INTRODUCTION TO RENAL DISEASES
• Introduction & Review of Renal Function
• Evaluation of renal diseases
• Urine examination
• Hematuria
• Proteinuria
FUNCTIONS OF KIDNEY

• Kidneys maintain the internal homeostasis for cellular metabolism and functions.

• The functioning unit of Kidney is the nephron - made up of glomerulus and tubules.

• Each kidney contains about one million nephrons.
FUNCTIONS OF KIDNEY

• Blood undergoes glomerular filtration followed by tubular secretion and re absorption

• Final product of excretion is Urine.

• Kidneys receive 20% of the cardiac output
# FUNCTIONS OF KIDNEY

**Excretory functions**
- Azotemic waste products
- Water balance
- Electrolyte balance
- Acid Base balance

**Endocrine functions**
- Erythropoetin
- Active Vitamin D
- Regulation Of Blood pressure
  - Renin
  - Prostaglandins
  - Kinins
<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>Pathological Correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Glomerular Diseases</strong></td>
<td><strong>Tubulointerstitial Disease</strong></td>
</tr>
<tr>
<td>Hematuria</td>
<td>Polyuria</td>
</tr>
<tr>
<td>Oliguria, anuria</td>
<td>Salt wasting</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>Acidosis</td>
</tr>
<tr>
<td>Oedema</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
</tr>
<tr>
<td><strong>Chronic Kidney Disease (CKD)</strong></td>
<td><strong>Abnormalities of Micturition</strong></td>
</tr>
<tr>
<td>Growth retardation</td>
<td>Poor urinary stream</td>
</tr>
<tr>
<td>Anemia</td>
<td>Enuresis</td>
</tr>
<tr>
<td>Bone Deformities</td>
<td>Dribbling</td>
</tr>
</tbody>
</table>
SYNDROMIC APPROACH TO RENAL DISEASES

• Acute Nephritic Syndrome
• Nephrotic Syndrome
• Urinary Tract Infection
• Acute Kidney Injury
• Chronic Kidney Disease
• Hypertension
• Obstructive Nephropathy
• Nephrolithiasis
• Tumors
• Voiding Dysfunction
• Asymptomatic Urinary Abnormalities
RENAL DISEASES : DIFFERENT AGE GROUPS

Newborns:
Congenital anomalies of Kidneys and urinary tract (CAKUT)

Infancy to 3 years:
UTI, HUS, Nephrotic Syndrome, RTA, Fanconi syndrome, Wilms tumour

3-6 yrs:
Nephrotic Syndrome (MCNS), UTI, AGN, Rickets

6-14 YRS:
PSGN, CKD, Hypertension, Nephrotic Syndrome, UTI, SLE
INVESTIGATIONS IN RENAL DISEASE

**Urinalysis** including Microscopy

**Biochemical Evaluation**-

- Blood Urea (Normal values - 20-35 mg/dl)
- Serum Creatinine:
  - Normal values - 0.2-0.5 mgm/dl below 6 years
  - 0.4-0.8 mgm/dl above 6 years
- Serum Sodium
- Serum Potassium
INVESTIGATIONS IN RENAL DISEASE

Disease specific Tests- Serum Cholesterol, Serum Albumin, Calcium, Phosphorus, Alkaline Phosphatase

Tubular diseases:
Serum HCO3, blood pH and Urine pH and Osmolality

Serology (special situations):
ASO, C3 Complement, ANA , Anti dS DNA
URINALYSIS

Urine is the liquid biopsy of the kidneys

Fresh is Best!

