The clinical presentation of renal disease

SUHARDJONO
Clinical symptoms of renal disease are non-specific

Underlying condition may not be suspected from the history alone,

Physical examination may be surprisingly unrevealing.

Routine Lab investigation; Urine, Kidney function (Creatinine/estimated GFR)
The presence of renal disease in a patient may be detected

1. Presentation with a symptom or clinical sign that indicates an underlying renal disorder (Back pain, edema, renal colic, etc)

2. The presence of a systemic disease known to involve the kidneys (DM, Hypertension, SLE, etc)

3. A family history of inherited renal disease (Polycystic disease, etc)

4. The finding of asymptomatic urinary abnormalities, disordered renal function tests, or abnormalities on kidney imaging
Asymptomatic presentation

- Many patients remain asymptomatic, even with advanced renal disease,
- The importance of urine analysis and the estimation of blood urea and serum creatinine in anyone suspected of having renal disease.
- Patients with renal failure may remain asymptomatic despite the loss of up to 80 per cent of excretory function.
- The importance of screening, general check-up
Clinical syndromes

- Asymptomatic urinary abnormalities
  - Asymptomatic proteinuria
  - Microalbuminuria
- Asymptomatic hematuria
- Nephrotic syndrome
- Acute nephritic syndrome (haematoproteinuria syndrome)
- Recurrent haematuria
- Disorders of micturition
  - Frequency, dysuria, polyuria, nocturia, oliguria and anuria
- Acute Kidney Injury
- Chronic Kidney Disease
- Hypo/Hypernatremia
- Hypo/Hyperkalemia
- High Blood Pressure, Hypertension
NEPHROTIC SYNDROME -
definition and clinical characteristics

• Proteinuria (> 3.5 g / 24 h)
• Hypoproteinemia (total protein < 60 g / l, albumin < 25 g / l)
• Dysproteinemia (relative increase in $\alpha_2$- and $\beta$-globulines, hypoalbuminemia, sometimes decrease in $\gamma$-globulin fraction)
• Hyperlipoproteinemia (hypercholesterolemia, sometimes hypertriglyceridemia)
• Edema
• Coagulation abnormalities (hypercoagulability-renal vein thrombosis)
• Endocrine abnormalities
• Infections
• Acute renal failure
A 28 year old soldier with a wonderful eruption of intracutaneous water whose urine, when evaporated over fire, formed itself into a white mass like the soft of an egg when boiled

Domenico Cotugno 1764
Skin blisters due to edema in nephrotic syndrome
Xantelasma in patient with nephrotic syndrome
The approximate frequency of different kidney diseases with nephrotic syndrome according to age
Proteinuria and prognosis in glomerular disease

![Graph showing renal survival over months for different proteiniuria conditions.]

- **Proteinuria never exceeds 5 g/day (n = 33)**
- **Nephrotic syndrome at onset (n = 200)**
- **Proteinuria exceeds 5 g/day during illness, never nephrotic (n = 20)**
ACUTE NEPHRITIC SYNDROME

Clinical syndrome

Sudden onset –

- visible haematuria

- oliguria
- fluid retention
- volume expansion
- hypertension

proteinuria – usually < 3g/24hr

haematuria – red cell casts
### Differentiation between nephrotic syndrome and nephritic syndrome

<table>
<thead>
<tr>
<th>Typical features</th>
<th>Nephrotic</th>
<th>Nephritic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>Insidious</td>
<td>Abrupt</td>
</tr>
<tr>
<td>Edema</td>
<td>++++</td>
<td>++</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>Normal</td>
<td>Raised</td>
</tr>
<tr>
<td>Jugular venous pressure</td>
<td>Normal/low</td>
<td>Raised</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>++++</td>
<td>++</td>
</tr>
<tr>
<td>Hematuria</td>
<td>May/may not occur</td>
<td>++++</td>
</tr>
<tr>
<td>Red-cell casts</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Serum albumin</td>
<td>Low</td>
<td>Normal/slightly reduced</td>
</tr>
</tbody>
</table>
ACUTE NEPHRITIC SYNDROME

Clinical syndrome

Characteristic of post-infectious GN

*Beta-haemolytic streptococcus*

is the commonest causative organism

...but not the only one
‘POST-STREPTOCOCCAL’ GLOMERULONEPHRITIS

Post-infectious glomerulonephritis

CLINICAL
Epidemic
Acute nephritic syndrome

Epidemics are uncommon in the developed world
WHY IS POST-STREPTOCOCCAL GN NOW SO UNCOMMON IN THE DEVELOPED WORLD?

