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The Potential Role of STARZ Score in Prediction of Neonatal Acute Kidney Injury: A Comprehensive Review

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Abstract
Background: Neonatal Due to its complicated aetiology and varying clinical manifestations, acute kidney injury (AKI) presents substantial problems in diagnosis and therapy. The absence of established diagnostic criteria and the vast variety of predisposing variables further hinder the understanding and prompt action for this disorder. The purpose of this review is to shed light on the complex nature of neonatal acute kidney injury (AKI), including its definition, epidemiology, clinical phenotypes, risk factors, evaluation, management strategies, and the potential role of scoring systems, with a particular emphasis on the STARZ score. Conclusions: Neonatal AKI originates as a complicated entity impacted by numerous prenatal and postnatal causes. The research highlights the critical need for standardised diagnostic criteria as well as the need of a holistic approach to diagnosis. It also draws attention to the changing landscape of management techniques and the promise of prognostic and therapy guidance scoring systems like STARZ for this at-risk group.

Keyword: Acute kidney damage (AKI) in newborns, diagnostic criteria, grading methods, the STARZ score.

1- Introduction

Acute Neonatologists consider acute kidney damage (AKI) a major problem since it complicates the management of severely unwell infants. As its occurrence in newborns has increased in recent years, accurate prognostic techniques are needed to better predict and treat this illness. In this quest for better prediction, the STARZ score stands out as a viable path that might completely alter how we detect and treat newborn acute kidney injury [1].

In the setting of a newborn's fragile physiology, neonatal acute kidney injury (AKI), characterised by a precipitous reduction in kidney function, poses a complicated challenge. Neonates are more vulnerable to AKI due to prematurity, perinatal hypoxia, sepsis, and the use of nephrotoxic medicines. Despite advancements in newborn care, the complicated interaction of these parameters frequently hinders early identification and exact risk assessment, requiring a powerful prediction tool adapted to the particular intricacies of neonatal physiology [2].

The STARZ score shows potential as a multifactoral scoring system developed specifically for predicting AKI in newborns, and it has only been in use for a short time in the field of neonatology. Comprising clinical characteristics such as blood creatinine levels, urine output, and the presence of comorbidities, this scoring system tries to utilise a holistic perspective of the neonate's health condition to estimate the risk of AKI development. It is based on a combination of known risk variables that have been shown to improve upon the accuracy and reliability of individual indicators [3].

Understanding the STARZ score requires diving into its components and their relative weightage in predicting the likelihood of acute kidney injury (AKI). There may be a gradient of importance in the newborn AKI landscape depending on factors including gestational age, birth weight, and the occurrence of sepsis or respiratory distress syndrome. By delving into these nuances, we may better understand the score's design and appreciate its potential to detect at-risk newborns before to clinical manifestation, paving the way for early intervention and individualised treatment [4].

The advent of the STARZ score corresponds with a growing interest in precision medicine in the field of neonatology, which is intriguing. Potential benefits include improved risk classification and individualised treatment plans, in addition to AKI prediction. The STARZ score is an example of the healthcare industry's shift toward customised methods; it suggests a future in which newborn acute kidney injury (AKI) therapy goes beyond reactive interventions and adopts a proactive posture based on individual risk assessment [5].

Therefore, the purpose of this extensive analysis is to examine how the STARZ score has developed in its ability to predict newborn AKI.

2-Neonatal acute kidney injury

Neonatal renal physiology

Understanding Managing and preventing newborn AKI requires a thorough understanding of neonatal renal physiology. The number of nephrons present in each kidney at birth varies greatly, from around 300,000 to over 1.8 million, depending on both hereditary and prenatal environmental

variables. Fetal urine production starts between weeks 9 and 10, and nephrogenesis continues until weeks 34 and 36 of pregnancy. The kidneys, which produce urine and regulate hormone levels, develop significantly throughout pregnancy. By the time a child is 2 years old, his or her renal blood flow (RBF) and glomerular filtration rate (GFR) have caught up to those of an adult [6]. Angiotensin II, prostaglandins, nitric oxide, and catecholamines are only few of the factors that control renal vascular resistance. However, angiotensin II levels are highest during the newborn period and steadily decrease until maturity. In addition, foetal kidneys respond better than neonatal kidneys to several vasoactive stimuli. Renal function and adaptability are also affected by changes in the foetal urine concentration capacity, electrolyte management, and potassium balance. Preterm newborns may still be developing their kidneys after delivery, according to certain studies [7]. This highlights the importance of the postnatal environment in nephrogenesis and the possible hazards of AKI on this developmental process.