First morning voiding (most concentrated)
Clean catch urine
Analyzed within 1 hour of collection

Urine Sp. Gravity: 1.000-1.030

Urine pH: 4.5-8.0
URINALYSIS

Protein

• Boiling test-
  10-15 ml urine in a test tube. Upper third is boiled-
  if turbidity add 3 drops of conc. Acetic acid.
  Turbidity if persists protein positive

• Semi quantitative method
  10% Sulfosalicylic Acid added to urine produces
  turbidity if protein positive
  Dipstick - Semi quantitative , mainly Albumin
Reducing substances
Benedict’s test for reducing substances;
Dipstick Glucose Oxidase test -specific for glucose
URINALYSIS- MICROSCOPY

Centrifuge 10 ml of urine for 5 minutes
Decant the supernatant
Re-suspend the sediment in 0.5 ml of urine
Place on a slide with a cover slip
  Count the number of RBCs in 20 fields
  Report the average-
    Positive test: 5 or more RBC / HPF

Count WBCs

Look for Casts & Crystals

Bacteria, Yeast, Parasites & Artifacts
GLOMERULAR FILTRATION RATE

Creatinine clearance:
24 hour urine is collected. Estimate Urinary creatinine(U) and serum creatinine(P) Assess urine volume (V).

Creatinine clearance = $\frac{UV}{P}$

Normal 80-120ml/mt/1.73 sq.m BSA
GLOMERULAR FILTRATION RATE

Calculated GFR (e GFR) by Schwartz Formula

\[ eGFR = \frac{K \times L}{S.Cr} \]

K (Schwartz constant)- 0.55 in children
L- height in cm, S.Cr –Serum creat in mgm/dl
Ultrasound- Base line investigation in renal diseases

Micturating cystourethrogram

Nuclear Imaging

Plain X-Ray Abdomen

IVU

MRI scan
MICROSCOPIC EXAM- CASTS

- Hyaline cast
- WBC cast
- Granular Cast
- RBC cast
- Waxy cast
- Fatty Cast
NOT ALL URINE THAT IS RED IS HEMATURIA!

- As little as 1 mL of blood per liter of urine cause a visible color change
- Pigments also color the urine

**RBC in the urine**

**Macroscopic hematuria** (visible)

Urine is pink, red, or cola colored

**Microscopic hematuria:**

Urine clear, RBCs seen only under microscope
RED URINE-HEME POSITIVE- DIPSTICK POSITIVE

Hematuria
Hemoglobinuria
Myoglobinuria

Centrifuge urine and serum
Look at the Appearance

Urine Clear, Serum Clear
Urine Microscopy 🕵️ RBC>5/hpf
Hematuria

Urine pink, Serum pink
Urine Microscopy ⇒ No RBC
Add ammonium sulfate to urine-clear
Hemoglobinuria

Add ammonium sulfate to urine - color persists
MYOGLOBINURIA
RED OR BROWN URINE WITH NEGATIVE DIPSTICK

A dye or pigment other than hemoglobin or myoglobin

Pink, red, brown or burgundy:
- Beets
- Blackberries
- Nitrofurantoin
- Rifampin
- Chloroquine
- Nitrofurantoin
- Deferoxamine
- Metronidazole
- Salicylates
- Ibuprofen
- Urates

Dark brown or black:
- Alkaptonuria
- Homogentisic aciduria
- Methemoglobinuria
- Tyrosinosis
- Melanin
- Porphyrin
HEMATURIA

More than 5 RBC / microlitre of centrifuged urine

Gross / microscopic hematuria

Causes

• Upper tract diseases
  Glomerular- cola coloured urine
  oedema, hypertension, oliguria
  Extraglomerular- bright red urine

• Lower Tract Diseases bright red with clots
  Cystitis
  Urethritis
UPPER TRACT VS LOWER TRACT HEMATURIA

UPPER TRACT BLEEDING
- Brown or cola urine
- Uniform color urine, no clots
- RBC casts, deformed RBC
- Leukocyte or ep cell casts (convoluted/CT)
- Proteinuria > 100 mg/dl

LOWER TRACT BLEEDING
- Non-uniform, clots present
- Terminal gross hematuria
- Irritative Voiding Symptoms
- Strangury
- RBC morphology - Eumorphic
- Proteinuria < 100 mg/dl