The progress of immunology? X

Antibiotics? X

Public health? YES

Spontaneous changes in streptococcal types? ?
RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS ‘RPGN’

A clinical syndrome ...

Renal failure over days or weeks

Proteinuria – usually < 3g/24hr

Haematuria – red cell casts

Blood pressure – often normal

May have features of vasculitis or other multisystem immune disorder
RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS

A clinical syndrome ...

With a pathological counterpart

Crescentic glomerulonephritis

Only very occasionally are clinical and serological findings sufficient to allow management to proceed without a renal biopsy
CRESCENTIC GLOMERULONEPHRITIS
Acute Kidney Injury

- Definition
  Acute Renal Failure ➔ Acute Kidney Injury
  An abrupt (within 48 hours) reduction in kidney function currently defined as an absolute increase in serum creatinine of more than or equal to 0.3 mg.dL, percentage increase of serum Cr of more than or equal to 50% (1.5 fold from baseline), or reduction in urine output (documented oliguria of less than 0.5 ml/kg per hour for more than six hours).
  Lack of a uniform definition

Mehta, 2008
RIFLE Criteria for Acute Renal Dysfunction

<table>
<thead>
<tr>
<th>Risk</th>
<th>GFR Criteria*</th>
<th>Urine Output Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Increased creatinine x1.5 or GFR decrease &gt; 25%</td>
<td>UO &lt; .5ml/kg/h x 6 hr</td>
</tr>
<tr>
<td>Injury</td>
<td>Increased creatinine x2 or GFR decrease &gt; 50%</td>
<td>UO &lt; .5ml/kg/h x 12 hr</td>
</tr>
<tr>
<td>Failure</td>
<td>Increase creatinine x3 or GFR decrease &gt; 75%</td>
<td>UO &lt; .3ml/kg/h x 24 hr or Anuria x 12 hrs</td>
</tr>
<tr>
<td>Loss</td>
<td>Persistent ARF** = complete loss of renal function &gt; 4 weeks</td>
<td></td>
</tr>
<tr>
<td>ESRD</td>
<td>End Stage Renal Disease</td>
<td></td>
</tr>
</tbody>
</table>
Clinical Classification of AKI

1. Reversible AKI
   Decreased effective renal perfusion
   Extrarenal obstruction to renal flow

2. Self Limited AKI
   Acute Tubular Necrosis
   Acute Interstitial Nephritis
   Intra renal obstruction, drug, uric acid

3. Irreversible AKI
   Cortical Necrosis
   Large vessel occlusion
   Certain nephrotoxin; metyloxyfluorane
   Microvascular occlusion
Principle for Management of AKI

- Preservation and optimization of renal function
  - **GOAL**: identify and correct any reversible factors such as volume depletion and obstruction
    - Restore effective renal perfusion and urine output
- Correction and maintenance of electrolyte, acid base and mineral homeostasis
- Minimize secondary organ damage from consequences of AKI
- Manage effects of decreased renal functions
Chronic Kidney Disease

Definition of Chronic Kidney Disease

1. Kidney damage for 3 months, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, manifest by either: Pathological abnormalities; or

- Markers of kidney damage, including abnormalities in the composition of the blood or urine, or abnormalities in imaging tests

2. GFR <60 mL/min/1.73m² for 3 months, with or without kidney damage.

Abbreviation: GFR, glomerular filtration rate
### Stages of Chronic Kidney Disease

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR (ml/min/1.73 m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney Damage with Normal or ↑ GFR</td>
<td>≥90</td>
</tr>
<tr>
<td>2</td>
<td>Mild ↓ GFR</td>
<td>60-89</td>
</tr>
<tr>
<td>3</td>
<td>Moderate ↓ GFR</td>
<td>30-59</td>
</tr>
<tr>
<td>4</td>
<td>Severe ↓ GFR</td>
<td>15-29</td>
</tr>
<tr>
<td>5</td>
<td>Kidney Failure</td>
<td>&lt;15 or Dialysis</td>
</tr>
</tbody>
</table>
At Risk Population

Stage 5
n=300,000

Stage 4
n=400,000

Stage 3
n=7,600,000

Stage 2
n=5,300,000

Stage 1
n=5,900,000

KDOQI Clinical Practice Guidelines for CKD
AJKD 2002


National Kidney Foundation
Patients With CKD Are More Likely to Die Than Reach Dialysis or Transplantation

Outcome of Patients With CKD Over a 5-Year Period

GFR/CREATININE

Serum Creatinine (mg/dl) vs. GFR (ml/min)

