RENAL FAILURE: OLIGURIA, ANURIA: An Overview

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State some major functions of the kidneys?

- Regulation of Fluid Balance,
- Regulation of Electrolyte Balance,
- Regulation of Acid-Base Balance,
- Excretion of products of Protein & Nucleic Acid metabolism: – Urea, Creatinine, Creatine, Uric Acid, Sulfate, Phosphate, etc.
- Endocrine Functions:
  - Kidneys produce a number of hormones, and are under the control of other hormones;

How can the functional state of the kidneys be assessed?

- To answer this question check your handout on “Renal Functions” for details

What do you understand by Renal Failure?

- Renal failure is the cessation of kidney function;
- Renal Failure can be:
  - Acute or
  - Chronic;
- Acute Renal Failure (**ARF**) is when the kidneys suddenly fail to carryout major functions,
  - It can occur over a period of hours or days;
- Chronic Renal Failure (**CRF**) develops over months or years and may lead to End Stage Renal Failure (**ESRF**);
- CRF usually cause irreversible damage to the kidneys;

- **ARF** is reversible and normal Renal Function can be regained;
- ARF can arise from a variety of problems affecting the kidneys and/or their blood circulation;
- ARF usually presents as a sudden deterioration of Renal function indicated by rapidly rising:
  - Serum urea concentration, and
  - Serum creatinine concentration;
- Severely ill patients may develop ARF thus monitoring of kidney function is important in some groups of patients;

What are the different phases of ARF?

- Oliguric phases;
- Diuretic Phase;
- Recovery Phase;

What are the Oliguric Phases?

- **Oliguric phase (Oliguria)**:
  - Urine output of patient falls to less than 400ml in 24hrs,
- **Non-Oliguric phase (Non-Oliguria)**:
  - Urine output of the patient is normal,
  - Glomerular Filtration rate is low,
  - Patient has Tubular Dysfunction ,
- **Anuric phase (Anuria)**:
  - Patients do not pass any urine,
- Within the first 24 hours of ARF: Serum and Urine tests for Renal Function might not reveal any abnormality;

What are some of the characteristics of Oliguric phase?

- **Oliguria is mainly due to a fall in the GFR**;
- In **Oliguric phase**:
- Urine Osmolality may be similar to Plasma, because:
  - Level of Na^+ ions in urine is relatively high,
  - Composition of the small amount of Glomerular Filtrate is slightly altered by the damaged Tubules;
- [Na^+] in Plasma may be low because of combination of factors:
  - Intake of water in excess of amount able to be excreted,
  - Increase in metabolic water from increased tissue catabolism,
  - A shift of Na^+ ions from ECF to (ICF);

- Plasma [K^+] may be increased because of:
  - Impaired Renal output, and
  - Increased tissue catabolism;
- Patient may develop metabolic acidosis because of failure to excrete H^+ ions and the increased formation of H^+ ions from tissue catabolism;
- Shift of K^+ ions out of cells accompanies the metabolic acidosis;

- Retention of:
  - Urea,
  - Creatinine,
  - Phosphate,
  - Sulfate and
  - Other waste products occurs
- Rate of increase of urea in plasma depends on the rate of tissue catabolism, which depends on the cause of the ARF;

How can the low urinary output in ARF be differentiated from Hypovolaemia?

- No specific lab tests are available to fully differentiate low urinary output of patient with suspected ARF from that due to severe circulatory impairment with reduced blood volume (Hypovolaemia);
- Careful assessment of fluid status of the patient, possibly including measurement of the central venous pressure, are required;
- **Table 1:** Lab results of Investigation of patient with low urine output

Table 1:

Lab results of Investigation of patient with low urine output

Investigation	**Simple Hypovolaemia**	**Acute Renal Failure**
Urine Osmolality	> 500mmol	< 400mmol
Urine [urea]:Plasma [urea]	> 10mmol	< 5
Urine [Na^+]	< 20mmol	> 40mmol

What lab parameters are used to monitor Oliguric phase?

