Original Article

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Predictors of Mortality in Out Born Neonates with Acute Renal Failure; an Experience of a Single Center

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Abstract

Objective: To evaluate the incidence, etiology, outcome, and predictors of mortality in neonates with Acute Renal Failure (ARF) in an out born Neonatal Intensive Care Unit (NICU) of India.

Methods: A retrospective analysis of case records of out born neonates, who had ARF at admission or developed ARF during NICU stay, from January to December 2011 (one year) was done.

Findings: Out of the total 456 neonates admitted during the study period, 44 (9.6%) neonates with ARF (32 males, 12 females) were studied. Their mean gestational age, weight, and age at admission was 34.7±3.9 weeks, 2100±630 grams, and 2.1±6.3 respectively. Causes of ARF were pre-renal in 22 (50%), intrinsic renal failure in 16 (36.3%), and post-renal in six (13.6 %). Oliguria was present in 29 neonates. Neonatal sepsis was the commonest cause of ARF, followed by perinatal asphyxia, respiratory distress syndrome, and genitourinary anomalies. ARF was present at admission in 37 neonates. The mortality rate was 15.9% (7/44). Thirty-seven (84%) were discharged with complete recovery of renal functions and followed for six months. Shock, oliguria, need for mechanical ventilation, and presence of disseminated intravascular coagulopathy (DIC) emerged as predictors of mortality in neonates with ARF.

Conclusion: The incidence and mortality rate of neonatal ARF were 9.6% and 15.9% respectively in our out born NICU. Neonatal sepsis was the commonest cause of ARF followed by perinatal asphyxia. Shock, oliguria, need for mechanical ventilation, and presence of DIC were associated with poor outcome.

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Introduction

The incidence of Acute Renal Failure (ARF) in neonates ranges from 2.6% to 25% of all admissions in Neonatal Intensive Care Units (NICU)[1-10]. The commonest cause of ARF in neonates is pre-renal failure, which may result in intrinsic kidney failure if not treated promptly[11]. In published studies, perinatal asphyxia and sepsis are the most common associated conditions followed by respiratory distress syndrome (RDS), dehydration, congestive heart failure, and nephrotoxic drugs[1-11]. The outcome depends on the underlying etiology of ARF, the condition of other organs, and the facilities available. Mortality and morbidity is more in neonates with multi-organ failure[12].

Most of the previous studies were done in inborn neonates. There is limited information available on the characteristics of out born

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neonatal ARF from India. Therefore, the present study was undertaken to know the incidence, etiology, outcome, and predictors of mortality in neonates with ARF in an out born NICU of India.

Subjects and Methods

This retrospective study was conducted in the 20-bedded NICU of Maulana Azad Medical College and associated Chacha Nehru Bal Chikitsalaya, Delhi (India) from January 2011 to December 2011(one year). The Institutional Scientific Committee approved the study.

All neonates, admitted with ARF or developed ARF during NICU stay, irrespective of their gestational age, birth weight, and postnatal age were included. Neonates who left against medical advice (LAMA), or died within 24 hours of admission were excluded. The demographic profile, clinical, and biochemical markers and presence of risk factors were collected in a predesigned proforma. Baseline values of serum creatinine, blood urea nitrogen (BUN), and repeat BUN/creatinine levels (done 24 hourly) were noted.

ARF was defined as an anuria (no urine voided for at least 24 hours) or documented oliguria less than 1 ml/kg/hr together with either BUN of more than 40 mg/dl or serum creatinine concentration of more than 1.5 mg/dl with normal maternal renal functions for both term and preterm babies. Non-oliguric ARF was defined when urine output was more than 1 ml/kg/hour with abnormal renal functions[6]. Oliguric neonates without fluid overload were considered to have pre-renal ARF, if their BUN/creatinine ratio was more than 20, their urinary concentration of sodium was less than 20 meq/L, and responded to fluid challenge. Response to fluid challenge was defined as resolving the oliguria after bolus of up to three doses of isotonic saline solution, 10 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) were considered as post-renal failure. The remaining patients in whom the ratio of BUN/creatinine was less than 20 and urine sodium concentration was more than 40 meq/l were considered to have intrinsic kidney failure if they did not respond to fluid challenge.

