



## ACUTE KIDNEY INJURY: EXPLORING THE COMPLEX INTERPLAY OF ETIOLOGY, PATHOLOGY AND EFFECTIVE MANAGEMENT APPROACHES

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**Abstract:** Acute kidney injury (AKI) is characterized by a rapid decline in kidney function, diagnosed by elevated levels of urea and creatinine or decreased urine output. This review article provides an overview of AKI, including its definition according to various criteria such as KDIGO. The epidemiology of AKI, etiological classifications (prerenal, intrinsic or renal, postrenal), pathophysiology, risk factors, clinical manifestations, and diagnostic approaches are discussed. Additionally, the article explores the treatment strategies for AKI, emphasizing the importance of maintaining renal perfusion, fluid resuscitation, electrolyte management, discontinuation of nephrotoxic medications, supportive therapies, and the use of renal replacement therapy when necessary.

**Index Terms :** AKI ,CKD, CREATININE

**Introduction:** Acute kidney injury (AKI) is a condition characterized by a rapid decline in kidney function within a short period. It can be diagnosed based on elevated levels of urea and creatinine or reduced urine output. Various criteria, such as KDIGO, are used to define and classify AKI. The understanding of AKI has evolved over time, leading to improved recognition and awareness of the condition. AKI imposes a significant burden on healthcare systems, with a rising incidence observed in recent years. This review aims to provide a comprehensive overview of AKI, including its etiology, pathology, and management.

### DEFINITION:

Acute kidney injury (AKI) is a condition characterized by a rapid reduction in kidney function within 48 hours, which can be diagnosed by the presence of elevated levels of urea and creatinine or decreased urine output, or both <sup>(1)(2)</sup>.

Various criteria have been employed in research studies to assess acute kidney injury, including RIFLE, AKIN (Acute Kidney Injury Network), and KDIGO (Kidney Disease: Improving Global Outcomes) criteria. Among these, KDIGO is the most widely used and recent tool. As per KDIGO, acute kidney injury is defined by the presence of any of the following criteria:

- An increase in serum creatinine by 0.3 mg/dL or more (equivalent to 26.5 micromoles/L or more) within a span of 48 hours.
- An increase in serum creatinine to 1.5 times or more the baseline level within the previous seven days.
- Urine volume less than 0.5 mL/kg/h for a minimum duration of 6 hours.

### EPIDEMIOLOGY:

In the United States, it is estimated that around 17 million admissions annually are affected by acute kidney injury (AKI), leading to an additional healthcare system expenditure of \$10 billion <sup>(3)</sup>. Moreover, over the past decade, there has been a noticeable increase in the incidence of AKI, rising from approximately 60 to 500 cases per 100,000 population <sup>(4)(5)</sup>. This rise in incidence could be attributed, at least in part, to improved recognition and awareness of AKI.

### ETIOLOGICAL CLASSIFICATION:

**Prerenal AKI:** Prerenal AKI is characterized by a decrease in blood flow to the kidneys, resulting in impaired renal perfusion. It is caused by various factors, including hypovolemia, hypotension, heart failure, and conditions affecting renal blood flow <sup>(6)(7)</sup>.

**Hypovolemia:** Examples include hemorrhage, severe burns, and fluid losses through diarrhea, vomiting, or high ostomy output.

**Hypotension due to decreased cardiac output:** Conditions such as cardiogenic shock, massive pulmonary embolism, or acute coronary syndrome can lead to decreased blood pressure.

**Hypotension due to systemic vasodilation:** Septic shock, anaphylaxis, anesthesia administration, or hepatorenal syndrome can cause systemic vasodilation and hypotension.

**Renal vasoconstriction:** Agents like NSAIDs, iodinated contrast, amphotericin B, calcineurin inhibitors, and conditions like hepatorenal syndrome can cause renal vasoconstriction.

**Glomerular efferent arteriolar vasodilation:** ACE inhibitors and angiotensin receptor blockers can cause vasodilation of the glomerular efferent arterioles.

**Intrinsic or Renal AKI:** Intrinsic or renal AKI occurs due to damage to the renal parenchyma itself. It can be further classified into different subtypes based on the specific structures affected.