- **For monitoring** patients in Oliguric phase of ARF:
- Very important parameters that must be determined at least once daily:
  - Plasma Creatinine,
  - Plasma Urea, and
  - [K^+] are particularly important,

- For Fluid and Electrolyte replacement requirement, the following must be regularly assessed:
  - Volume of urine and its Electrolyte composition;
  - Volume and composition of any other measurable sources of fluid loss;

DIURETIC PHASE

- With the onset of the Diuretic phase:
  - Urine volume increases,
  - Clearance of Urea, Creatinine and other waste products may not improve to the same extent,
  - Plasma Urea and Creatinine levels may continue to rise, at least, at the start of the Diuretic phase;

  - Loss of Electrolytes may occur in urine; this should be monitored and replaced as appropriate;

- [K^+] in plasma may fall as diuretic phase continues, because of:
  - Shift of K^+ ions back into the cells, and
  - Increased losses in urine due to impaired regulation of K^+ ions by the damaged tubules;
- Loss of Na^+ ions may also occur because of failure of regulation by the damaged renal tubules;

- During **Diuretic phase**, measure plasma:
  - Creatinine,
  - Urea,
  - Na^+ and K^+ ions at least once daily,
- Monitor the urine flow rate and electrolyte output;

How is ARF classified?

- **Pre-Renal**:
  - When blood supply to the kidneys is affected;
  - May be due to vascular obstruction or to reduced perfusion;
- **Renal**:
  - When the kidneys are damaged;
  - May be due to a variety of diseases,
  - Renal damage may be due to prolonged Pre or Post-renal problems;
- **Post-Renal**:
  - Problems occurring after the Kidneys,
  - Urinary drainage of kidneys impaired by obstruction,
  - May be due to Renal Stones, Carcinoma of Cervix, Prostate, or Bladder;

State some factors that can cause Pre-renal ARF

- Factors associated with reduced effective ECF Volume, may include:
- Decreased Plasma Volume because of:
  - Blood loss,
  - Burns,
  - Prolonged Vomiting or Diarrhea,
- Diminished Cardiac Output;
- Local factors such as an Occlusion of Renal Artery;

- Pre-renal factors may lead to:
  - Decreased Renal Perfusion, and
  - Reduction in Glomerular Filtration Rate (GFR);

- Both Arginine Vasopressin (AVP) and Aldosterone are secreted maximally and a small volume of concentrated urine is produced;

State some Biochemical findings in patient with Pre-renal ARF?

- Serum Urea and Creatinine are increased:
  - Urea is increased proportionally more than Creatinine because of its reabsorption by Tubular cells at low urine flow-rates;
- Hyperkalemia due to decreased GFR and Acidosis;
- Metabolic Acidosis due to inability of Kidneys to excrete H^+ ions;
- High urine Osmolality;

State some factors that can cause Post-renal ARF?

- Post-renal factors may cause decreased Renal function, because:
  - Effective Filtration pressure of Glomeruli is reduced due to back-pressure caused by obstruction;
- Obstruction may be caused by:
  - Renal Stones,
  - Carcinoma of Cervix,
  - Prostate or
  - Occasionally Bladder;

- Failure to correct the Pre-renal or Post-renal factors can lead to Intrinsic Renal damage (Acute Tubular Necrosis);

- Patients in early stages of Acute Tubular Necrosis may have only a modestly increased Serum Urea and Creatinine, which then rises rapidly over a period of days, in contrast to the slow increase over months and years seen in Chronic Renal Failure;

What are the biochemical features that distinguish pre-renal ARF from Intrinsic Renal damage?

