**Value of RIFLE criteria in AkI in ICU patients**

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**Abstract:-**

**Purpose of review :** to show the prognostic value of RIFLE (Risk / Injury / Failure /Loss of kidney function/ESRD) criteria in prediction of outcome of intensive care unit ( ICU ) patients with Acute renal failure .

**Recent finding :**The development of Acute Kidney Injury( AKI) in hospitalized patients is common and carries with it a significant independent risk of mortality. Up to 20% of hospitalized patients may develop AKI . Of patients who are critically ill , 35%-40% will develop AKI . Acute Tubular Necrosis (ATN) accounts for the majority of causes of AKI in ICU patients. Currently, the mortality rate for hospital-acquired AKI ranges between 40% up to70% .

**Conclusion :**As with many conditions in acute medicine, early detection affords a better opportunity to intervene. Furthermore, milder forms of renal dysfunction have clinical importance and therefore staging (mild to severe) is desirable in order to better describe the syndrome .For these reasons, the Acute Dialysis Quality Initiative (ADQI).proposed the RIFLE criteria to define and stage acute kidney dysfunction. The acronym RIFLE stands for the three severity stages of risk, injury, and failure (in order of increasing severity) and the two outcome stages of loss and end-stage kidney disease. The RIFLE criteria for AKI are more sensitive than more traditional definitions of ARF. The incidence of AKI defined by the RIFLE criteria is much higher (2-10 times higher) than the incidence of more traditionally defined ARF .

**Keywords : -** RIFLE – AKI – ICU .

**Background :-**

Recent information of the definition, epidemiology, pathophysiology, and clinical causes of AKI in the ICUs is a fundamental prerequisite for prevention of this disorder. A multidisciplinary approach, which nephrologist and intensivist work side by side to achieve optimal care for a given patient, is essential for successful management [1].The variety of definitions used in clinical studies may be partly responsible for the large variations in the reported incidence (1–31%) and the associated mortality (19–83%) of acute kidney injury. Indeed, the lack of a uniform definition for acute kidney injury is believed to be a major impediment to research in the field [2] . Because the most powerful tool to improve outcome of AKI is prevention, the definition should have a high sensitivity, be multifaceted, and allow detection of patients who are at risk to develop kidney injury, as well as those with already established AKI and those with established ARF. This distinction in different stages might prove valuable to guide therapeutic recommendations and to allow reasonable comparisons on outcome between various treatment strategies in equivalent patient groups [3] .Recently, the acronym RIFLE which includes three levels of renal dysfunction of increasing severity-namely, Risk of renal dysfunction, Injury to the kidney, and Failure of kidney function and two outcome categories-Loss of function, and End-stage kidney disease) has been delivered. Based on recent clinical studies, the increasing use of the RIFLE criteria is justified, as this approach appears to be a robust method for both the diagnosis of and prognostication in ARF [1,4] .

**From acute renal failure to acute kidney injury:**

The concept of acute renal failure (ARF) has undergone significant reexamination in recent years. Mounting evidence suggests that acute, relatively mild dysfunction of the kidney, manifest by changes in urine output and blood chemistries, portends serious clinical consequences. Although the term acute renal failure is relatively new, its first description as is churiarenalis was by William Heberden in 1802. During the First World War the syndrome was named “War Nephritis” and was reported in several publications. The syndrome was then largely forgotten until the Second World War, when Bywaters and Beall published their classical paper on crush syndrome. It is Homer W. Smith who is credited for the introduction of the term acute renal failure (1951) [5] .In recent years, it has been recognized that the time-honored term ARF fails to adequately describe what is a dynamic process extending across initiation, maintenance, and recovery phases, each of which may be of variable duration and severity. The alternative proposed term acute kidney injury (AKI) better captures the diverse nature of this syndrome, and has entered into widespread clinical use [1,4] .

**AKI in ICU patients :**

The development of AKI in hospitalized patients is common and carries with it a significant independent risk of mortality. Based on RIFLE and AKIN criteria, up to 20% of hospitalized patients may develop AKI. Of patients who are critically ill, 35%-40% will develop AKI. The most common causes of AKI in hospitalized patients include ischemia, sepsis, medications, and radio-contrast dye. Pre-renal causes are common in ward patients, however, acute tubular necrosis (ATN) accounts for the majority of causes of AKI in ICU patients. ATN in the ICU is typically multifactorial and is frequently part of multisystem organ failure syndrome [6,7]. Currently, the mortality rate for hospital-acquired AKI ranges between 40% up to70% (ICU mortality up to 52%) and is directly correlated to the severity of the patient's other disease processes. The mortality rate among patients presenting to the emergency department with prerenal AKI may be as low as 7% and up to 30%. The most common causes of death associated with AKI are sepsis, heart failure, and respiratory failure [8]. The commonest causes of AKI in ICU are intra-renal causes especially ATN (ischemic ATN), while the least common causes of AKI in ICU the post-renal causes [9].

