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 carry out 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>
<thead>
<tr>
<th>Investigation</th>
<th>Simple Hypovolaemia</th>
<th>Acute Renal Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine Osmolality</td>
<td>&gt; 500mmol</td>
<td>&lt; 400mmol</td>
</tr>
<tr>
<td>Urine [urea]:Plasma [urea]</td>
<td>&gt; 10mmol</td>
<td>&lt; 5</td>
</tr>
<tr>
<td>Urine [Na⁺]</td>
<td>&lt; 20mmol</td>
<td>&gt; 40mmol</td>
</tr>
</tbody>
</table>
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 $\text{H}^+$ 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

<table>
<thead>
<tr>
<th>Biochemical features</th>
<th>Pre-Renal Failure</th>
<th>Intrinsic Renal Damage</th>
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<tbody>
<tr>
<td>Urine sodium</td>
<td>&lt; 20 mmol/L</td>
<td>&gt; 40 mmol/L</td>
</tr>
<tr>
<td>Urine [urea] : Serum [urea]</td>
<td>&gt; 10:1</td>
<td>&lt; 3:1</td>
</tr>
<tr>
<td>Urine/Plasma Osmolality</td>
<td>&gt; 1.5:1</td>
<td>&lt; 1.1:1</td>
</tr>
</tbody>
</table>
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

\[ \text{CO}_2 + \text{H}_2\text{O} \rightleftharpoons \text{H}_2\text{CO}_3 \rightleftharpoons \text{H}^+ + \text{HCO}_3^- \]
Equation for calculating the pH of Bicarbonate buffer is shown below;

The equation shows that the pH (H\textsuperscript{+} ion conc.) in blood varies as the Bicarbonate ion conc. ([HCO\textsubscript{3}\textsuperscript{-}]) and Partial Pressure of CO\textsubscript{2} (PCO\textsubscript{2}) changes;

\[
pH = pK_a + \log_{10} \left( \frac{[HCO_3^-]}{PCO_2} \right)
\]
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 ([HCO₃⁻]) in blood plasma;

• Examples:
  • Reduction of [HCO₃⁻] 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,
  • [HCO₃⁻] 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 $[\text{HCO}_3^-]$;

• Metabolic Alkalosis:
  • Primary disorder is an increased $[\text{HCO}_3^-]$;

• 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 [HCO₃⁻] or PCO₂ when [H⁺] changes as a result of Primary Acid – Base disorders are show below

<table>
<thead>
<tr>
<th>PRIMARY DISORDER</th>
<th>COMPENSATORY RESPONSES</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑ PCO₂ (Respiratory acidosis)</td>
<td>↑ HCO₃⁻</td>
</tr>
<tr>
<td>↓ PCO₂ (Respiratory alkalosis)</td>
<td>↓ HCO₃⁻</td>
</tr>
<tr>
<td>↓ HCO₃⁻ (Metabolic acidosis)</td>
<td>↓ PCO₂</td>
</tr>
<tr>
<td>↑ HCO₃⁻ (Metabolic alkalosis)</td>
<td>↑ PCO₂</td>
</tr>
</tbody>
</table>
Kidneys & Lungs are involved in compensatory mechanism for regulation of Bicarbonate buffer and maintenance of Acid-Base Balance in blood; (See the equations below)

\[
pH = pK_a + \log_{10} \frac{[HCO_3^-]}{PCO_2}
\]

\[
pH = pK_a + \log_{10} \frac{\text{Kidneys}}{\text{Lungs}}
\]
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