Biochemical features in the differential diagnosis of Oliguric patient

Biochemical features	**Pre-Renal Failure**	**Intrinsic Renal Damage**
Urine sodium	< 20 mmol/L	> 40 mmol/L
Urine [urea] : Serum [urea]	> 10:1	< 3:1
Urine/Plasma Osmolality	> 1.5:1	< 1.1:1

BICARBONATE BUFFER SYSTEM

- Bicarbonate buffer is the major buffer in blood;
- It is regulated by Carbonic Anhydrase;
- The expression for the Bicarbonate buffer is:

Carbonic Anhydrase

$$CO_2 + H_2O \leftarrow\!=\!=\!=\!=\!=\!=\rightarrow H_2CO_3 \leftarrow\!=\!=\!=\!=\!=\rightarrow H^+ + HCO_3^-$$

Equation for calculating the pH of Bicarbonate buffer is shown below;

The equation shows that the pH (H^+ ion conc.) in blood varies as the Bicarbonate ion conc. ($[HCO_3^-]$) and Partial Pressure of CO_2 (PCO_2) changes;

$$\mathbf{pH = pKa + \log_{10} \frac{[HCO_3^-]}{PCO_2}}$$

What are the factors that affect the Bicarbonate buffer?

- Factors that affect Bicarbonate buffer:
- Those that increases [H^+] ions; i.e., decrease pH.
  - Adding H^+ ions,
  - Removing HCO_3^- ion, or
  - Increasing PCO_2
- Those that decreases [H^+] ions; i.e., increase pH.
  - Removing H^+ ions,
  - Adding HCO_3^- or
  - Lowering PCO_2

What is “Metabolic” Acid – Base disorders?

- **“Metabolic” Acid – Base** disorders are those that directly affect the concentration of Bicarbonate ions ([HCO_3^-]) in blood plasma;
- Examples:
  - Reduction of **[HCO_3^-]** in Extracellular Fluid, or
  - Build up of **H^+ ions** in blood caused by accumulation of Lactic acid or Ketone bodies (Acetoacetic acid, Beta-Hydroxybutyric acid) or any other acid,
- [HCO_3^-] ions in blood is regulated by the Kidneys;

What is "Respiratory" Acid – Base disorders?

- "**Respiratory" Acid – Base** disorders are those that directly affect the Partial Pressure of CO_2 (PCO_2) in blood plasma;
- Example:
  - Impaired Respiratory function causes build up of CO_2 in blood plasma,
  - Hyperventilation causes decrease of PCO_2 in plasma;
- Partial Pressure of CO_2 (PCO_2) in blood plasma is regulated by the Lungs;

State the Primary disorders in Acid – Base disorders?

- **Metabolic Acidosis**:
  - Primary disorder is a decrease in [HCO_3^-];
- **Metabolic Alkalosis:**
  - Primary disorder is an increased [HCO_3^-]
- **Respiratory Acidosis**:
  - Primary disorder is an increased PCO_2
- **Respiratory Alkalosis:**
  - Primary disorder is a decreased PCO_2

What are the compensatory responses for Primary Acid – Base disorders?

Predicted Compensatory response in $[HCO_3^-]$ or PCO_2 when $[H^+]$ changes as a result of Primary Acid – Base disorders are show below

PRIMARY DISORDER	COMPENSATORY RESPONES
↑ PCO_2 (Respiratory acidosis)	↑ **HCO_3^-**
↓ PCO_2 (Respiratory alkalosis)	↓ **HCO_3^-**
↓ HCO_3^- (Metabolic acidosis)	↓ **PCO_2**
↑ HCO_3^- (Metabolic alkalosis)	↑ **PCO_2**

Kidneys & Lungs are involved in compensatory mechanism for regulation of Bicarbonate buffer and maintenance of Acid-Base Balance in blood; (See the equations below)

$$\mathbf{pH} = \mathbf{pKa} + \log_{10} \frac{[\mathbf{HCO_3^-}]}{\mathbf{PCO_2}}$$

$$\mathbf{pH} = \mathbf{pKa} + \log_{10} \frac{\mathbf{Kidneys}}{\mathbf{Lungs}}$$

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