Acute renal injury: what it means

Kidney function may suddenly drop, resulting in structural damage and functional loss within hours; this condition is now referred to as acute kidney injury (AKI), which has replaced the term acute renal failure (ARF). Diagnosing and treating AKI may be difficult since it often occurs outside of the critical care setting and has several causes, including sepsis, ischemia, and nephrotoxicity. Classification-wise, AKI covers pre-renal, acute post-renal obstructive nephropathy, and intrinsic acute kidney disorders. Acute kidney injury (AKI) may be classified as either intrinsic (indicating true kidney disease) or non-renal (arising from extra-renal diseases affecting glomerular filtration rate) (GFR). Acute reduction in GFR, measured by abrupt increases in serum creatinine (sCr) levels and/or decreases in urine output (UO) within a specific period, is the primary way to diagnosis [8].

The insensitivity of sCr to acute renal alterations and its heterogeneity among populations make it necessary to investigate other biomarkers. It is difficult to analyse these indicators, and it is unclear what standard of care should be used to make a diagnosis of AKI. Understanding the many clinical presentations and underlying pathophysiologies of AKI is necessary for better diagnosis and treatment options [9], and the fluctuation in sCr levels and the difficulty surrounding determining its genuine baseline further complicate AKI assessment.

Epidemiology

Acute kidney injury (AKI) has been reported at variable rates since there is no agreed-upon definition for the condition. Incidence diverges dependent on categories utilised, patient demographics, and geographical locations analysed, revealing considerable disparities between developing and industrialised nations. Community-acquired AKI is more prevalent in rural parts of impoverished countries owing to diseases like diarrhoea, dehydration, infections, and animal venoms, whereas hospital-acquired AKI is more common in metropolitan areas due to reasons including renal ischemia, sepsis, and nephrotoxic medications. Underreporting is a frequent problem, particularly in poor countries, hampering a thorough knowledge of AKI's worldwide effect [10]. On the other hand, the incidence of AKI is rising, especially among hospitalised and severely sick people in industrialised nations. Acute kidney injury (AKI) is more common in those over the age of 65 owing to a combination of factors, including the ageing kidney, hypertension, cardiovascular disease, and chronic renal disease, which are itself aggravated by medical procedures and drugs. Results vary by region's healthcare accessibility and prompt referrals [11], but AKI may occur in children mostly owing to volume-related difficulties, sepsis, and particular diseases.

According to the KDIGO criteria for defining and staging AKI (Tables 1 and 2):

Table (1) AKI is defined as any of the following [12].

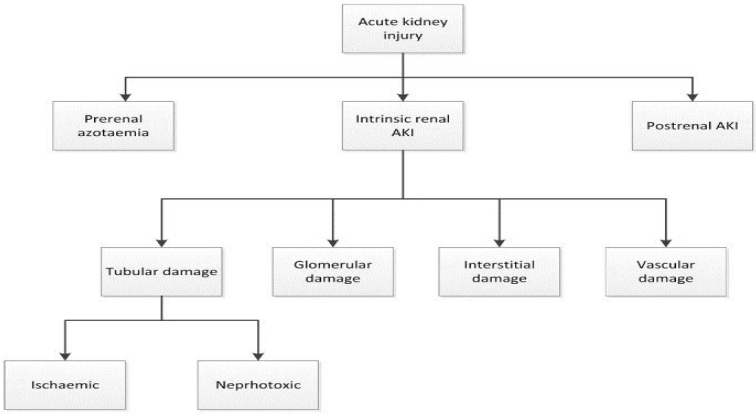
1	Increase in sCr ≥0.3 mg/dL (≥26.5 μmol/L) within 48 hours; or
2	Increase in sCr ≥1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or
3	Urine volume <0.5 mL/kg/h for 6 hours.

Table 2: AKI is staged for severity according to the following criteria [6].

