

Acute Kidney Failure in Neonatal Period

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Introduction. Acute kidney failure (AKF) is a common clinical problem in neonatal intensive care units and is usually associated with a contributing condition such as sepsis, asphyxia, and heart failure. The aim of this study was to determine the types, frequency of associated contributing conditions, and short-term outcome of neonatal AKF.

Materials and Methods. Medical records of neonates with a diagnosis of AKF from March 2003 to September 2006 were studied in a tertiary care children's hospital in Tabriz, Iran.

Results. Of 6042 hospitalized neonates, 151 with documented AKF (100 boys and 51 girls) were reviewed in the study. Ninety-one patients (60.3%) had been referred from other cities. Fifty-seven patients (37.7%) developed AKF following a surgery. Causes of AKF were intrinsic kidney failure in 52.3%, prerenal in 42.4%, and postrenal in 5.3%. Oliguria was observed in 72.2% of the patients. Perinatal asphyxia was present in 29.8% of the neonates, sepsis in 28.5%, respiratory distress syndrome in 25.2%, dehydration in 24.2%, and heart failure in 21.2%. Most patients (85.4%) had more than 1 associated contributing condition. Mortality rate was 20.5%. Most patients (76.2%) were discharged with normal kidney function and 3.3% with diminished kidney function. Initial admission to NICU, female sex, septicemia, and the need for mechanical ventilation were associated with a higher mortality rate.

Conclusions. The frequency of associated contributing conditions and short-term outcome of neonatal AKF in our institution is comparable with other studies; however, intrinsic kidney failure comprises the most common form of AKF in our patients.

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INTRODUCTION

Acute kidney failure (AKF) occurs in 3.4% to 24% of neonates admitted to neonatal intensive care units (NICUs).¹⁻³ The most common form of AKF in neonates is prerenal failure which is due to renal hypoperfusion or ischemia.⁴ Prerenal failure may result in intrinsic kidney failure if not treated promptly. The kidneys of neonates are particularly susceptible to hypoperfusion, because of the physiologic characteristics of neonatal kidneys; high renal vascular resistance, high plasma renin activity,

low glomerular filtration rate, decreased intercortical perfusion, and decreased reabsorption of sodium in the proximal tubules are the susceptibilities of the kidneys in the first days of a neonate.⁵ Thus, newborn infants are vulnerable to acute tubular necrosis or cortical necrosis.

The cause of AKF in neonates is multifactorial, and usually there is one or more associated contributing factors with neonatal AKF.⁶⁻⁷ In most studies, perinatal asphyxia and sepsis are the most common associated conditions.⁸⁻¹¹ The

other conditions associated with the development of AKF in the newborns are respiratory distress syndrome, dehydration, congestive heart failure, and nephrotoxic drugs.⁴ The short-term outcome of therapy for AKF in newborns is highly dependent on the underlying etiology of AKF, the condition of other organs, and the facilities for renal replacement therapy. Mortality is more frequent and morbidity is much worse in neonates with multiorgan failure.¹²

There are limited information on the characteristics of AKF in the medical institutions of Iran. The aim of this study is to evaluate the types, frequency of associated contributing conditions, and short-term outcomes of AKF in neonates admitted in our institution, which is a referral and tertiary care center in north-west of Iran, and to compare the results with those reported in the literature.

MATERIALS AND METHODS

This study was conducted in the neonatal unit of the Children's Hospital of Tabriz, Iran. The study was approved by Ethical Committee of Tabriz University of Medical Sciences. Medical records of admitted neonates diagnosed with AKF between March 2003 and September 2006 were studied. Acute kidney failure was defined as a plasma creatinine level higher than 1.5 mg/dL,¹⁴ or a blood urea nitrogen (BUN) level higher than 20 mg/dL on 2 separate occasions at least 12 hours apart, while maternal kidney function was normal.⁵ Oliguria was defined as urinary output less than 1 mL/kg/h. Oliguric neonates without fluid overload were considered to have prerenal AKF if their BUN-creatinine ratio was more than 20, their urinary concentration of sodium was less than 20 mEq/L, and they rapidly responded to fluid challenge. Response to fluid challenge was defined as resolving the oliguria after infusion of up to 3 doses of hypertonic saline solution, 20 mL/kg, and restoration of creatinine level to less than 1.5 mg/dL in a control measurement after 12 hours. Neonates who had obstruction in the urinary tract system based on imaging studies (ultrasonography or renal scintigraphy) were considered as postrenal failure. The remaining patients in whom the ratio of BUN to creatinine was less than 20 and urine sodium concentration was greater than 40 mEq/L were considered to have intrinsic kidney failure if they did not respond to fluid challenge.

