



## Evaluation of factors responsible for acute renal failure in septicemic neonates from Bihar region

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### Abstract

Acute renal failure (ARF) is defined as a significant acute decline in glomerular filtration rate (GFR), usually associated with uraemia, which may or may not be associated with a fall in urine output. It is a frequent complication in critically ill patients and associated with an excess mortality. In fact, ARF is nowadays mostly observed as part of the multi-organ dysfunction syndrome in severe sepsis and septic shock. [7] Hence based on above findings the present study was planned for Evaluation of Factors Responsible for Acute Renal Failure in Septicemic Neonates from Bihar Region.

The present study was planned in Department of Pediatrics, Mata Gujri Memorial Medical College and Lions Seva Kendra Hospital, Kishanganj, Bihar, India. In the present study 100 cases of neonates diagnosed with the neonatal sepsis were enrolled in the present study. Out of that 28 cases were diagnosed with the Acute Renal Failure (ARF) were evaluated and discussed with the already reported literature. Risk factors evaluated for fatality in sepsis associated ARF included gestational age, weight, early onset, culture positivity, associated meningitis, asphyxia, shock, administration of nephrotoxic drugs and presence of oliguria.

The data generated from the present study concludes that ARF is a very common entity among septic neonates. Low birth weight is an important risk factor for the development of ARF in septic neonates. The latent period for the development of ARF in neonatal sepsis is short. The high mortality among septic neonates with ARF stresses the need for septic neonates to be screened for renal failure.

**Keywords:** acute renal failure; neonatal sepsis, factors, Bihar, etc

### 1. Introduction

Acute kidney injury (AKI), formerly called acute renal failure (ARF), is commonly defined as an abrupt decline in renal function, clinically manifesting as a reversible acute increase in nitrogen waste products (measured by blood urea nitrogen [BUN] and serum creatinine levels) over the course of hours to weeks. Acute kidney injury is a common entity in the emergency department (ED). Emergency physicians play a critical role in recognizing early AKI, preventing iatrogenic injury, and reversing the course. [1]. Imaging studies are important in the emergent workup of suspected postrenal azotemia. The distinction between community- and hospital-acquired AKI is important for the differential diagnoses, treatment, and eventual outcome of patients with AKI.

In critically ill patients, renal dysfunction severity can also be evaluated by combining renal function with functional parameters of other organs (eg, the Sequential Organ Failure Assessment [SOFA] score). In a study to assess the definition of renal dysfunction in multicenter, randomized, controlled trials involving critically ill patients, the renal SOFA score is the most commonly used system to quantify renal function at baseline or as a secondary outcome. [2]. Changes have been assessed in critically ill patients over time or during treatment and have also been used to evaluate

the degree of organ dysfunction in sepsis. In addition to assessing patient status, renal criteria can be used for prognosis. In patients with kidney injury, measuring changes in the SOFA score in the first 24 hours of renal replacement therapy (RRT) can identify patients at high risk for mortality. However, individual SOFA scores have been shown to be poor at predicting early (7 day) mortality in patients with septic AKI who require continuous RRT [3].

Stabilize acute life-threatening conditions and initiate supportive therapy. Watch for electrocardiographic evidence of hyperkalemia. Treatment of AKI ideally should begin before the diagnosis is firmly established. A high index of suspicion often is necessary to diagnose early AKI. Significant decreases in GFR frequently occur before indirect measures of GFR reveal a problem. All seriously ill medical patients (eg, elderly patients, diabetic patients, hypovolemic patients) should have AKI included early in their differential diagnosis. After providing an adequate airway and ventilation, focus on fluid management of the patient with AKI.

Reversal of hypovolemia by rapid fluid infusion often is sufficient to treat many forms of AKI. However, rapid fluid infusion can result in life-threatening fluid overload. Placement of a urinary catheter early in the workup of a patient with KI not only allows diagnosis and treatment of

urethral and bladder outlet urinary obstruction but also allows for accurate measurement of urine output. Routine use of urinary catheters should be tempered by consideration of the inherent risks of catheter-associated infections. The principal methods of renal replacement therapy (RRT) are intermittent hemodialysis (IHD), continuous venovenous hemodiafiltration (CVVHD), and peritoneal dialysis (PD). Each has advantages and limitations.

Mortality rates for AKI have changed little since the advent of dialysis at 50%.<sup>[4]</sup> This curious statistic simply reflects the changing demographics of AKI from community- to hospital-acquired settings. The mortality for hospital-acquired AKI is reported to be as high as 70% and is directly correlated to the severity of the patient's other disease processes. The mortality among patients presenting to the ED with prerenal AKI may be as low as 7%.

