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L6. CHRONIC KIDNEY DISEASE

Definitive criteria: Patient has CKD if ***either*** of the following criteria are present:

- Kidney damage for ≥3 mo with or without decreased GFR, which manifested by 1 or more of the following features:
  - Abnormal blood or urine findings
  - Abnormal imaging tests
  - Abnormal kidney biopsy

OR

- GFR <60 mL/min/1.73 m2 for ≥3 mo, with or without the above signs of kidney damage.

Stages of CKD: depending on degree of renal damage and reduction in renal function (GFR):

STAGE	DESCRIPTION	GFR (mL/min/1.73 m2)
1	Kidney damage with normal or increased GFR	>90
2	Kidney damage with mild decrease in GFR	60-89
3	Moderate decrease in GFR	30-59
4	Severe decrease in GFR	15-29
5	Kidney failure or End-stage renal disease	<15 or on dialysis

Etiology:

Below 5 year of age	1. Congenital renal abnormalities (most common causes) e.g. renal hypoplasia, dysplasia, or obstructive uropathy. 2. Congenital nephrotic syndrome 3. Prune belly syndrome 4. Cortical necrosis 5. Focal segmental glomerulosclerosis 6. Autosomal recessive polycystic kidney disease 7. Renal vein thrombosis 8. HUS.
After 5 year of age	1. Acquired diseases (various forms of glomerulonephritis including lupus nephritis) 2. Inherited disorders e.g. Alport syndrome
Throughout childhood	1. Metabolic disorders (cystinosis, hyperoxaluria) 2. Inherited disorders (both autosomal dominant and recessive polycystickidney disease)

Clinical manifestations: Its varies depending on the underlying cause of CKD:

1. Children and adolescents with CKD caused by chronic GN present with edema, hypertension, hematuria, and proteinuria.
2. Infants and children with congenital disorders such as renal dysplasia and obstructive uropathy can present in the neonatal period with failure to thrive, polyuria, dehydration, urinary tract infection, or overt renal insufficiency.

3. Congenital kidney disease can diagnosed by prenatal ultrasonography, allowing early diagnostic and therapeutic intervention.

Complications:

1. **Growth failure (short stature):** due to poor nutrition, renal osteodystrophy (ROD), metabolic acidosis, hormonal abnormalities, resistance to growth hormone and decreased insulin-like growth factor 1.
2. **Anemia** due to decrease erythropoietin production ,iron, folic acid or B12 deficiencies and reduced RBCs survival.
3. **Renal osteodystrophy ROD** due to **secondary hyperparathyroidism**
4. **Hypertension** and **left ventricular hypertrophy**.
5. **Delayed puberty** due to altered gonadotropin secretion and feedback patterns.
6. Impaired learning and school performance.

Laboratory findings:

1. Increased BUN and S. creatinine.
2. Electrolyte disturbances: hyperkalemia, hyponatremia (due to volume overloaded), hypernatremia (due to loss of free water), hypocalcemia, and hyperphosphatemia,
3. Acidosis and increase plasma uric acid.
4. Hypoalbuminemia due to heavy proteinuria
5. CBC may show a normochromic, normocytic anemia.
6. Elevated S. cholesterol and triglyceride levels
7. Decrease GFR measured by endogenous creatinine clearance.

Renal Osteodystrophy (ROD):

Is a spectrum of bone disorders seen in patients with CKD. The most common condition seen in children is high-turnover bone disease caused by secondary hyperparathyroidism causing skeletal pathologic finding called osteitis fibrosa cystica.

Pathophysiology :

When the GFR declines to approximately 50% of normal early in the course of CKD, there is decrease in functional kidney mass which leads to a decline in renal 1α-hydroxylase activity, with decreased production of activated vitamin D (1,25-dihydroxycholecalciferol).

This deficiency in activated vitamin D results in decreased intestinal calcium absorption, hypocalcemia, and increased parathyroid gland activity (secondary hyperparathyroidism). Excessive PTH secretion attempts to correct the hypocalcemia by increasing bone resorption.