Sepsis was diagnosed in symptomatic patients on the basis of either a positive blood culture for microorganisms or a positive sepsis screen (if 2 or more of the following criteria were present: high erythrocyte sedimentation rate for age, leukocyte count less than $5 \times 10^9/L$, immature/total neutrophil count greater than 0.2, and positive serum C-reactive protein).⁵ The short-term outcome was determined by following the clinical course until discharge from hospital and was categorized into 3 groups of "death," "discharge with normal kidney function," and "discharge with diminished kidney function." Neonates who did not have enough data in their records, those who died within the first 24 hours of admission, and patients with maternal history of kidney failure were excluded.

The data collected for each patient were demographic features, clinical and laboratory findings, short-term outcome, and presence of any associated contributing conditions including perinatal asphyxia, sepsis, respiratory distress syndrome, dehydration, heart failure, exposure to nephrotoxic drugs (indomethacin, angiotensin-converting enzyme inhibitors, aminoglycosides, and vancomycin), congenital anomalies of the urinary tract system, and history of surgical operation. The collected data were analyzed by the SPSS software (Statistical Package for the Social Sciences, version 14.0, SPSS Inc, Chicago, Ill, USA). All quantitative data were expressed as mean \pm standard deviation. The chi-square test was used for comparison of mortality frequencies between groups. A *P* value less than .05 was considered as significant.

RESULTS

Of 6042 admitted neonates during the studied 3.5 years, 162 patients were diagnosed with AKF (2.7%). Eleven neonates were excluded based on the criteria determined for the study, and data of 151 patients, including 100 boys (66.2%) and 51 girls (33.8%), were reviewed. Of the 151 neonates, 106 (70.2%) were full-term, 38 (25.2%) were preterm, and 7 (4.6%) were postterm. Parents of 60 patients (39.7%) lived in Tabriz and 91 patients (60.3%) had been referred from other cities of the East Azarbaijan province, in the northwest of Iran. Oliguria was observed in 109 patients (72.2%). Sixty-two patients (41.1%) were initially admitted to the NICU and 89 (59%) to the neonatal unit. Table 1 demonstrates the age, weight, and laboratory findings of the

Table 1. Demographic Features and Laboratory Findings of 151 Neonates With Acute Kidney Failure

Characteristics	Mean Value (Range)
Age at admission, d	5.3 ± 6.2 (2 to 28)
Gestational age, w	37.7 ± 3.5 (28 to 44)
Weight at admission, g	2769.0 ± 764.9 (1100 to 4600)
Plasma creatinine, mg/dL	3.98 ± 2.40 (1.6 to 12.0)
Blood urea nitrogen, mg/dL	74.2 ± 29.3 (35 to 179)
Plasma sodium, mEq/L	135.2 ± 12.9 (114 to 174)

neonates at admission.

The cause of AKF was prerenal failure in 64 patients (42.4%), intrinsic kidney failure in 79 (52.3%), and postrenal failure in 8 (5.3%). The frequency of each associated contributing condition is shown in Table 2. One hundred and twenty-nine patients (85.4%) had more than 1 associated contributing condition. Seventy-three patients (48.3%) developed AKF after admission to the hospital, 57 of whom (37.7%) developed AKF following a surgical operation. The most common cause of surgery was gastrointestinal anomalies (82.4%), including imperforated anus in 29, intestinal obstruction in 9, esophageal atresia in 7, and intestinal volvulus in 2 patients. Urinary anomalies were diagnosed in 26 patients, including vesicoureteral reflux in 6; renal hypoplasia in 5; posterior urethral valve in 4; unilateral renal agenesis in 2; and polycystic kidney, multicystic dysplastic kidney, and ureteropelvic junction obstruction, each in 3 patients.

Thirty-one neonates (19 girls and 12 boys; 20.5%) died during their hospital stay in the NICU, 115 (76.2%) were discharged with normal kidney function, and 5 (3.3%) with infantile polycystic kidney and bilateral renal hypoplasia were discharged with diminished kidney function. The frequency of death in the NICU (22 of 62; 35.5%) was significantly more than that in the neonatal unit (9 of 89; 10.1%). Girls were significantly more

Table 2. Associated Contributing Conditions to Acute Kidney Failure in 151 Neonates

Contributing Condition	Number (%)
Perinatal asphyxia	45 (29.8)
Sepsis	43 (28.5)
Respiratory distress syndrome	38 (25.2)
Dehydration due to feeding problem	37 (24.2)
Heart failure	32 (21.2)
Nephrotoxic drug administration	31 (20.5)
Urological anomalies	26 (17.2)

frequent (19 of 51; 37.2%) than boys (12 of 100; 12%) among the dead cases ($P = .001$). Sepsis was significantly more frequent in the patients who died than in those who survived ($P = .01$). Also, of 37 patients who needed mechanical ventilation, 14 died (37.9%). This rate was significantly higher than in those who did not need mechanical ventilation ($P = .005$).