Sepsis was diagnosed in symptomatic neonates 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: leukocyte count less than 5×10^9/l, high erythrocyte sedimentation rate for age, immature/total neutrophil count greater than 0.2, and positive C-reactive protein)[6]. Sarnat and Sarnat staging was used for defining hypoxic-ischemic encephalopathy (HIE). Complete recovery was defined when urine output was more than 1ml/kg/hour with normal serum BUN/creatinine for that age. Ultrasonic imaging of kidneys was carried out for size, echo texture, and cortico-medullary differentiation.

The SPSS software (Statistical Package for the Social Sciences, version 12.0) analyzed the collected data. All quantitative data were expressed as mean±standard deviation. The chi-square test was used for comparison of mortality frequencies between groups. *P* value of <0.05 was considered as significant.

Findings

Of 456 neonates admitted during the study period, 44 (9.6%) were diagnosed with ARF (32 males and 12 females), 24 were term and 20 preterm. ARF was present at admission in 37 neonates. Seven neonates developed ARF during hospital stay, of which four had RDS and three sepsis. Twenty-one, nine, and three were low birth weight (LBW), very low birth weight (VLBW), and extremely low birth weight (ELBW) respectively. Twenty-nine were appropriate for gestational age (AGA), and 15 were small for gestational age (SGA). Table 1 demonstrates the demographic profile and laboratory findings of neonates with ARF. Thrombocytopenia was present in 22, hyperkalemia in 21, hypocalcaemia in 12, and hyponatremia in four neonates.

The causes of ARF were pre-renal in 22 (50 %), intrinsic renal failure in 16 (36.3%), and post-renal in six (13.6 %). Oliguria was present in 29 (65.9%) neonates at the time of admission. Eight

Table 1: Demographic profile and laboratory findings of neonates with acute renal failure (n=44)

Parameter	Mean (SD)	Median
Age at admission (days)	2.1 (6.3)	3
Gestational age (weeks)	34.7 (3.9)	36
Weight at admission (grams)	2100 (630)	2098
Systolic blood pressure (mm Hg)	58.6 (4.8)	-
Plasma creatinine (mg/dL)	2.78 (0.88)	-
Blood urea nitrogen (mg/dL)	63.8 (64.1)	-
Serum sodium (mEq/L)	138.4 (5.2)	-
Serum potassium (mEq/L)	4.8 (0.6)	-
Bicarbonate level (mEq/L)	16.3 (4.3)	-
Duration of NICU stay (days)	6.02 (7.33)	-

SD: Standard Deviation

neonates had proteinuria, four had microscopic hematuria, and three had both proteinuria and hematuria. Etiology of neonatal ARF and their outcome is shown in Table 2.

Neonatal sepsis, the commonest cause of neonatal ARF in the present study, accounted for 61.3% and was associated with the highest mortality rate of 57.1%. Oliguria was present in 70.3%. Peritoneal dialysis (PD) was required in two neonates, both died. Organisms grew in ten (37%) neonates with sepsis and the rest were sepsis screen positive.

Perinatal asphyxia, the second common cause accounted for 22.7%, but did not account for any mortality. All neonates were in HIE stage II at the time of admission. Oliguria was present in four and none required PD. Seven were term, three preterm, and two LBW.

RDS accounted for four (9.0%) neonates, out of which three died. Their median gestational age, birth weight, and age of presentation were 26 weeks, 860 grams and 2 days respectively. Oliguria was present in three. Three were ELBW and ≤28 weeks. Genitourinary anomalies were diagnosed in three term neonates, viz posterior urethral valve, unilateral renal agenesis and polycystic kidney. Oliguria was present in all three but none required PD. Of the study group, seven (15.9%) neonates died, five were preterm and two terms. Oliguria was present in six. Thirty-seven (84.1%) neonates were discharged with complete recovery of renal functions and followed for six months. Sonographic abnormalities were seen in six neonates. The median duration of NICU stay was 11 days (range: 2-33days). Ventilator support was required in 15 (34.0%) neonates for median duration of 6 days (range: 2-11 days). Ionotropes were required in 25 (56.8%) neonates. The factors associated with poor outcome in neonatal ARF are shown in Table 3.