Stage	1.5–1.9 times baseline OR ≥0.3 mg/dL (≥26.5 μmol/L) absolute	Urine volume <0.5 mL/kg/h

1	increase in sCr	for 6–12 hours
Stage 2	sCr ≥2.0–2.9 times baseline sCr ≥3.0 times from baseline OR	Urine volume <0.5 mL/kg/h for ≥12 hours
Stage 3	Increase in sCr to ≥4.0 mg/dL(≥353.6 μmol/L) OR Initiation of renal replacement therapy OR, In patients <18 years, decrease in eGFR to <35 mL/min per 1.73 m^2	Urine volume <0.3 mL/kg/h for ≥24 hours OR Anuria for ≥12 hours

Among the many possible root causes of AKI is an imbalance between the nephrons' higher energy needs and the decreased oxygen and nutrients they get as a result of poor microcirculation [13]. Diagnosis and treatment of AKI have traditionally relied on separating cases into pre-renal, intrinsic, and post-renal stages (Figure 1).



Causes of acute renal damage are shown in Figure 1. Inspired by [14].
causes of acute renal damage in newborns (Table 3):
Neonatal Acute Kidney Injury Causes (Table 3)

Cause	Description
Pre-renal AKI	Results from decreased renal perfusion without renal parenchymal damage due to extra-renal insults. Can stem from systematic or intra-renal circulation failure.
Respiratory Distress Syndrome (RDS)	Severe hypoxemia in neonates due to RDS, persistent pulmonary hypertension, or post-traumatic deliveries, impacting renal function via hormonal and vasoactive changes.
Perinatal Asphyxia	Non-oliguric ARF in asphyxiated neonates, often unnoticed without daily serum creatinine monitoring. Linked to hypoxic response impacting kidney perfusion.
Renal Artery Thrombosis	Bilateral thrombosis causing neonatal ARF, often related to umbilical artery catheterization and high renal vascular resistance.
ARF in Twin Pregnancies	Occurs in donor fetuses in feto-fetal transfusion syndrome, leading to oligohydramnios, hypovolemia, and renal insufficiency.
Closure of Abdominal Wall Defects	Post-operative complications from primary fascial closure, including reduced cardiac output, hypotension, and renal failure.
Post-renal AKI	Acute obstruction of urinary flow resulting in increased intra-tubular pressure, impaired renal blood flow, and decreased GFR.

3-Intrinsic renal aetiologies of AKI

It may be difficult to diagnose since there are so many different types of kidney damage. The tubules, glomeruli, interstitium, and intrarenal blood arteries are the four main sites of involvement in the kidney. Acute kidney injury (AKI) caused by tubule destruction is medically referred to as acute tubular necrosis (ATN). This kind of intrinsic kidney damage occurs more often than any other. Finally, acute interstitial nephritis is caused by an allergic response to certain drugs or an infection [15], and it contributes to AKI from vascular damage since injury to intra-renal arteries reduces renal perfusion and reduced GFR.

Pathophysiology and the various AKI clinical phenotypes

When renal function suddenly decreases, causing waste buildup and disturbances in electrolyte, acid-base, and water balance, this condition is known as acute kidney injury (AKI). Ischemia plays a crucial role in the complex pathophysiology by causing cell

death, vasoconstriction, and inflammation, all of which have an effect on the outer medulla of the kidney, which is where the arteries and tubules meet. Ischemia disrupts oxygen and substrate delivery, leading to cell damage or death; this is especially true for the delicate proximal tubular cells [16]. Rapid declines in GFR are induced by sepsis, another prevalent cause of AKI, and are characterised by the intricate interaction of inflammation, oxidative stress, and cytokine production by tubular cells. Animal models provide insights primarily through extreme conditions like ischemia-reperfusion, but they cannot precisely replicate human AKI, where renal blood flow rarely ceases completely, raising debates on damage extent and affected cell types [17]. This presents a challenge to the traditional AKI classification (pre-renal, intrinsic-renal, post-renal), which is based on histological diagnoses that are uncommon.