3 tube test
1st - Urethra
2nd - Anywhere in the tract
3rd - Bladder (trigone)
## CAUSES OF HEMATURIA

### GLOMERULAR DISEASES

**ISOLATED RENAL**
- IgA NEPHROPATHY
- Alport syndrome
- Thin GBM DISEASE
- PSGN
- Membranous nephropathy
- MPGN
- FSGS
- Anti GBM Disease
- RPGN

**MULTI SYSTEM DISEASE**
- SLE
- HSP
- HUS
- Vasculitis
- Goodpasture’s Disease
- HIV
- Sickle cell
### Extra Glomerular Causes

#### Tubulointerstitial Diseases
- Pyelonephritis
- Acute Tubular Necrosis
- Papillary Necrosis
- Nephrocalcinosis
- Interstitial nephritis
- Toxic nephropathy
- Cortical necrosis
- Crystalluria
- Sickle Cell disease
- Idiopathic hypercalciuria

#### Anatomic
- PCKD
- MCDK
- Hydronephrosis
- Tumours
- Trauma

#### Vascular
- Arterial thrombosis
- Venous thrombosis
- Hemangioma
- Aneurysm

#### Hematological
- Sickle cell disease
- Coagular abnormalities
- Thrombocytopenia
EVALUATION OF RENAL DISEASES
COMMON MANIFESTATIONS

- Oedema
- Hematuria
- Oliguria (Urine volume less than 1hr /ml/kg)
- Growth Failure
- Anuria
- Dysuria
- Anemia
- Rickets
- Hypertension
- Ureteric colic
- Renal mass
- Flank pain
- Abnormalities of micturition
HISTORY

PSGN
Recent URI, skin infection
Headache, visual problems, epistaxis
Features s/o heart failure

HUS
Diarrhoea, GI infection - Rash, arthritis
HSP/Collagen vascular Disease
Good pasture’s Disease
Hemoptysis-
Bleeding Diathesis

UTI
Dysuria, Flank pain
Renal colic - calculus
Trauma, Sexual abuse
Previous similar episodes

Family history
Hematuria
Renal problems
Hearing problems (Alport Syndrome)
Renal stones
EVALUATION - PHYSICAL EXAMINATION

Assess for
- Growth failure
- Bony deformities.
- Hypertension
- Pallor
- Edema
- Chromosomal abnormality
  - Low set ears
  - Ear tags
  - Supernumerary nipples
  - Congenital anomalies e.g.. Ano rectal malformations
  - Prune belly syndrome
  - Single umbilical artery
  - VATER Association

Skin
- Purpura, neurocutaneous markers.

Blood Pressure

CVS
- Gallop Rhythm, Murmur
- Lung for Rales

Spinal & Sacral anomalies.
- Lower limb deformities or wasting
- Anal tone

Always look for
- Distended bladder
- Ballotable kidneys
- Ext Genitalia
INVESTIGATIONS

Urinalysis

• Hemogram with ESR
• Blood Urea , Serum Creatinine
• Glomerular Hematuria - C3, ASO/ anti DNAse B, ANA/ANCA, creatinine clearance
• Extra glomerular Hematuria - Urine C&S, Urine spot calcium creatinine ratio(>0.2), 24 hr urine oxalate, calcium, uric acid and creatinine
• Urinalysis of 1st degree relatives
IMAGING

• USG abdomen
  Hydronephrosis-renal scan
  Urolithiasis - 24 hr urine for Calcium, Creatinine, Oxalate, Uric acid
• MCU: Indication- UTI, renal scar, hydro ureter, pyelocaliectasis
• Radionucleotide scan - less radiation, sensitive
  Radioactive technetium- DMSA, DTPA, MAG-3
  DMSA- morphology, scarring of kidney
  DTPA- freely filtered, perfusion & function
  Mag 3- structure & function
CAUSES OF PERSISTENT MICROSCOPIC HEMATURIA