Discussion

The incidence of neonatal ARF was 9.6% in the present study, with a male:female ratio of 2.6:1. The high frequency of ARF in males may be due to susceptibility of males to perinatal disorders. Secondly, more number of male neonates seeks medical treatment as compared to females due to the gender bias persisting in our society. The incidence of oliguria was 65.9% in our study, which falls in the reported range of 8% to 82% in recent studies[3-6,9,10]. The recent studies on

Table 2: Etiology of Neonatal Acute Renal Failure and their outcome

Etiology	Number (%) (n=44)	Mortality (%) (n=7)
Septicemia	27 (61.3%)	4 (57.2%)
Perinatal asphyxia	10 (22.7%)	0 (0%)
Respiratory Distress syndrome	4 (9.0%)	3 (42.8%)
Genitourinary Anomalies	3 (6.8%)	0 (0%)

Table 3: Poor prognostic factors associated with acute renal failure in neonates

Factors	Survived (n=37)	Expired (n=7)	*P.* value
Shock	18	7	0.01
Oliguria	22	7	0.04
Need for mechanical ventilation	8	7	0.0001
Disseminated Intravascular Coagulopathy	7	7	<0.0001

Neonatal ARF are shown in Table 4.

The causes of ARF in neonate are pre-renal failure in more than 80% of cases, intrinsic renal and post-renal failure in about 11% and 3% respectively[13]. We found pre-renal failure in 50% and intrinsic renal failure in 36.3% of neonates.

Table 4: Recent studies on neonatal acute renal failure

Study	Design & Setting	Characteristics	Incidence of ARF	Causes/Comments	Mortality
Airede et al[1] (1997)	Prospective study. Both inborn/outborn.	n= 43. M:F= 3.3:1. Term: 26, preterm: 14, post term: 3	3.9%	Causes : Asphyxia: 53.4%, Sepsis: 32.6%, Obstructive Uropathy: 9.3%, Misc.: 4.7%	51.2 %
Abu et al[2] (1998)	Retrospective study. Inborn only.	n=38, MGA: 37.6 weeks. MBW: 1900 grams, MAD: 5.6 days, Preterm=12	8%	Causes: Asphyxia: 42%, Drugs: 14%, Sepsis: 15.7%, Urinary anomalies: 9.3%, Misc.: 4.7%	45%
Agras et al[3] (2004)	Retrospective study. Inborn only.	n= 45. Both term & preterm (31.1%). MBW: 2863 grams. MAD: 6.2 days. Oliguria: 53%. PD done in 22.2%	3.4%	Causes: Asphyxia: 40%, Sepsis: 22.2%, Feeding problems: 17.8%.	24.4%
Cataldi et al[4] (2005)	Retrospective case control study. Inborn only.	Cases=71, control= 101, MGA: 27.8 weeks, MBW: 1115.98 grams, ELBW: 79%, oliguria: 8%	---	RDS: 89%, Low apgar score: 42%, PDA: 44%, Sepsis: 23%	11%
Gupta et al[5] (2005)	Prospective case–control. Inborn asphyxiated neonates.	Cases = 70, control = 28, Oliguria: 22%.	47.1%,	Oliguria, hyponatremia and abnormal sonographic scan are bad prognostic signs in ARF secondary to asphyxia.	14.1%
Mathur et al[6] (2006)	Prospective case–control. Outborn neonates with sepsis.	Case-52, control-146 mostly term, Oliguria: 15%	26%	Those with AKI more likely to have shock, DIC, meningitis and prematurity	70.2%
Lunn et al[7] (2006)	Retrospective study. Outborn neonates.	n=41. VLBW: 79%, acidosis in 59% at onset of ARF, 39% received ionotropes.	8.8%	Causes: Sepsis: 39%, Prematurity: 32%, Asphyxia: 17%, Hypotension: 10%.	24%
Mortazavi et al[8] (2009)	Retrospective study Outborn neonates.	n=151. M:F=2:1, MGA: 37.7 weeks, MBW: 2769 grams, oliguria: 72.2%, MAD: 5.3 days, term: 106, preterm: 38	2.6%	Causes: Asphyxia: 29.8%, Sepsis: 28.5%, RDS: 25.2%, Dehydration: 24.2%, Heart failure: 21.2%	20.5%
Doronjski et al[9] (2009)	Retrospective study. Inborn premature neonates.	n=16, MBW: 1265 g, Oliguria: 38%, PD done in 3 cases	25%	BW<1500 grams demonstrated the highest sensitivity, while GA< 28 weeks, sepsis and ICH grade III/IV showed high specificity in relation to ARF	25%
Viswanathan et al[10] (2012)	Retrospective case control study. Inborn ELBW neonates.	n=46, MGA: 24.7 days, MBW: 614 grams, oliguria: 82.6%	12.5%	ARF in ELBW infants is associated with an increased mortality, especially in presence of oliguria.	71.3%

