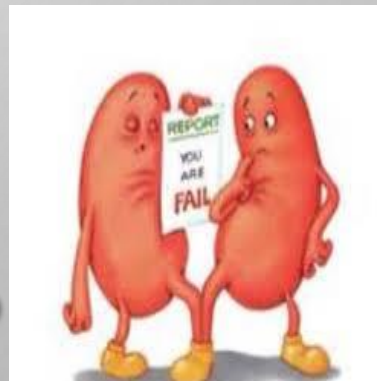
CKD

DEFINITION

- CKD is defined as abnormalities of kidney structure or function, present for >3 months

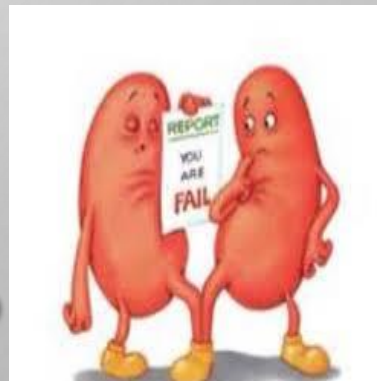
- Term *end-stage renal disease* represents a stage of CKD where the accumulation of toxins, fluid, and electrolytes normally excreted by the kidneys results in the *uremic syndrome*



DIAGNOSIS

- Bilateral Small size Kidneys
- Lab data
- Previous history (3 months ago)
- Nocturia

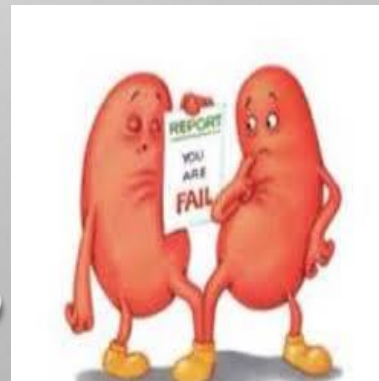
- Risk of worsening of kidney function is closely linked to the amount of *albuminuria*
  - CKD staging system according to Scr and albumin excretion
  - marker for the presence of microvascular disease



AT RISK PATIENT

:

- Small for gestational age
- Low birth weight
- Childhood obesity
- Hypertension
- Diabetes mellitus
- Autoimmune disease
- Advanced age
- African ancestry
- Family history of kidney disease
- Previous episode of acute kidney injury
- Presence of proteinuria
- Abnormal urinary sediment
- Structural abnormalities of the urinary tract
- Hereditary disorders: ADPKD, Alport



- Stages 1 & 2: no sign and symptom
- Stages 3 & 4: clinical and laboratory complications of CKD
  - *Anemia and associated easy fatigability*;
  - decreased appetite with progressive malnutrition
  - Ca/P
  - mineral-regulating hormones, such as 1,25(OH)2D3 (calcitriol), PTH, FGF-23
  - Na/K, water, acid-base homeostasis
- Stage 5: ESRD (uremic Syndrome)

- *GFR in many elderly patients is compatible with stage 2 or 3 CKD.*

ETIOLOGIES OF CKD

- Diabetic nephropathy
- Glomerulonephritis
- Hypertension-associated CKD (includes vascular and ischemic kidney disease and primary glomerular disease with associated hypertension)
- Autosomal dominant polycystic kidney disease
- Other cystic and tubulointerstitial nephropathy

CLINICAL & LABORATORY MANIFESTATIONS OF CKD AND UREMIA

SODIUM AND WATER HOMEOSTASIS

- Total-body content of sodium and water: modestly increased, may not be apparent clinically
- Disruption in urinary excretion
  - Retention
    - HTN
      - Accelerate nephron loss

- Hyponatremia: not commonly
  - Often responds to water restriction

Potassium Homeostasis

- Augmented potassium excretion in the GI tract : defense mechanism

- *Hyperkalemia causes:*
  - increased dietary potassium intake, protein catabolism, hemolysis, hemorrhage, transfusion of stored red blood cells, and metabolic acidosis.
  - Medications: RAS inhibitors and spironolactone and amiloride, eplerenone, triamterene

METABOLIC ACIDOSIS

- Daily proton production: 50-100 meq
- common in advanced CKD
  - less ammonia production as urinary buffer.
  - Hyperkalemia further depresses ammonia production
- *Hyperkalemia and hyperchloremic metabolic acidosis is often present even at earlier stages of CKD.*
  - *In more advanced disease:*
    - high anion gap (Limited urinary excretion of acid)
- In most patients
  - Metabolic acidosis is mild
  - pH is rarely < *7.32*
  - *corrected with oral sodium bicarbonate supplementation*

Bone Manifestations of CKD

- high bone turnover with increased iPTH levels
  - osteitis fibrosa cystica
  - classic lesion of secondary hyperparathyroidism
  - bone pain and fragility, brown tumors, compression syndromes, and erythropoietin resistance
  - PTH as uremic toxin (muscle weakness, fibrosis of cardiac muscle, and nonspecific constitutional symptoms)

- low bone turnover with low or normal PTH levels:
  1. Adynamic bone disease
     - Risk factor: diabetics and the elderly
     - reduced bone volume and mineralization may result from: excessive suppression of PTH production, chronic inflammation, or both.
     - Suppression of PTH: use of vitamin D preparations or from excessive calcium exposure in the form of calcium-containing phosphate binders or high calcium dialysis solution
     - Complications: increased incidence of fracture and bone pain and an association with increased vascular and cardiac calcification or soft tissue calcification (tumoral calcinosis")
  2. Osteomalacia: AL overload, vit D deficiency