The inhospital mortality rate for AKI is 40-50%. The mortality for ICU patients with AKI is higher (>50% in most studies), particularly when AKI is severe enough to require dialysis treatment. ICU patients with sepsis-associated AKI have significantly higher mortality rates than do nonseptic AKI patients. In addition, the pooled estimate for general ICU patients with AKI shows a stepwise increase in relative risk for death through the risk, injury, and failure classifications of the RIFLE criteria in AKI patients versus non-AKI patients. The survival rate is nearly 0% among patients with AKI who have an Acute Physiology and Chronic Health Evaluation II (APACHE II) score higher than 40. In patients with APACHE II scores of 10-19, the survival rate is 40%.<sup>[5]</sup>

AKI is not a benign disease. One study noted a 31% mortality rate in patients with AKI not requiring dialysis, compared to a mortality rate of only 8% in matched patients without AKI. Even after adjusting for comorbidity, the odds ratio for dying of AKI was 4.9, as compared to patients without AKI.

With the advent of dialysis, the most common causes of death associated with AKI are sepsis, cardiac failure, and pulmonary failure. Interestingly, patients who are older than 80 years with AKI have mortality rates similar to those of younger adult patients. Pediatric patients with AKI represent a different set of etiologies and have mortality rates averaging 25%.

Mortality rates are generally lower for nonoliguric AKI (>400 mL/day) than for oliguric (< 400 mL/day) AKI, reflecting the fact that nonoliguric AKI is usually caused by drug-induced nephrotoxicity and interstitial nephritis, which have few other systemic complications. Renal ultrasonography is the test of choice for urologic imaging in the setting of acute renal failure. [6] It has excellent sensitivity and specificity for detecting hydronephrosis due to obstruction, and it can also give valuable information other than ruling obstruction in or out. In critically ill patients, bedside ultrasonography warrants special consideration, because it can quickly diagnose treatable etiologies of the patient's condition and give guidance for fluid resuscitation. Renal ultrasonography is useful for evaluating existing renal disease and obstruction of the urinary collecting system. However, obtaining images of the kidneys can be technically difficult in patients who are obese, as well as in those with abdominal distention from ascites, gas, or retroperitoneal fluid collection. The degree of hydronephrosis found on ultrasonograms does not

necessarily correlate with the degree of obstruction. Mild hydronephrosis may be observed with complete obstruction if found early. Small kidneys suggest chronic renal failure.

Bipolar renal length is easy to assess, and kidneys smaller than 9 cm suggest chronic renal failure. Renal parenchyma should be isoechoic or hypoechoic when compared with that of the liver and spleen; hyperechogenicity indicates diffuse parenchymal disease. Color Doppler ultrasound allows assessment of renal perfusion and can allow diagnosis of large-vessel etiologies of AKI. Doppler scans can be quite useful in the diagnosis of thromboembolic or renovascular disease. Increased resistive indices can be observed in patients with hepatorenal syndrome.

Acute renal failure (ARF) is defined as a significant acute decline in glomerular filtration rate (GFR), usually associated with uraemia, which may or may not be associated with a fall in urine output. It is a frequent complication in critically ill patients and associated with an excess mortality. In fact, ARF is nowadays mostly observed as part of the multi-organ dysfunction syndrome in severe sepsis and septic shock<sup>[7]</sup>. Hence based on above findings the present study was planned for Evaluation of Factors Responsible for Acute Renal Failure in Septicemic Neonates from Bihar Region.

### Methodology

The present study was planned in Department of Pediatrics, Mata Gujri Memorial Medical College and Lions Seva Kendra Hospital, Kishanganj, Bihar, India. In the present study 100 cases of neonates diagnosed with the neonatal sepsis were enrolled in the present study. Out of that 28 cases were diagnosed with the Acute Renal Failure (ARF) were evaluated and discussed with the already reported literature. Risk factors evaluated for fatality in sepsis associated ARF included gestational age, weight, early onset, culture positivity, associated meningitis, asphyxia, shock, administration of nephrotoxic drugs and presence of oliguria.

A thorough clinical examination to see for urethral, meatal abnormalities, palpable bladder and kidneys was done. None of the neonates included in the study had any gross congenital anomaly of the kidney or urinary tract on clinical examination. All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

### Results and Discussion

Sepsis, a commonly encountered scenario in an intensive care unit (ICU), often leads to multi-organ dysfunction and the kidney is one of the organs frequently afflicted. Acute kidney injury (AKI) occurs in about 19% patients with moderate sepsis, 23% with severe sepsis and 51% with septic shock, when blood cultures are positive.

Neonatal AKI is usually transient and reversible with appropriate treatment of underlying disorders<sup>[8]</sup>. Some known contributing factors for AKI include: neonatal septicemia, respiratory distress syndrome, low birth weight, prematurity, cesarean section, intracranial hemorrhage, perinatal asphyxia, intubation at birth, preeclampsia, premature rupture of membranes, male gender, surgical procedures, mechanical ventilation with high positive airway pressure, dehydration, genitourinary abnormality,

necrotizing enterocolitis, drug nephrotoxicity, and antenatal steroid treatment. The kidneys of neonates are particularly susceptible to hypo-perfusion because of the physiologic characteristics of neonatal kidneys, including high renal vascular resistance, high plasma renin activity, low glomerular filtration, decreased intra-cortical perfusion rate and decreased re-absorption of sodium in the proximal tubules in the first days of a neonate.<sup>[9]</sup> Thus, newborn infants are vulnerable to acute tubular necrosis or cortical necrosis. Acute renal failure (ARF) is commonly present among sick neonates.<sup>[10-11]</sup> While asphyxia, Respiratory distress syndrome (RDS) and urogenital anomalies are commonly reported causes of ARF in the West.<sup>[12]</sup> Sepsis is the leading cause of ARF in the preliminary reports from India.<sup>[9, 39]</sup> Earlier studies have focused on perinatal asphyxia as the cause of ARF.