- IgA nephropathy
- Alport Syndrome
- Benign familial Hematuria
- Thin Glomerular Basement Membrane Disease
- Idiopathic hyper calciuria

**Persistent asymptomatic isolated microscopic hematuria**

Keep under Follow up: Urinalysis every 3 months

Annual Renal Function Tests

If persists more than one year, further detailed evaluation
RENAL BIOPSY - INDICATIONS

Persistent microscopic hematuria
Recurrent gross Hematuria
Hematuria with hypertension
Hematuria with Significant Proteinuria
Renal dysfunction
PROTEINURIA

Glomerular capillary wall- Effective barrier
Normal 24 hour Protein in urine - 150 mg/day
Proteinuria is more than 100mg/sq.m BSA/day of protein in urine

Dipstick – semi quantitative Assessment

No change   Negative
Trace      10-30 mg/dl
1+         30-100 mg/dl
2+         100 -300 mg/dl
3+         300-1000 mg/dl
4+         more than 1000mg/dl (Heavy or Nephrotic Proteinuria)
QUANTITATIVE ASSESSMENT

24 hr urine protein – Accurate but difficult in small child
Normal <150mg/day (<4 mg/m2/hr)
Nephrotic Range >40 mg/m2/hr

Urine spot protein- creatinine ratio in first morning void
Normal Ratio Below 0.2(mg/mg)
Significant Proteinuria: 0.2-2 in >2 yrs
(NonNephrotic)
Nephrotic range proteinuria: more than 2
PROTEINURIA

False negative

- Highly concentrated urine
- Hematuria
- pH > 7.0
- Antiseptic contamination

Transient proteinuria

- Fever
- Exercise
- Dehydration
- Stress
- Seizures
ORTHOSTATIC/POSTURAL PROTEINURIA

Commonest cause of persistent proteinuria
Asymptomatic
No hematuria
No hypertension
No edema
Normal renal function
Benign Condition
Pathogenesis not clear
Follow up till proteinuria abates
DIAGNOSIS OF ORTHOSTATIC/POSTURAL PROTEINURIA

• Void before going to bed
• Collect 1st morning urine sample
• Dipstick –ve or trace for protein & Urine P/C <0.2 for 3 consecutive days
• No or minimal proteinuria in sample collected after overnight recumbence
• Ambulant sample - Significant proteinuria up to 1g/24 hrs
SIGNIFICANT PERSISTENT PROTEINURIA - CAUSES

Glomerular proteinuria-
Heavy proteinuria especially albumin or any degree proteinuria with edema, hypertension, renal dysfunction. Glomerular diseases damage glomerular basement membrane

• Selective proteinuria—chiefly albumin - Minimal change disease
• Nonselective proteinuria - Significant lesion Nephrotic syndrome

Eg. FSGS, Reflux Nephropathy, IgA Nephropathy
SIGNIFICANT PERSISTENT PROTEINURIA - CAUSES

Tubular proteinuria- Mild to moderate proteinuria
  • Renal tubular disease alter tubular function
  • Low MW proteins usually reabsorbed in proximal tubules.
  • Glomerular function normal
    Eg. Pyelonephritis, Interstitial Nephritis, Renal hypoplasia, Fanconi syndrome.
GLOMERULAR CAUSES

Isolated proteinuria
- FSGS
- MPGN
- Membranous nephropathy
- Diabetic nephropathy
- Obesity
- Sickle cell Nephropathy

Proteinuria and hematuria
- A/c PSGN
- IgA nephropathy
- Alports
- HSP
- Lupus nephritis
DIAGNOSTIC APPROACH

• Quantify protein in urine
• Assess GFR
• Ultrasound KUB
• Serum albumin
• Serum Cholesterol
• C3 complement
• Renal biopsy if indicated
THANK YOU