# Estimated GFR

<table>
<thead>
<tr>
<th>TABLE 1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GFR prediction equations</strong></td>
</tr>
</tbody>
</table>

## Cockroft-Gault equation

\[
C_{Cr} = \frac{(140-\text{age}) \times \text{weight}}{72 \times S_{Cr}} \times (0.85 \text{ if female})
\]

## Four-variable (abbreviated) MDRD Study equation

\[
\text{GFR} = 186 \times (S_{Cr})^{-1.154} \times \text{(age)}^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if black})
\]

**Key:** \(C_{Cr}\), creatinine clearance in mL/min; GFR, glomerular filtration rate in mL/min/1.73 m\(^2\); \(S_{Cr}\), serum creatinine in mg/dL; MDRD, modification of diet in renal disease.
Manifestations of the Uremic Syndrome; Neurologic

- **Central**
  - Daytime drowsiness and a tendency to sleep, which progresses to increasing obtundation and, eventually, coma
  - Attentiveness and performance of cognitive tasks <<
  - Imprecise memory
  - Slurred speech
  - Asterixis and myoclonus
  - Seizures
  - Disorientation and confusion

- **Peripheral**
  - Sensorimotor peripheral neuropathy, often with burning dysesthesia
  - Singultus (hiccup)
  - Restless leg syndrome
  - Increased muscle fatigability and muscle cramps
- Cardiovascular
  - Accelerated atherosclerosis
  - Cardiomyopathy
  - Pericarditis

- Pulmonary
  - Atypical pulmonary edema
  - Pneumonitis
  - Fibrinous pleuritis
- Gastrointestinal
  - Anorexia progressing to nausea and vomiting
  - Stomatitis and gingivitis
  - Parotitis
  - Peptic ulcer diathesis
  - Gastritis and duodenitis
  - Enterocolitis
  - Pancreatitis
  - Ascites

- Dermatologic
  - Pruritus
  - Dystrophic calcification
  - Changes in skin pigmentation
Vascular calcification predicts cardiovascular risk

Adragao score ≥ 3 CAD, PAD, VD
RR 3.9 CV mortality; 2.8 CV hospitalization; 2.3 fatal and non-fatal CV events

CAD, coronary artery disease; PAD, peripheral artery disease; VD, vascular disease; RR, relative risk; CV, cardiovascular
Hematologic
- Anemia
- Altered neutrophilic chemotaxis
- Depressed lymphocyte function
- Bleeding diathesis with platelet dysfunction

Ophthalmic
- Conjunctival or corneal calcifications

Endocrinologic
- Secondary hyperparathyroidism
- Carbohydrate intolerance due to insulin resistance
- Type IV hyperlipidemia
- Altered peripheral thyroxine metabolism
- Testicular atrophy
- Ovarian dysfunction with amenorrhea, dysmenorrhea, dysfunctional uterine bleeding, cystic ovarian disease
Differentiation of Acute from Chronic Kidney Disease

- **History**
  - Long-standing history suggests chronic kidney disease
  - Radiographic evidence of osteitis fibrosa cystica, osteomalacia

- **Renal osteodystrophy**
  - Chronic kidney disease of any cause

- **Renal size (length)**
  - Small kidneys (e.g., <9 cm)
  - Acute kidney disease of any cause

- **Normal or enlarged kidney disease (9–12 cm)**
  - Nephropathy DM, Amyloidosis, HIVN
Chronic Kidney Disease: A Public Health Problem That Needs a Public Health Action Plan

Anton C. Schoolwerth, MD, MSHA, Michael M. Engelgau, MD, Thomas H. Hostetter, MD, Kathy H. Rufo, MPH, Dolph Chianchiano, JD, MPA, William M. McClellan, MD, MPH, David G. Warnock, MD, Frank Vinicor, MD
Table 3. Chronic Kidney Disease: A Clinical Action Plan

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR (mL/min/1.73m²)</th>
<th>Action*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>At increased risk</strong></td>
<td>≥90 (with CKD risk factors)</td>
<td>Screening CKD risk reduction</td>
</tr>
<tr>
<td>1.</td>
<td>Kidney damage with normal or ↑ GFR</td>
<td>≥90</td>
<td>Diagnosis and treatment Treatment of comorbid conditions, slowing progression, CVD risk reduction</td>
</tr>
<tr>
<td>2.</td>
<td>Kidney damage with mild ↓ GFR</td>
<td>60-89</td>
<td>Estimating progression</td>
</tr>
<tr>
<td>3.</td>
<td>Moderate ↓ GFR</td>
<td>30-59</td>
<td>Evaluating and treating complications</td>
</tr>
<tr>
<td>4.</td>
<td>Severe ↓ GFR</td>
<td>15-29</td>
<td>Preparation for kidney replacement therapy</td>
</tr>
<tr>
<td>5.</td>
<td>Kidney Failure</td>
<td>&lt;15 (or dialysis)</td>
<td>Replacement (if uremia present)</td>
</tr>
</tbody>
</table>
MANIFESTATIONS OF HYPOKALEMIA