ARF: Acute renal Failure; M; Male; F: Female; RDS: Respiratory Distress Syndrome; MBW: Mean Birth Weight; BW: Birth Weight; VLBW: Very Low Birth weight; ELBW: Extremly Low Birth Weight; GA: Gestational age; MGA: Mean Gestational Age; Birth Weight; PDA: Patent Ductus Arteriosus; ICH: intracranial hemorrhage; MAD: Mean Age at admission

This difference could be because our institute is a tertiary care out born NICU, receiving neonates from surrounding regions and probably most cases of pre-renal failure had already received primary healthcare in another health center. Agras et al found intrinsic renal failure in 31.1% and pre-renal in 64.4% of neonates, whereas Mortazavi et al reported intrinsic renal failure in 52% and pre-renal in 42.4% of neonates[3,8].

Neonatal sepsis was the commonest cause of neonatal ARF in our study, and accounted for 61.3% of neonates, which is higher than the reported incidence of 15.7% to 39% in previous studies [1-4,7,8]. This might be due to fact that ours is a tertiary care out born NICU and most of the neonates were sick and septic at the time of admission. Moreover, inadequate supportive care (hypothermia, hypoxia and hypoglycemia) during transportation of neonates may further predispose them to ARF. Jayashree et al reported 15% of neonates with sepsis had ARF, which was predominantly oliguric[14]. Whereas Mathur et al reported 26% of neonates with sepsis had ARF; only 15% of ARF was oliguric. We found oliguric ARF in 70.3% of neonates; however, the mortality rate was only 57.2% in comparison to 70.2% reported by others[6].

Perinatal asphyxia accounted for 22.7% of neonates, and reported incidence was 17%-56% in recent studies[1-3,5,7-8,15]. The average mortality of asphyxia associated with ARF was reported to be 14% in oliguric ARF[5]. In our study, four of the asphyxiated neonates had oliguria but none of them died. This could be because neonates with asphyxia in present study were having moderate perinatal asphyxia. Pejovac et al also demonstrated good prediction of the severity of oliguric ARF according to the degree of perinatal asphyxia[16].

Agras et al showed ARF of renal origin; need for dialysis and need for mechanical ventilation to be associated with significantly increased mortality in neonatal ARF[3]. Mortazavi et al described initial admission to NICU, female sex, septicemia, and the need for ventilation to be associated with higher mortality rate[8]. Vishwanathan et al described oliguria to be associated with increased mortality in ELBW neonates with acute kidney injury[10]. Mathur et al found shock to be a significant predictor of fatality in neonates with sepsis and ARF[6]. We found shock, oliguria, need for mechanical ventilation and presence of disseminated intravascular coagulopathy as indicators of poor prognosis.

The overall mortality was 15.9%, which is consistent with the reported mortality rates of 11-71%[1-10]. The limitations of this study include its retrospective design, small sample size, and lack of a control group. Large prospective studies are needed to understand the risk factors, incidence, and outcomes of out born neonatal ARF.

Conclusion

The incidence and mortality rate of neonatal ARF were 9.6% and 15.9% respectively in our out born NICU. Neonatal sepsis was the commonest cause of ARF followed by perinatal asphyxia, RDS, and genitourinary anomalies. Shock, oliguria, need for mechanical ventilation, and presence of DIC were identified as indicators of poor prognosis in these neonates.

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Conflict of Interest: None

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