiding or a neurogenic bladder. Current infections should also be treated. Prophylactic antibiotics may be indicated in patients with recurrent infections and/or abnormal anatomy.
Regular dipsticks and RFTs should be done. Surgery may be required to correct any anatomical anomalies.

NEPHROLITHIASIS (RENAL STONES)

Nephrolithiasis is the formation of a precipitate in the genitourinary system.

Pathophysiology

It may be due to:

- Recurrent UTIs
- Neurogenic bladder
- Presence of sutures (act as a nidus)
- Obstruction
- Metabolic causes:
    - Familial hypercalciuria
    - Cystinuria

Clinical Features

The child may present with:

- Acute obstruction

- Renal colic
- Flank, lower abdominal or groin pain/mass
- Vomiting
- Features of infection – fever, irritability, lethargy
- Haematuria
- Fever
- Renal angle tenderness
- Tachycardia
- Tachypnoea

Investigations

They should include:

- Urinalysis:
    - Urine dipstick
    - Urine MCS
    - Urine biochemistry
- Blood tests:
    - U&E and uric acid levels
    - Calcium, phosphate and parathyroid hormone levels
- Imaging:
    - Abdominal X-ray and CT scans are more helpful than USS as the stones can be radio-opaque (e.g. calcium stones) or radio-lucent (e.g. magnesium/ammonium/phosphate stone or struvites due to infective causes).

Management

General management includes:

- Relieve acute obstruction
- Give analgesia
- Start antibiotics (if there are signs of infection)
- Alkalinise urine with oral agents
- Keeping the child hydrated
- Making dietary changes (decrease salt, protein and oxalate intake)

HYPOSPADIAS

It forms part of a triad of congenital anomalies:

- Urethral meatus that is ventral and proximal to its normal opening (hypospadias)
- Dorsal hood
- Chordee

It is associated with genital ambiguity rather than urinary anomalies.

Clinical Features

The child may have:

- Meatal opening on the glans, corona or distal third of the shaft
- Phimosis or paraphimosis
- Ventral hood
- Chordee
- Undescended testes (10% of patients)
- Inguinal hernia

Investigations

The diagnosis is clinical and investigations are usually unnecessary.

Management

Surgical intervention before 18 months of age is best.

CHRONIC KIDNEY DISEASE (CKD)

It refers to continuous injury to the kidneys that results in progressive decline in kidney function until end stage renal failure develops.

Aetiology

Causes include congenital and obstructive diseases. After puberty, acquired conditions and the inability to support the growing body become more common causes of chronic renal failure.

Clinical Features

They may include:

- FTT
- Pallor
- Hypertension (may have headaches and heart failure)
- Polyuria
- Dehydration
- Oedema
- Anaemia
- Renal osteodystrophy
- Rickets (pigeon chest, curved weight bearing bones, etc.)
- Uraemic symptoms (nausea, vomiting, confusion, convulsions)
- Delayed puberty
- Impaired learning and poor school performance

Investigations

They should include:

- Urinalysis:
    - Urine dipstick (to look for proteinuria and haematuria)
    - UPCR
    - UMCS
- Blood tests:
    - U&E
    - FBC
    - Creatinine clearance and eGFR (to grade severity)
- Imaging:
    - X-ray (to look for osteomalacia)
    - Ultrasound to exclude anatomical anomalies

Management

A multidisciplinary approach should be used. Treatment should include:

- Daily weight, BP and dipstick checks
- Dietary management:
    - The child should be put on a high-energy diet with supplemental multivitamins and folic acid.
    - Salt- and potassium-intake should be restricted but not protein-intake.
- Fluid management
- Avoidance of nephrotoxic drugs
- Managing electrolyte dysfunction (metabolic acidosis and hyperkalaemia), anaemia, HPT and dyslipidaemia
- Following the appropriate immunisation schedule (especially for pneumococcus, VZV and HBV)

The child must be assessed for the need for chronic dialysis or renal transplantation.

PAEDIATRIC HYPERTENSION (HPT)

This is defined as systolic or diastolic BP >95th percentile for age, sex and height.

There is an increased risk of sequelae with severe or chronic hypertension.

The HPT may be due to:

- Primary cause (essential HPT)
- Secondary cause (renal disease is the most common cause)

Clinical Features

Children are usually asymptomatic but can present with target organ damage. The child may have:

- Family history of HPT
- Truncal obesity and poor dietary history
- Headache
- Blurry vision
- Stroke
- Heart attack or heart failure

- Bruits
- Diminished leg pressure
- Flank masses
- Signs of Cushing syndrome

Investigations

One should perform investigations which help one assess target organ damage, assess cardiovascular risk factors and identify causes. Further focused investigation should be done based on initial findings.

Management

It includes:

- Finding and treating identifiable causes
- Adjusting risk factors and making lifestyle changes
- Initiating anti-hypertensive therapy (start with a single agent and add other agents as required)
- Managing hypertensive crises