Renal failure brought on by medication

High drug and metabolite levels may have toxic effects on the kidney, damaging glomerular, interstitial, and tubular cells. Important for filtrate concentration and reabsorption, renal tubular cells are also very susceptible to medication toxicity. Hemodynamic changes, direct cellular damage, inflammatory reactions, and restriction of renal excretion are all potential causes of this kind of toxicity. Subtle renal damage and urine irregularities are generally missed until overt alterations in renal function, usually evidenced by elevated blood creatinine levels, become evident. Renal damage is a complicated issue, but it is better understood because to reviews that dive deeply into the mechanisms of renal injury associated to routinely used therapeutic drugs [18].

Acute Kidney Injury Caused by Contrast Medium (CI-AKI)

Acute renal dysfunction may occur after intravascular injection of contrast agents, which are often used for diagnostic and therapeutic purposes, and is known as contrast-induced acute kidney injury (CI-AKI) or contrast-induced nephropathy (CIN). Its prevalence and risk factors in newborns are unknown, despite being well-documented in adults undergoing contrast imaging. Due to their underdeveloped kidneys, newborns are especially vulnerable to renal damage, which may occur when the toxicity of contrast agents causes acute tubular necrosis and subsequent impairment of renal function. Neonates are at risk when they are born prematurely, have a low birth weight, suffer from sepsis, become dehydrated, or have preexisting renal problems [19].

Changing definitions, such as the KDIGO criteria for AKI, attempt to standardise clinical and research terminology for CI-AKI, which has been related to prolonged hospital admissions, advancement to end-stage renal disease, dialysis demands, increased mortality, and increased expenditures. While animal models show many possible nephrotoxic processes, their direct relevance to human CI-AKI remains contested, partially owing to numerous insults required to recreate the syndrome, possibly leading to overestimations of its incidence and severity in clinical investigations [20].

4-Acute kidney injury and extra-renal organ dysfunction

Evidence Recent advances in our understanding of AKI, from both the laboratory and the clinic, are shifting our perspective from one of a condition of isolated organ failure to one in which the kidney is an integral part in the development of systemic dysfunction. Clinical data demonstrates that AKI not only serves as a measure of sickness severity but also causes the beginning of multi-organ dysfunction at an early stage, which has a major impact on mortality [21].

Remote organ dysfunction, including in the lungs, heart, liver, intestines, and brain, is a consequence of AKI [22]. This dysfunction is caused by a pro-inflammatory process including neutrophil cell migration, cytokine production, and elevated oxidative stress.

Interaction between the kidneys and lungs in the severely unwell

When many organs fail at once, the kidneys and lungs tend to go first. Both ALI and AKI are frequent sequelae of sepsis, and both significantly increase mortality. Interest is rising in the possibility that one organ might cause or contribute to harm in the other when both are compromised. Both AKI and ALI have been linked in animal research. It is still not fully known what causes the lung damage seen in people with AKI. Pro-inflammatory and pro-apoptotic factors have been linked in several studies (leukocyte trafficking, cytokines activation of caspases, oxidative stress and uraemic toxins). Through metabolic and biochemical disturbances [23], AKI causes lung damage and inflammation, and ALI then promotes and exacerbates renal failure.

Interaction between the heart and the kidneys: cardiorenal syndrome

Both kidney illness and heart disease are prevalent, and they often occur together. Renal function may decline acutely and/or chronically in response to both acute and chronic heart illness. This illness, which serves as a useful model for studying the aetiology

and pathophysiology of cardiac and renal failure, is often referred to as cardiorenal syndrome (CRS). The CRS has been suggested with a unified definition and taxonomy. This classification system identifies five distinct forms of CRS. The origins of the names for these subtypes reflect the underlying cardiac and renal illness, as well as the secondary dysfunction caused by systemic disease [24].

The Hepatorenal Syndrome: A Liver-Kidney Interaction

Differentiating between AKI-induced hepatic dysfunction and HRS is difficult because the degree to which AKI impairs liver function by inducing oxidative stress, inflammation, and hepatocyte destruction is generally proportional to the severity of the kidney injury. Approximately 40% of patients with advanced cirrhosis develop HRS, a reversible renal impairment manifesting as a substantial reduction in GFR and renal blood flow without other renal damage causes. The renal function declines rapidly and steadily in Type 1 HRS, whereas it is milder and more gradual in Type 2. Cirrhosis patients provide a unique challenge for the HRS diagnostic criteria because of the changed creatinine dynamics that may lead to an overestimation of renal function or an underestimating of the degree of damage. The concept of "acute-on-chronic" was created to better capture the developing renal alterations in cirrhosis patients, and criteria were revised to classify Type 1 HRS as a type of AKI and Type 2 HRS as a form of CKD [25].