Later in the course of CKD, when the GFR declines to 20-25% of normal, compensatory mechanisms of renal phosphate excretion become inadequate, resulting in hyperphosphatemia, which further increase the hypocalcemia and increased PTH secretion.

Clinical manifestations:

Muscle weakness, bone pain, and fractures with minor trauma.

In growing children, rachitic changes, varus and valgus deformities of the long bones, and slipped capital femoral epiphyses may be seen.
Laboratory investigation shows a decreased serum calcium level and increased serum phosphorus, alkaline phosphatase, and PTH levels.
Radiographs of the hands, wrists, and knees show subperiosteal resorption of bone with widening of the metaphyses.

Treatment of ROD:
The goals of treatment are to prevent bone deformity and normalize growth velocity using both dietary and pharmacologic interventions.
The target phosphorus level for adolescents is between 3.5 and 5.5 mg/ dL, and for children 1-12 yr of age it is 4-6 mg/dL, this treatment is achieved by:

1. Low-phosphorus diet for children and adolescents, and infants should be provided with a low-phosphorus formula such as Similac PM 60/40.
   Phosphate binders are used to enhance GI phosphate excretion.
2. The cornerstone of therapy for renal osteodystrophy is vitamin D administration in form of 0.01-0.05 µg/kg/24 hr of calcitriol (activated vitamin D)

Treatment of CKD:

Aims of treatment:

1. Replacement of decreased or absent renal functions.
2. Slowing the progression of renal dysfunction.

Monitoring:

3. Blood tests include S. electrolytes, BUN, creatinine, calcium, phosphorus, albumin, alkaline phosphatase, and hemoglobin levels.
4. Periodic measurement of parathyroid hormone (PTH) levels and bone XR for early detection of renal osteodystrophy.
5. Periodic Echocardiography to identify left ventricular hypertrophy and cardiac dysfunction.

The treatment of CKD and its complications include the following:

1. Fluid restriction indicated only in oliguric patients and those with Lt. ventricular dysfunction.
2. Poor growth managed by Increased caloric intake, treatment of acidosis, treatment of renal osteodystrophy, and recombinant GH (rHuGH) therapy
3. Treatment of anemia with Erythropoietin (rHuEPO) when Hb level below 10 g/dL, at a dose of 50-150 mg/kg/dose subcutaneously 1-3 times weekly. The dose is adjusted to maintain the Hb level between 11 and 12 g/dL.
   All patients receiving rHuEPO therapy should be provided with either oral or intravenous iron supplementation
4. Treatment of renal osteodystrophy and secondary HPT.
5. Treatment of HT by salt restriction (< 2g\24 hr), diuretics (hydrochlorthiazide in mild cases and furosemide in severe cases) plus anti-hypertensive agents including **ACE inhibitors** (enalapril, lisinopril) and **angiotensin II receptor blockers** (losartan) which are the antihypertensive of choice in all children with proteinuric renal disease because of their potential ability to decrease proteinuria

and slow the progression to ESRD (by mechanisms still not completely understood).
6. Treatment of LVH by volume control
7. Treatment of electrolyte abnormalities including Hyperkalemia, Hyponatremia and Metabolic acidosis

The optimal treatment of ESRD is **renal transplantation.**
Maintenance (chronic) dialysis is effective for a child awaiting renal transplantation or for whom renal transplantation is not possible. **Peritoneal dialysis** is done at home by the family and **Hemodialysis** is typically done three times a week at a dialysis units.

Indications of chronic dialysis are:
1. Poor growth.
2. Stage 5 chronic kidney disease (end-stage renal disease).

Prognosis of CKD:

1. Children with mild CKD (stages 1 and 2) may do well but need to be monitored for progressive loss of kidney function.
2. Children with stages 3 and 4 CKD have a high possibility of progressing to ESRD.
3. Children with kidney transplants generally do well but have to take immunosuppressive medications associated with a variety of side effects, including infections, nephrotoxicity, cardiovascular complications, and increased risk for certain malignancies. Unfortunately most transplanted kidneys dye over time but can last for several years.
4. Children on maintenance dialysis have the highest morbidity and mortality, especially with longer time spent on dialysis.