- proportionate to the degree and duration of hypokalemia
- Symptoms generally do not become manifest until the serum potassium is below 3.0 meq/L, unless the serum potassium falls rapidly
- usually resolve with correction of the hypokalemia.
Severe muscle weakness or paralysis
- begins with the lower extremities, progresses to the trunk and upper extremities, and can worsen to the point of paralysis
- Respiratory muscle weakness
- gastrointestinal muscles, resulting in ileus

- Cramps, paresthesias, tetany, muscle tenderness and atrophy

- Cardiac arrhythmias and ECG abnormalities

- Rhabdomyolysis

- Renal abnormalities
  - nocturia, polyuria and polydipsia
  - hypokalemic nephropathy
High potassium content foods

Highest content (>25 meq/100 g)
- Dried figs
- Molasses
- Seaweed

Very high content (>12.5 meq/100 g)
- Dried fruits (dates, prunes)
- Nuts
- Avocados
- Bran cereals
- Wheat germ
- Lima beans

An increase in the amplitude of U waves, which occur at the end of the T wave, are characteristic of hypokalemia.
MANIFESTATIONS OF HYPERKALEMIA

- Severe muscle weakness or paralysis
- Muscle weakness usually begins with the lower extremities and progresses to the trunk and upper extremities
- Cardiac conduction abnormalities
  - A tall peaked T wave with shortened QT interval
  - Ventricular fibrillation or standstill are the most severe
  - Right bundle branch block, left bundle branch block, bifascicular block, and advanced atrioventricular block
Pseudohyperkalemia, which is most often due to hemolysis of the blood specimen, is the most common cause of a reported elevation in serum potassium and must be excluded. It does not reflect true hyperkalemia and does not produce ECG changes.

Peaked T waves
Prolonged PR and QRS intervals, and small P waves
Loss of P wave, further prolongation of QRS interval ("sine wave" pattern), and conduction delay that can manifest as bundle branch or AV nodal block.
Ventricular fibrillation or asystole can result.
Hyponatremia or hypernatremia

The symptoms:
primarily neurologic
related both to the severity
rapidity of onset of the change in the plasma sodium concentration
may have complaints; related to concurrent volume depletion, and to possible underlying neurologic diseases that predispose to the electrolyte abnormality. These include:
(1) **impaired mental status of any cause**, leading to lack of expression of thirst, which is normally the major protective mechanism against the development of hypernatremia; and
(2) **a wide variety of neurologic disorders** that can lead sequentially to the inappropriate secretion of **antidiuretic hormone**, water retention, and hyponatremia.
HYPONATREMIA

- primarily occur with acute and marked reductions in the plasma sodium concentration
- reflect neurologic dysfunction induced by cerebral edema
- possibly adaptive responses of brain cells to osmotic swelling
  - the associated fall in plasma osmolality creates an osmolar gradient that favors water movement into the cells, leading in particular to brain edema
Clinical manifestations of acute hyponatremia

- The severity of symptoms generally reflects with severity of cerebral overhydration
- Nausea and malaise are the earliest findings, and may be seen when the plasma sodium concentration falls below 125 to 130 meq/L.
- followed by headache, lethargy, and obtundation and eventually seizures, coma, and respiratory arrest (Na below 115 to 120 meq/L)
- Noncardiogenic pulmonary edema
HYPERNATREMIA

- is basically a mirror image of hyponatremia
- The rise in the plasma sodium concentration and osmolality causes acute water movement out of the brain; this decrease in brain volume can cause rupture of the cerebral veins, leading to focal intracerebral and subarachnoid hemorrhages and possible irreversible neurologic damage
The clinical manifestations

- Begin with lethargy, weakness, and irritability, and can progress to twitching, seizures, and coma.
- Severe symptoms usually require an acute elevation in the plasma sodium concentration to above 158 meq/L. Values above 180 meq/L are associated with a high mortality rate, particularly in adults.
- Although rarely reported, osmotic demyelination can also occur in association with hypernatremia, primarily with extremely plasma sodium concentrations.