5-Risk factors for neonatal AKI

The The decline in renal function that characterises AKI likely results from a web of risk and protective variables. Risk factors intrinsic to newborn renal development and physiology [26] must be taken into account despite the fact that neonates are vulnerable to the same risk factors prevalent in critically sick children of all ages.

Events and Exposures During Pregnancy

Numerous maternal exposures and perinatal events might cause neonatal AKI due to the special physiology of the newborn kidney. Nonsteroidal anti-inflammatory medication exposure during pregnancy, for instance, increases the risk of oliguria and acute kidney injury in newborns. Renal agenesis to acute kidney injury (AKI) are only two of the many possible outcomes for babies exposed to angiotensin-converting enzyme inhibitors because of the renin-angiotensin system's many functions in renal development during pregnancy and in maintaining renal blood flow after birth. Low Apgar scores, intubation, a low cord pH, and asystole are all risk factors for acute kidney injury (AKI) in the newborn period [27].

Sepsis

Neonatal sepsis is a major contributor to morbidity and death. In newborn populations, sepsis has been demonstrated to be a risk factor for the development of AKI, contributing to as many as 78% of instances of AKI [28]. Acute kidney injury (AKI) was reported in 52 of 200 term newborns with sepsis by Mathur et al., 2006. Meningitis, disseminated intravascular coagulation, and septic shock were more common in those with AKI, and they were also born at a lower weight [29]. Neonates that develop sepsis are generally assumed to be susceptible to AKI related to the hypotension associated with systemic inflammation, but there also seems to be a direct effect on the kidneys [30]. Furthermore, AKI may occur despite the preservation of systemic blood pressures and renal blood flow, indicating that sepsis may directly harm the kidney via effects on microvasculature [31].

Drugs That Harm the Kidneys

Among the wide range of critically sick and hospitalised children, nephrotoxic medicines are a recognised cause of AKI. Another potentially preventable risk factor for AKI in newborns is their exposure to nephrotoxic drugs [32]. The effects and prevalence of nephrotoxic drug exposure in 107 very low birth weight (VLBW) newborns were analysed by Rhone et al., 2014. Eighty-seven percent of neonates in this research were given at least one nephrotoxic medicine, and these infants were given these drugs for an average of 14 days during their time in the NICU. While this research is a start in the right direction, further research is needed to fully understand the epidemiology of nephrotoxic drug exposure in NICU populations as a whole [33].

Small for Gestational Age and Very Low Birth Weight Newborns

Three major single-center studies have assessed AKI in very low birth weight (VLBW) newborns (500-1500 g) thus far [34]. Two hundred and twenty-nine very low birth weight babies were prospectively monitored from birth to 36 weeks postmenstrual age and reported in 2011. According to the neonatal modified KDIGO criteria, 18% of the infants had AKI. Infants with AKI had a far greater death rate than those without the condition. Those with AKI had a considerably greater risk of dying, even after controlling for other factors [35]. Viswanathan et al., (2012) found similar results in a retrospective single centre analysis, where 12.5 percent of all ELBW babies had AKI and death among those with

AKI was considerably greater than controls [36]. In a large retrospective study of VLBW newborns, Carmody et al., (2014) studied 455 VLBW infants and reported an AKI incidence of 39.8 percent . Independent analyses showed that AKI increased mortality and hospitalisation duration in this research [34].

6-Perinatal Asphyxia

Infants experiencing perinatal asphyxia are known to be at increased risk for AKI. Two studies utilising up-to-date definitions of AKI have looked at the frequency of AKI in a single centre. Kaur et al. (2011) found that AKI occurred in 41.7% [37] of their study population. Newborns treated with therapeutic hypothermia for perinatal asphyxia were assessed by Selewski et al., (2013), and they discovered that 38% of them developed AKI. Even after correcting for key potential confounders, children with AKI on average were ventilated 4 days longer and hospitalised 3.4 days longer [38]. Also, these researchers demonstrated that acute kidney injury (AKI) during therapeutic hypothermia was linked to aberrant brain MRI findings at 7-10 days of life, suggesting that AKI might serve as a marker for neurologic outcomes [39].