- a) Tubular Damage: The most common form is acute tubular necrosis (ATN), often caused by ischemic or nephrotoxic injury to the renal tubules.
- b) Glomerular Damage: Severe cases of acute glomerulonephritis, involving inflammation and damage to the glomeruli, can lead to AKI<sup>(8)</sup>.
- c) Interstitial Damage: Acute interstitial nephritis, typically triggered by allergic reactions to medications or infections, can result in AKI.
- d) Vascular Damage: AKI can occur due to vascular injury to the intrarenal blood vessels, seen in conditions like malignant hypertension, atheroembolic disease, preeclampsia/eclampsia, and hemolytic-uremic syndrome/thrombotic thrombocytopenic purpura<sup>(9)</sup>.

**Postrenal AKI:** Postrenal AKI arises from acute obstruction of the urinary tract, leading to impaired urine flow and subsequent kidney dysfunction. Causes include conditions like benign prostatic hyperplasia, urinary tract stones, tumors, and other obstructive lesions<sup>(10)(11)</sup>.

**PATHOPHYSIOLOGY:** The development of acute kidney injury (AKI) is influenced by its underlying causes. The pathophysiology of AKI is intricate and involves multiple factors. Ischemia, which occurs when blood flow to the kidneys is diminished, is the most common cause of AKI. Initially, physiological adaptations attempt to compensate for the reduced blood flow. However, if there is an inadequate supply of oxygen and metabolic substrates, cellular injury and organ dysfunction ensue<sup>(12)</sup>. The kidneys are particularly vulnerable to ischemic injury, leading to vasoconstriction, endothelial damage, and activation of inflammatory processes. In all forms of acute tubular necrosis, the common outcome is cellular injury caused by ischemia or direct exposure to toxins. This results in the loss of the brush border and eventual cell death, leading to the impairment of tubular cell function<sup>(13)</sup>. Additionally, intratubular obstruction caused by substances like myoglobin or crystals such as uric acid in conditions like tumor lysis syndrome or monoclonal gammopathy can have similar consequences. On the other hand, the mechanism of injury in glomerulonephritis may involve direct immune-mediated damage to the blood vessels or immune complex deposition, triggering an immune response and resulting in glomerular damage<sup>(14)(15)</sup>.

#### **RISK FACTORS:**

Several factors increase the risk of acute kidney injury (AKI). These include older age, shock, diabetes, sepsis, hypertension, exposure to nephrotoxic substances, chronic kidney disease (CKD), cardiovascular disease, undergoing surgery, chronic liver disease, hyperuricemia, chronic obstructive pulmonary disease (COPD), hypoalbuminemia, HIV infection, hyperglycemia, obesity, and anemia<sup>(6)(7)</sup>.

#### **CLINICAL MANIFESTATIONS:**

The clinical presentation of AKI varies depending on the underlying cause, severity of renal injury, and presence of associated conditions. In many cases, patients with mild to moderate AKI do not exhibit symptoms and are identified through laboratory tests<sup>(16)</sup>. However, individuals with severe cases may experience symptoms such as listlessness, confusion, fatigue, loss of appetite, nausea, vomiting, weight gain, or edema. Oliguria, defined as urine output less than 400 mL per day, anuria (urine output less than 100 mL per day), or normal urine volumes (nonoliguric AKI) may also be observed. Additional manifestations of AKI can include the development of uremic encephalopathy, characterized by a decline in mental status, asterixis, or other neurological symptoms, as well as anemia or bleeding caused by uremic platelet dysfunction.

#### **DIAGNOSIS:**

The diagnosis of acute kidney injury (AKI) involves a comprehensive evaluation that includes various laboratory tests and imaging studies. The initial laboratory assessment typically includes measuring the serum creatinine level, complete blood count, urinalysis, and fractional excretion of sodium. Additional tests, such as urine electrolytes, urine protein, urine osmolality, and urine albumin to creatinine ratios, can provide valuable information about the underlying cause of AKI. In older patients without an apparent etiology, serum and urine protein electrophoresis (SPEP and UPEP) may be conducted to rule out conditions like monoclonal gammopathy and multiple myeloma<sup>(17)</sup>.