- Calciphylaxis:
  - Livedo reticularis and advances to patches of ischemic necrosis, especially on the legs, thighs, abdomen, and breasts
  - vascular occlusion in association with extensive vascular and soft tissue calcification
- Matrix GLA protein: preventing vascular calcification
- Warfarin: decrease regeneration of matrix GLA protein

CKD MBD TREATMENT

- Hyperphosphatemia:low phosphate diet , phosphate-binding agent(calcium-containing or non-calcium-containing)

- Hyperparathyroidism : calcitriol, cinacalcet

CARDIOVASCULAR ABNORMALITIES

- Cardiovascular disease: occlusion coronary, cerebrovascular, and peripheral vascular disease
- compared to the age- and sex-matched general population ranges from ***10- to 200-fold***, depending on the stage of CKD
- Between 30 and 45% of those patients who do reach stage 5 CKD have advanced cardiovascular complication
- ***Risk factors****:*

1. Traditional (“classic”):hypertension, hypervolemia, dyslipidemia, sympathetic over activity, and hyper homocysteinemia
2. nontraditional (CKD-related): anemia, hyperphosphatemia, hyperparathyroidism, increased FGF-23, sleep apnea, and generalized inflammation

CVD TREATMENT

- CKD with diabetes or proteinuria >1gr per 24h,BP should be reduced to <130/80mmHg.
- Salt restriction first line
- ACE inh /ARB:<30% Reduction of GFR can be tolerated
- Cardiovascular risk factors ; Traditional and non-traditional

HEMATOLOGIC ABNORMALITIES

- **ANEMIA**
- A normocytic, normochromic anemia:
  - stage 3 CKD
  - almost universal by stage 4

- Adverse effects:
  1. decreased tissue oxygen delivery
  2. increased cardiac output
  3. ventricular dilation
  4. ventricular hypertrophy.

ABNORMAL HEMOSTASIS

- prolonged bleeding time
- decreased activity of platelet factor III
- abnormal platelet aggregation and adhesiveness
- impaired prothrombin consumption
- Decreased vwf
- Susceptibility to VTE

Treatment:

- DDAVP
- Cryoprecipitate
- IV conjugated estrogens
- Blood transfusions
- ESA therapy
- Optimal dialysis

NEUROMUSCULAR ABNORMALITIES

- Neuropathy
  1. CNS:
     - Mild disturbance : memory and concentration and sleep disturbance
     - Hiccup , cramps and twitching
     - In advanced untreated kidney failure : asterixis, myoclonus, seizures, and coma
  2. PNS: stage4 CKD
     - sensory nerves > motor
     - lower extremities > upper
     - distal parts of the extremities > proximal
  3. Autonomic
- Myopathy
- Subtle clinical manifestations of uremic neuromuscular disease usually become evident at stage 3 CKD

GASTROINTESTINAL AND NUTRITIONAL ABNORMALITIES

- Uremic fetor:
  - a urine-like odor on the breath
  - Breakdown of urea to ammonia in saliva
  - often associated with an unpleasant metallic taste (dysgeusia). Gastritis, peptic disease, and mucosal ulcerations at any level of the GI tract
- prone to constipation: worsened by of calcium and iron supplements.
- Retention of uremic toxins: anorexia, nausea, vomiting
- Protein restriction may put patient at risk for malnutrition that is indication for RRT

ENDOCRINE-METABOLIC DISTURBANCES

- Glucose metabolism:

1. Slower decline in blood glucose after a glucose load.
2. FBS: normal or only slightly elevated
3. slight to moderate elevation in insulin levels both in the fasting and postprandial states.

- Progressive reduction in insulin requirement
- Oral anti-hyperglycemic agent : dose reduction or avoidance
- SGLT2inh(empagliflosin):reduction in kidney function decline and cardiovascular event

DERMATOLOGIC ABNORMALITIES

- Pigmentation: deposition of retained pigmented metabolites, or *urochromes* in CKD or ESRD
- Pruritus: often tenacious even after dialysis
  - R/o scabies, and hyperphosphatemia
  - Local moisturizers
  - mild topical glucocorticoids
  - oral antihistamines
  - ultraviolet radiation

MANAGEMENT OF PATIENTS WITH CKD

- History(PMH,FH,DH,GYN) and P/E : often subtle(BP , organ damage, fundoscopy in DM , edema,..)

- Laboratory investigation : Search for underlying disease (Viral marker , vasculitis marker , pro electrophoresis),CKD consequences(iron study , ca , cr vitD,PTH,VitB12,folate,urine pr…)

- Imaging studies : sono (presence of two kidneys , size, symmetry , mass , obstruction , length), CT, MRI, Nuclear medicine , VCUG(reflux nephropathy),radiographic contrast(precaution)

Kidney biopsy : not advised in CKD(likelihood of bleeding , scarring, time of specific therapy has passed)contraindication include HTN , active UTI , bleeding diathesis , severe obesity
If indicated : desmopressin , dialysis prior to bx

SLOWING THE PROGRESSION

- Control of Blood Glucose
- Control of intraglomerular hypertension
- Antihypertensive therapy
- Antihyperlipidemic therapy

CKD TREATMENT

- Superimpose processes: ECFV depletion , uncontrolled HTN ,UTI , nephrotoxic, obstructive urophathy , flare of original disease
- Slowing the progression of CKD: decline glomerular HTN and Proteinuria with ACE inh or ARB,NDHP CCB(diltiazem , verapamil) ،SGLT2 inh . Target BP:130/80
- Other targets for renal protection : Protein restriction Smoking cessation . Treatment of chronic metabolic acidosis with supplemental bicarbonate may slow the progression to end-stage kidney disease. Glycemic control
- Dose adjustment : may not be needed for agents >70% excretion nonrenal . some drugs should be avoided
- RRT : Dialysis , TX
- Patient education , social support