ECMO

ECMO-supported neonates are a special group at risk for AKI because of the severity of their sickness and the inflammatory response that comes with being connected to an extracorporeal circuit [40]. Evaluation of AKI in 242 newborns on ECMO over a 14-year period by Zwiers et al. (2013) found a 64% prevalence of AKI and a 66% fatality rate at the most severe stage of AKI [41]. These results are consistent with those shown by Gadepalli et al., (2011) in ECMO-treated infants with congenital diaphragmatic hernia, in which AKI developed in 71% of neonates and the death rate for those with the most severe form of AKI was 73% [42].

Heart Operations on Newborns

There is conclusive evidence linking AKI with an increased risk of death after heart surgery in children aged one year old or older. In a retrospective analysis of 122 newborns, Alabbas et al. (2013) found that 62% of the infants had AKI. There was a correlation between the highest stage of AKI and an increased risk of death and duration of stay in the intensive care unit [43]. Blinder et al. (2012) observed similar results after studying the outcomes of heart surgery in 430 newborns.

Diagnosis and treatment of newborn acute kidney injury

In newborn AKI examination, a comprehensive approach is necessary, spanning pre-renal, intrinsic, and post-renal causes. Clinical history examination, including gestational age, prenatal, maternal, and postnatal events, is critical. Differentiating prerenal from intrinsic reasons may be accomplished by assessment of volume status and vital signs in addition to the fractional excretion of sodium. Evaluation of postrenal causes is facilitated by ultrasound. Nephrotoxicity may be avoided by carefully reviewing medications, keeping track of fluid intake and output, and enlisting the help of a pharmacist. Although effective ways to prevent or cure AKI in newborns remain limited, monitoring cumulative fluid overload is crucial and may dictate treatments and nephrology consultation [45]. Despite efforts to sustain urine output, there is a lack of strong data supporting the use of diuretics in AKI. In contrast, the use of theophylline and dopaminergic agonists have showed promise but lack solid recommendations owing to inconsistent trial results. In extreme situations, renal replacement treatment is essential, particularly in the presence of persistent acidosis, uremia, electrolyte imbalances, insufficient nutrition, or fluid overload. Despite equipment limitations and a lack of research on the effects of fluid overload in neonates, peritoneal dialysis continues to be the modality of choice for treating severely sick newborns.

- A major cause of death in newborns in intensive care is fluid overload, which has brought attention to the treatment of this condition and the timing of renal replacement therapy. Since fluid overload may be a modifiable risk factor in newborn outcomes, further study is needed to help doctors decide when to start giving their patients dialysis and how much fluid to give them. Although renal replacement therapy has progressed from a measure of last resort to an early intervention in adult and paediatric care, its incorporation into neonatal care has lagged behind, in part because of the risks involved, ethical considerations, and the lack of comprehensive studies demonstrating fluid overload's role in neonatal outcomes. Although peritoneal dialysis is the modality of choice for newborns, modifying equipment meant for larger children remains a difficulty. Improving the care for critically unwell newborns with AKI requires further research on the effects of fluid overload on neonatal outcomes. [47].
- Scoring methods for acute renal injury in newborns
- Neonates with acute kidney damage have been the focus of several scoring systems designed to estimate their likelihood of death

and determine if they would need renal replacement therapy (RRT) (AKI). Among these grading schemes are [48]:

- Scoring System for Neonatal Acute Renal Zest (STARZ):
- Serum creatinine, urine output, the need for mechanical ventilation, and the presence of sepsis are the four characteristics used to determine a newborn's STARZ score. The overall score may be anything from 0 (not good) to 4 (excellent) depending on how well each criterion is satisfied. In [49], we have the values and parameters as follows:
- Serum creatinine: ≤ 0.9 mg/dL: 0 points
- 1.0-1.9 mg/dL: 1 point
- Two points if your blood sugar levels are between 2.0 and 3.9
- 3.0 to 3.9.9 mg/dL: 2 points
- In the event that your urine production is less than 1 mL/kg/h, you will not get any points.
- 1 point for every 1 mL/kg/h for 6-24 hours
- If the rate is less than 1 mL/kg/h for more than 24 hours, you get 2 points.
- If you've been anuric for more than 24 hours, you lose 3 points.
- Those not receiving mechanical ventilation are penalised with zero points.
- Using a ventilator for less than seven days: 1 point.
- Two points for using a ventilator for 7-14 days.
- Three points if you've been on a ventilator for more than 14 days.
- Score 0 if you don't have sepsis.
- Suspected or treated sepsis: 1 point
- The STARZ score has been proven to have high discriminative power for predicting death in newborns with AKI. It may be used to determine whether infants need to be monitored more closely or given additional interventions like renal replacement therapy or referral to a newborn critical care unit. Patients in clinical trials of novel therapeutics for AKI in newborns may be stratified using this score [49].
- Risk, Injury, Failure, Renal function decline, and End-Stage Kidney Disease in Children (pRIFLE) criteria:
- To standardise the diagnosis and severity grading of AKI in children, the pRIFLE criteria were initially suggested in 2004. The RIFLE (Risk, Injury, Failure, Loss, End-stage kidney disease) criteria for AKI in adults served as the basis for the development of these pediatric-specific criteria, which were modified to account for the physiological and clinical variations between children and adults. Both serum creatinine and urine volume are considered vital signs in the pRIFLE criterion. Indicators of renal perfusion and function include urine production and serum creatinine levels. The clinical condition of the patient is also considered (for example, whether they have hypotension, fluid overload, or acid-base abnormalities; see criterion [50]).
- The pRIFLE criteria classify AKI into three grades: at-risk, injured, and failed. To further characterise the long-term effects of AKI, the criteria contain two additional phases, loss and end-stage renal disease [51]:
- A blood creatinine 1.5 times baseline or a urine output 0.5 mL/kg/h or less for 6 hours constitutes the risk stage. Mild AKI is associated with a favourable prognosis at this point. If your serum creatinine level rises to double its normal level or if your urine output drops to less than 0.5 mL/kg/h for 12 hours, you have reached the injury stage. Moderate AKI is present, along with an increased risk of complications.
- An rise in serum creatinine of three times the normal range, a decrease in urine production to less than 0.3 mL/kg/h for 24 hours, or anuria for 12 hours, all indicate the onset of the failure stage. Severe AKI and a dismal outlook define this phase.

Complete kidney failure that has persisted for more than four weeks is considered to be at the loss stage of chronic acute renal injury. At this point, kidney damage is permanent and long-term monitoring is required.

Permanent loss of kidney function needing renal replacement treatment for more than three months characterises the end-stage kidney disease stage. Damage to the kidneys is permanent at this point, necessitating renal replacement treatment for the rest of the patient's life.

Good predictive value for outcomes including renal replacement treatment required, duration of hospital stay, and death has been shown using the pRIFLE criteria. Patients may be stratified for clinical studies based on these criteria, and the criteria can also be used to guide treatment choices like determining who needs renal replacement therapy. Serum creatinine and urine output are used in the pRIFLE criterion, however these variables might be impacted by other factors such age, weight, and hydration status. The criteria also fail to account for comorbidities or the underlying aetiology of AKI, both of which may significantly affect outcomes [50].

Criteria for Acute Kidney Injury (AKI-Net):

To standardise the diagnosis and categorization of AKI in adults, the AKI-Net criteria were initially suggested in 2007. The RIFLE (Risk, Injury, Failure, Loss, End-stage renal disease) and pRIFLE (Acute Kidney Injury in Children) criteria [52] served as inspiration for the development of these new criteria.

According to the AKI-Net criteria, there are three distinct degrees of AKI, as measured by serum creatinine and/or urine output. Timeframes for these alterations and the existence of additional clinical variables are also included in the criterion [53]:

A serum creatinine rise of 0.3 mg/dL (26.5 mol/L) within 48 hours, a serum creatinine increase of 1.5 times baseline within 7 days, or a urine output of less than 0.5 mL/kg/h for 6 hours all constitute the initial stage of AKI. Mild AKI is the condition at this point.