Renal ultrasound imaging may be beneficial when obstructive causes of AKI are suspected, although it is not required for every AKI patient. Non-contrast CT imaging can be employed to identify the presence of nephrolithiasis or urolithiasis. Certain markers of tubular function, such as fractional excretion of sodium and urea, as well as urine osmolality, can aid in distinguishing between prerenal causes and renal/postrenal causes of AKI. However, it's important to note that these markers have limited sensitivity and can be influenced by the use of certain medications, such as diuretics<sup>(18)</sup>.

#### **TREATMENT :**

The treatment of acute kidney injury (AKI) involves various strategies aimed at restoring and maintaining renal function and addressing complications. Here are the key aspects of AKI treatment:

**Ensure adequate renal perfusion:** Maintaining hemodynamic stability and avoiding hypovolemia are crucial to ensure sufficient blood flow to the kidneys. This involves achieving and maintaining stable blood pressure levels and avoiding low blood volume<sup>(19)</sup>.

**Assess intravascular volume status:** Assessing the intravascular volume status can be challenging in some cases. Central venous pressure measurement in an intensive care setting can help determine the volume status<sup>(20)</sup>.

**Fluid resuscitation:** If intravascular volume depletion requires fluid resuscitation, isotonic solutions like normal saline are preferred over hypertonic solutions. The goal is to restore and maintain a mean arterial pressure greater than 65 mm Hg. In cases of persistent hypotension, vasopressors may be necessary<sup>(21)</sup>.

**Electrolyte management:** Close attention should be paid to electrolyte imbalances such as hyperkalemia, hyperphosphatemia, hypermagnesemia, hyponatremia, hypernatremia, and metabolic acidosis. Specific interventions may be required, such as insulin and dextrose to shift potassium into cells in severe hyperkalemia, or calcium gluconate to stabilize the membrane and reduce the risk of arrhythmias. Dietary potassium restriction may also be recommended<sup>(22)</sup>.

**Diuretics:** Diuretics can be used to manage volume overload. Intravenous loop diuretics, given as a bolus or continuous infusion, can be beneficial. However, it's important to note that diuretics do not improve morbidity, mortality, or renal outcomes and should not be used to prevent or treat AKI in the absence of volume overload<sup>(23)</sup>.

**Discontinue medications affecting renal function:** Medications that can be toxic to the kidneys or impact renal function should be discontinued. Adjustments to the dosages of essential medications may be necessary based on the level of kidney function<sup>(24)</sup>.

**Avoid nephrotoxic agents:** Nephrotoxic agents such as iodinated contrast media and gadolinium should be avoided. Noncontrast imaging studies should be considered when imaging is necessary.

**Supportive therapies:** Implement standard supportive therapies, including appropriate antibiotic use, adequate nutrition, mechanical ventilation when necessary, glycemic control, and management of anemia.

**Treatment for rapidly progressive glomerulonephritis:** In cases of rapidly progressive glomerulonephritis, treatment options may include pulse steroids, cytotoxic therapy, or a combination, typically after confirming the diagnosis through a kidney biopsy.

**Renal replacement therapy:** In cases where conservative management fails to adequately address metabolic consequences, renal replacement therapy (such as hemodialysis or peritoneal dialysis) may be required. Indications for initiating renal replacement therapy include refractory hyperkalemia, volume overload unresponsive to medical management, uremic pericarditis or pleuritis, uremic encephalopathy, intractable acidosis, and certain poisonings and intoxications<sup>(23)</sup>.

### Conclusion:

Acute kidney injury (AKI) is a complex condition with diverse etiological factors and pathological mechanisms. Early recognition and management of AKI are essential to prevent further kidney damage and improve patient outcomes. The use of established criteria, such as KDIGO, aids in the diagnosis and classification of AKI. Treatment strategies focus on restoring and maintaining renal perfusion, addressing electrolyte imbalances, discontinuing nephrotoxic medications, and providing supportive care. In severe cases, renal replacement therapy may be necessary. Further research and advancements in AKI management are required to enhance patient care and reduce the burden of this condition on healthcare systems.

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