Although the etiology of AKI in critically ill patients is likely often multifactorial, sepsis is consistently been found to be an important contributing factor. Several studies have shown that approximately 40% to 50% of patients with AKI on presentation to an ICU have concomitant sepsis and that approximately 11% to 64% of patients with a diagnosis of severe sepsis or septic shock have concomitant AKI [10] . The length of stay in ICU for the patients with AKI increases when sepsis is the contributing factor, also mortality rate increases as shown in **figure1**[11] .

Contrast-induced nephropathy (CIN) has become an important cause of iatrogenic acute renal impairment. In fact, CIN is the third leading cause of new acute kidney injury in hospitalized patients and the incidence in ICU about 11.5 % [12] .

Table (1) :- Differential diagnosis of AKI by urinary diagnostic indices [13]

|  |  |  |  |
| --- | --- | --- | --- |
| **Urinary diagnostic indices** | **Pre -renal** | **Intra- renal** | **Post renal** |
| Urine osmolality (mOsm/kg) | >500 | **<**350 | Usually not useful in the diagnosis of post renal AKI |
| Urine/plasma creatinine ratio | > 40 | < 20 |
| BUN to serum creatinine ratio | > 20 | < 10 |
| Urine sodium level (mEq/L) | < 20 | > 40 |
| Fractional sodium excretion (%) | < 1 | > 1 |

Studies in which variables such as levels of urea and creatinine and urine output have been used as indicators of kidney function or injury have not provided interventions that decrease the need for dialysis or reduce mortality. At the same time, the inability to diagnose AKI quickly and accurately places an enormous financial burden on society. Therefore, the use of biomarkers that could be used to detect early renal injury may affect timely diagnosis and, possibly, outcomes in AKI [14] .

Table (2): Summary of Novel biomarker in AKI [15] .

|  |  |  |
| --- | --- | --- |
| **Marker** | **Substrate-Test** | **Comments** |
| Interleukin 18(IL18) | Urine-ELISA | IL-18 elevated in human kidney ATN (native and transplanted kidneys) |
| Sodium/hydrogen exchanged isoform3 (NHE3)  | Urine-semiquantitativeimmunoblotting | (NHE3)differentiated prerenal from intrarenal ischemic ATN from other intrarenal causes of ARF |
| Kidney Injury Molecule -1(KIM-1) | Urine, kidney-multiple methods | Specific for ischemic AKI/ATN when compared with other forms of kidney disease |
| Human Growth-related- oncogen- α (Gro-α) | Urine, blood-ELISA | Gro-α correlates well with renal recovery from AKI/DGF in transplant, early increase in urine and blood well before rise in serum creatinine in AKI models |
| NeutrofilGelatinin Associated Lipocalin(NGAL) | Blood, urine-western blot and ELISA | NGAL sensitive, specific and predictive marker of AKI in blood and urine of patients after cardiopulmonary bypass |

Given the high morbidity and mortality associated with AKI and absence of specific pharmacological therapy for AKI, prevention is crucial strategy include maintaining an adequate intravascular volume; avoiding nephrotoxic exposure; saline expansion prior to, during, and after radio-contrast exposure in at-risk patients; titrating drug dosages to the level of renal function. Restoration of renal blood flow (RBF) with early and active volume replacement may reduce renal tubular cell injury in the initiation phases of ischemic ATN [16] .From a renal standpoint, fluid therapy is used to restore glomerular filtration and thus increase urine output. Glomerular filtration requires an adequate trans-glomerular pressure gradient, which is mostly determined by total renal blood flow, glomerular arteriolar tone and the colloid osmotic pressure of proteins in the plasma. Fluid therapy is aimed at restoring systemic blood pressure (a major determinant of renal perfusion pressure) and cardiac output (a prerequisite for adequate renal blood flow). Restoration of these parameters might relax the neuroendocrine reflexes responsible for increasing renal vascular resistance and diminishing GFR [17] . Ultimately the best method of assessing fluid status and responsiveness is the fluid challenge technique. However the fluid challenge must be done correctly and carefully so that fluid administrations interrupted immediately if there is no benefit, hence, patient must be closely monitored at least every 10 minutes during administration of the fluid. Fluid chart should be done accurately [18] .