Severe sepsis and septic shock are the most common causes of mortality in non-coronary intensive care units (ICUs) accounting for an estimated annual number of 60 000 deaths in Germany<sup>[4]</sup>. The 90-day mortality rates of severe sepsis and septic shock are as high as 54%.<sup>[13]</sup> the combination of ARF and severe sepsis was reported to carry a mortality of up to 70% whereas the mortality of ARF alone is 40–45%.<sup>[14-15]</sup> However, it is unclear whether such estimates are truly representative for all hospitalized patients, since tertiary care centres are probably overrepresented in clinical trials. Moreover, especially in septic patients, it remains controversial whether ARF is an independent predictor of death or merely an indicator of disease severity and whether ARF-associated mortality is related to other organ failures.

**Table 1:** Clinical Profile of Study Population

Total number of neonates with sepsis	100
Mean gestational age	33 – 39 weeks
Preterm	85
Mean weight at presentation	1550 –2620 gm
Mean age at presentation	6 – 7days
Early onset sepsis (≤ 72 hrs)	52
Late onset sepsis (> 72 hrs)	48
Culture positive sepsis	19
Meningitis	21
Survival	63
ARF	28
Oliguric	4
Non oliguric	24
ARF at presentation	17

**Table 2:** Comparison of Septic Neonates with ARF and Without ARF

	With ARF	Without ARF
No. of Subjects	28	72
Mean gest. Age (wks)	33 – 38	32 – 39
Term ≥ 37 wk	12	42
Preterm < 37 wk	14	30
Mean weight (gms)	1620 – 2459	1599 – 2540
Wt< 2500 g	16	46
Mean age at presentation days	5 – 6	7 – 8
Sepsis Early	14	37
Sepsis Late	12	35
Culture positive sepsis	4	14
Meningitis	13	18
Co morbid conditions	11	19
Shock	21	19
Mortality	5	16

It is common knowledge that optimization of systemic

hemodynamics and effective intravascular volume is important to prevent ARF in patients with sepsis. Unfortunately, what constitutes optimal hemodynamics remains largely undefined. In a multicenter randomized trial, volume expansion and vasopressor therapy aimed at achieving supranormal values for cardiac index and normal values for mixed venous oxygen saturation had no effect on mortality or on the incidence and severity of ARF.<sup>[16]</sup> In contrast, early institution of treatment to increase central venous oxygen saturation to 70% or higher resulted in a lower mortality and less severe organ dysfunction in patients with severe sepsis or septic shock.<sup>[17]</sup>

The exact pathophysiology of sepsis-induced AKI is not known, however, it is generally accepted that it has a multi-pronged injury pathway. This form of AKI has components of: ischemia-reperfusion injury, direct inflammatory injury, coagulation and endothelial cell dysfunction, and apoptosis.<sup>[18]</sup>

Moreover, based on recent evidence we may presume that the pathophysiologic mechanisms of sepsis-induced AKI are different from non-septic AKI.<sup>[19]</sup> this would translate to the issue that sepsis-induced AKI may entail different therapeutic strategies.

Gram-negative sepsis, which is more common in India, is independently associated with AKI.<sup>[20]</sup> An elevated plasma concentration of endotoxin (lipopolysaccharide; LPS) is often found in the systemic circulation during sepsis, regardless of the type of the infecting microorganism,<sup>[21]</sup> possibly as a result of the translocation of LPS originating from the resident Gram-negative flora of the gut.<sup>[22]</sup> during the inexorable downward spiral of sepsis, LPS, then cytokines, and consequently nitric oxide (NO) is released.

The neonatal kidney is particularly vulnerable to the effects of hypoperfusion since the renal vascular resistance and plasma renin activity are high. Consequently, renal blood flow is proportionately more reduced in neonates. Acute tubular necrosis (ATN) has many parallels with the physiologic characteristics of neonatal kidney-the low glomerular filtration rate (GFR), decreased intercortical perfusion, decreased proximal reabsorption of sodium and increased plasma renin activity<sup>[23]</sup>.

**Conclusion:**

The data generated from the present study concludes that ARF is a very common entity among septic neonates. Low birth weight is an important risk factor for the development of ARF in septic neonates. The latent period for the development of ARF in neonatal sepsis is short. The high mortality among septic neonates with ARF stresses the need for septic neonates to be screened for renal failure.

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