If your serum creatinine has increased by 2 times your baseline level in the last 7 days, or if your urine production has been less than 0.5 mL/kg/h for 12 hours, then you have progressed to stage 2 AKI. This degree of AKI is classified as moderate.

The third stage of AKI is defined as an increase in serum creatinine by 3 times baseline within the previous 7 days, or a serum creatinine level of more than 4.0 mg/dL (353.6 μmol/L) with an acute increase of at least 0.5 mg/dL (44.2 μmol/L), or a urine output of less than 0.3 mL/kg/h for 24 hours, or anuria for 12 hours. Severe acute kidney injury is the hallmark of this phase.

Other clinical variables, such as hypotension, oliguria, or anuria, and the necessity for renal replacement treatment, are also included in the AKI-Net criteria. The severity and clinical course of AKI are evaluated in relation to these parameters. Good predictive value for outcomes including renal replacement treatment need, duration of hospital stay, and death has been shown for the AKI-Net criteria. Because they depend on measurements of serum creatinine and urine output, the AKI-Net criteria are susceptible to confounding variables such as age, body mass index, and hydration status. Comorbidities and the underlying aetiology of AKI [54] are not included in the criteria, which may have a significant effect on outcomes.

Baby KDIGO (kidney disease: Improving Global Outcomes) Criteria for Acute Kidney Injury

In order to standardise the process of diagnosing and categorising AKI in neonates, the Neonatal KDIGO AKI criteria were created in 2014. The AKI-Net criteria for adults served as inspiration for these standards, which also account for the special physiology of newborns. The Neonatal KDIGO AKI criteria classify AKI into three phases according to variables such as blood creatinine levels, urine output, birth weight, and postnatal age. Here are the conditions [53]:

Serum creatinine elevation of 0.3 mg/dL (26.5 mol/L) or more within 48 hours, serum creatinine elevation of 1.5 times baseline or higher within 7 days, or less than 0.5 mL/kg/hour urine output for 6-12 hours constitutes stage 1. Mild AKI is the condition at this point.

Second-stage disease is characterised by a 2-fold or higher rise in serum creatinine within 7 days or by fewer than 0.5 mL/kg/hour urine output for 12-24 hours. This degree of AKI is classified as moderate.

Levels of serum creatinine more than 4.0 mg/dL (353.6 mol/L) with an abrupt rise of at least 0.5 mg/dL (44.2 mol/L) or a urine output of less than 0.3 mL/kg/hour for 24 hours or anuria for 12 hours characterise Stage 3 disease. Severe acute kidney injury is the hallmark of this phase.

When determining whether a baby has AKI, the Neonatal KDIGO AKI criteria also factor in the child's postnatal and gestational ages. Adjusting for variations in creatinine levels at birth is done using gestational age, whereas postnatal age is utilised to account for the physiological changes that occur in the neonatal period [52].

Prediction of outcomes, such as the requirement for renal replacement treatment and death, in newborns with AKI, has been validated using the Neonatal KDIGO AKI criteria. They are also helpful in determining whether or not fluid and electrolyte management or renal replacement therapy are required. Nonetheless, the criteria do contain certain restrictions. Serum creatinine and urine output are used, and both are affected by variables including fluid balance and drug use. They also fail to account for comorbidities or the underlying aetiology of AKI, both of which might have a significant bearing on outcomes [51].

Perspectives and suggestions for the future:

Consistent efforts are needed to improve diagnostic precision by investigating new biomarkers and standardising scoring systems like STARZ in order to advance the field of neonatal acute kidney injury (AKI). Risk factors for acute kidney injury (AKI) may be reduced by measures such as improving fluid management, minimising exposure to nephrotoxic medications, and providing individualised care to high-risk newborns. Innovations in management tactics, especially

in designing individualised renal replacement medicines and understanding the effect of fluid excess, offer promise. For holistic treatment models and better newborn AKI outcomes, it is essential to conduct longitudinal research for thorough outcome evaluation and to collaborate across healthcare domains.

7-Conclusions

There are several prenatal and postnatal variables that contribute to the development of neonatal acute kidney injury. The research highlights the critical need for standardised diagnostic criteria as well as the need of a holistic approach to diagnosis. It also draws attention to the changing landscape of management techniques and the promise of prognostic and therapy guidance scoring systems like STARZ for this at-risk group.

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