**RIFLE criteria in AKI :**

As with many conditions in acute medicine, early detection affords a better opportunity to intervene. Furthermore, milder forms of renal dysfunction have clinical importance and therefore staging (mild to severe) is desirable in order to better describe the syndrome [19] . A classification system should therefore include and distinguish between mild or severe, and early or late cases. This would allow such a classification to detect patients in whom renal function is mildly affected (high sensitivity for the detection of kidney malfunction ) and patients in whom renal function is markedly affected (high specificity for true renal dysfunction) [20]. For these reasons, the Acute Dialysis Quality Initiative (ADQI), an international consensus group comprised of nephrologists and intensivists with expertise in acute kidney dysfunction, proposed the RIFLE criteria to define and stage acute kidney dysfunction. The acronym RIFLE stands for the three severity stages of risk, injury, and failure (in order of increasing severity) and the two outcome stages of loss and end-stage kidney disease. The three severity stages are defined on the basis of either increases in serum creatinine or decreases in urine output, where the more severe of either criterion is used. The two outcome criteria, loss and end-stage kidney disease, are defined by the duration of loss of kidney function [2] .**figure 2**



|  |  |  |
| --- | --- | --- |
|  | GFR criteria | Urine output criteria |
| Risk | Cr increased 1.5x or GFR decrease >25% | <0.5ml/kg/h for 6hrs |
| Injury | Cr increased 2.0x or GFR decrease >50% | <0.5ml/kg/h for 12hrs |
| Failure | Cr increased 3.0x or GFR decrease >75% or Cr ≥ 4mg/dL when there was an acute rise of >0.5mg/dl | <0.3ml/kg/h for 24hrs or anuria for 12hrs |
| Loss | Persistent ARF; complete loss of kidney function for >4 weeks |
| End-stage renal disease | ESRD for 3 months |

Table (3): The RIFLE criteria [2].

Since its original publication in 2004, many investigators have already implemented the RIFLE classification for research purposes. Most of these studies are epidemiological and evaluated mortality of critically ill patients with AKI comparing subjects in the R, I, and F classes to verify if outcome progressively worsened with increasing severity of AKI. Although most deal with adults, one study validated the RIFLE criteria in a cohort of critically ill pediatric patients [21]. The authors concluded that RIFLE classification might improve the ability of such older and established ICU scoring systems as APACHE II and Simplified Acute Physiology Score II in predicting outcome of ICU patients with AKI [22] ***.***

RIFLE classification system can serve well to improve understanding of AKI epidemiology in critically ill burn patients. AKI lead to a poor outcome in patients with severe burn injury [23] . When compared with AKI of other etiologies, crush induced AKI shows highly specific features due to a high incidence of life threatening electrolyte disturbances, such as hyperkalemia; the frequent simultaneous presence of medical and surgical problems in the clinical course, resulting in a high number of complications and high need for therapeutic interventions such as blood and blood product transfusions and dialysis. RIFLE correlated well with most outcome parameters [24].

The first stratum of the RIFLE criteria (risk) might be the most important one, because at this stage, a positive test should increase the physician’s awareness of the presence of risk for renal injury, at a moment when the situation still is reversible by preventive or therapeutic intervention [25] .

In the RIFLE criteria, the stratum of injury is defined by a doubling of serum creatinine or a reduction of urinary output below 0.5 ml/kg per h during at least 12 h. importantly of the patients who develop injury 50% later will develop established renal failure [25] .

ARF is defined as the need for RRT. Although this seems to be a clear cut definition at first glance, it is far from an objective one. Because the decision to start RRT is to some extent subjective, In RIFLE, failure is defined as a threefold increase of serum creatinine or decrease in GFR of 75% or a urine output of 0.3 ml/kg per h for 24 h or anuria for 12 h. Alternatively, failure also is defined by a serum creatinine of 4 mg/dl (353.6 mol/L) with an acute rise of 0.5 mg/dl (42.2 mol/L) [26] .

LOSS is defined as need for renal replacement therapy (RRT) for more than 4 weeks, whereas ESRD is defined as the need for RRT for more than 3 months [20].

The RIFLE criteria for AKI are more sensitive than more traditional definitions of ARF. The incidence of AKI defined by the RIFLE criteria is much higher (2-10 times higher) than the incidence of more traditionally defined ARF [5] .

The prognostic value of RIFLE criteria in prediction of outcome of ICU patients with Acute renal failure is very important. (In-hospital mortality for ICU patients without AKI and ICU patients with increasing RIFLE class) [27] as in **figure 3**



**Conclusion :**

AKI is a common and serious complication in critically ill patients with high mortality rate .the prognosis of patients is important in risk stratification and for efficient use of hospital resources . predicting the outcome of patients in the intensive care environment is of particular significance to ensure that resources are used appropriately , Thus the Acute Dialysis Quality Initiative ( ADQI ) group has put forward a working definition of AKI which is called RIFLE acronym indicating Risk for renal dysfunction , Injury to the kidney , Failure of kidney function , also includes two clinical outcomes Loss and ESRD . RIFLE classification is as dependable as other scoring system regarding mortality prediction in patients with sepsis and systemic inflammatory response syndrome(SIRS) presented with acute renal shutdown . The combination of the different scoring models strongly supports and highly improves the prognostic performance of either model alone. So, we do recommend the combined use of Acute Physiology and Chronic Health Evaluation (APACHE) II score ,Sequential Organ Failure Assesment (SOFA) score together with RIFLE score for prediction of mortality of critically ill patients in intensive care unit.

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