DISCUSSION

The frequency of AKF in our study (2.6%) is lower than that reported in the literature, probably because we enrolled all admitted neonates (both in the NICU and neonatal unit) in the study. The male-female ratio in our study was 2:1. Airede and colleagues reported a male-female ratio of 3.3:1 in neonates with AKF.³ The high frequency of AKF in boys may be due to the susceptibility of boys to some perinatal disorders such as sepsis and respiratory distress syndrome.

Acute kidney failure in neonates predominantly manifests with oliguria. The incidence of oliguria varies from 46% to 93% in different studies.⁶ In our study, 72% of patients were oliguric, that is similar to other studies. We found intrinsic kidney failure more frequently than prerenal failure (52% versus 42.4%) that is different from other studies. It should be noted that our hospital is a referral tertiary care center, and about 60% of patients had been referred from other surrounding cities, and probably most cases of prerenal failure had received primary treatment in another health centers. Moreover, inadequate supportive care during transportation of neonates should be considered as a possible cause of developing AKF. Hypothermia, inadequate feeding, and hypoxia during transportation may cause acute injury to the kidneys in a neonate who is referred for any other reason. Further studies on the quality and safety of neonatal transportation system in our area are needed in order to evaluate this hypothesis.

Acute tubular necrosis is the most common form of intrinsic kidney failure in newborns,⁴ which is reversible unless it is associated with cortical necrosis. In our study, of 79 patients with intrinsic kidney failure, 47 recovered completely. Although we did not have enough evidence, these cases might be considered as acute tubular necrosis. However, definite diagnosis of acute tubular necrosis is not possible without a Histopathological examination

of the kidney tissue.

A large number of our patients (37.7%) developed AKF following a surgical operation. This shows the necessity of a careful attention to perioperative supportive management of neonates undergoing operation. Although surgery per se is not a predisposing factor of AKF, a constellation of associated risk factors such as dehydration, hypotension, hypoxia, nephrotoxic drugs, hemorrhage, and infections may cause AKF in neonates undergoing surgery.

In line with other studies, perinatal asphyxia and sepsis were the most frequent conditions accompanying AKF in our study. Perinatal asphyxia was detected in 29.8% of our patients. In the study of Airede and colleagues, perinatal asphyxia was found in 53.4% of AKF neonates.³ Renal involvement is frequent in neonates with perinatal asphyxia, which correlates with the severity of neurological damage.¹³⁻¹⁵ Nouri and coworkers observed AKF in 17.2% of neonates who admitted for hypoxic-ischemic encephalopathy.¹³ Since AKF associated with asphyxia is predominantly nonoliguric, serum creatinine level should be monitored daily in severely asphyxiated neonates.¹ If only urinary output is considered as indicator of AKF, most kidney failure cases in asphyxiated neonates will be missed.

Sepsis was observed in 28.5% of our patients and in 22.2% of the patients studied by Agras and associates.² A variety of mechanisms, including shock, disseminated intravascular coagulation, hemorrhage, and cardiac failure may cause AKF in septic neonates. In a study by Mathur and coworkers in India, 26% of septic neonates developed AKF.⁵ Mortality of AKF among septic neonates is high, and reportedly 50% to 78% of the cases end up with death.⁵ Like other studies, mortality of septic neonates was significantly higher than nonseptic patients in our study.

In our study, the overall mortality frequency of neonates with AKF was 20.5%; however, this in neonates admitted to NICU was higher (35.4%). Airede and colleagues reported a mortality rate of 51.2% in Nigerian newborns with AKF,³ and Agras and coworkers reported a rate 24.4% in neonates with AKF in NICU.²

CONCLUSIONS

The frequency of associated contributing

conditions and short-term outcome of neonatal AKF in our study was similar to those reported in the literature; however, in contrast to other studies, intrinsic kidney failure was the most common form of AKF in our patients. Initial admission to NICU, female sex, septicemia, and the need for mechanical ventilation were associated with higher rate of mortality. This study showed that in our hospital, most neonates with AKF had been referred from other surrounding cities and 37.3% of the patients developed AKF after a surgical operation. Multivariate analysis is necessary to evaluate the accurate risk factors of developing AKF in neonates and in particular, those who undergo surgery. We recommend that neonates undergoing surgery and those associated with contributing factors such as asphyxia, sepsis, dehydration, and heart failure be carefully evaluated for kidney failure.

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CONFLICT OF INTEREST

None declared.

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