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Prognostic Factors and Mortality Rate in Neonates with Acute Renal Injury in NICU

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Nasrin Esfandiar,[1] *
Masoumeh Mohkam,[1]
Abolfazl Afjeii,[1]
Farshid Kompani,[2]
Ilnaz Shahrazad, [1]
Mandana Naderi,[1]
Babak Otoukesh,[1]
Hamid Raiati[1]

1 Pediatric Infection research center, Shahid Beheshti University of medical science, Faculty of medicine, Tehran-Iran
2 Ahvaz University of medical science, Ahvaz-Iran

*** Corresponding Author:**
Nasrin Esfandiar
Pediatric nephrologist
Assiss. Prof.
Mofid children's hospital
Shariati ave. Tehran-Iran
Telfax: 021-22227033
E-mail:
nasrinesfandiar@gmail.com

Introduction: Acute Renal Injury (AKI) is a frequent clinical condition in the Neonatal Intensive Care Units (NICUs). Most AKI causes are preventable; performing rapid preventive, diagnostic, and therapeutic measures could prevent the potential complications. The present study was conducted to define the risk factors and mortality rates of neonates with and without AKI admitted in the NICU of a tertiary care hospital.
Materials and Methods: Demographic and biochemical data of NICU of Mahdieh Hospital were collected and analyzed. More than twofold increase in normal serum creatinine level or >0.8 mg/dl (for infants > 4 days age) was defined as AKI. All newborns were divided into two groups: with and without AKI. Risk factors and mortality rates were compared in the 2 groups.
Results: The mortality rate of newborns with AKI was 4.5%. The other risk factors for mortality in neonates with AKI were as follows: Hyaline Membrane Disease (HMD) (P <0.03), using mechanical ventilation (P <0.041), using surfactant (P <0.04), first minute Apgar score <5, PCO2 >60 mmHg (P <0.035), birth weight < 2500 g (P <0.003) and serum creatinine (SCr) level >1 mg/dl (P <0.003). ROC Curve revealed that low birth weight was the most significant risk factor for mortality of neonates with AKI admitted in the NICU.
Conclusions: Mortality related to AKI was associated with HMD, using mechanical ventilation, the need to surfactant use, low Apgar score, high blood PCO2, high serum creatinine level, and low birth weight.

Keywords: Acute Kidney Injury; Prognosis; Hospital mortality; Intensive Care Units; Neonate.

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Running Title: Prognostic Factors in Neonates with AKI

Introduction

Acute Renal Injury (AKI) is a frequent and prominent problem in Neonatal Intensive Care Units (NICUs) and it can increase mortality rate in the affected newborns per se[1]. Due to advances in pediatrics, the survival rate for critically ill neonates has improved dramatically although the mortality and morbidity rates are still considerable. The mortality rate of neonates with AKI ranges from 14 to 73% [2] and even higher in multiple organ failure patients [3]. In VLBW neonates the mortality rate is found rather higher [4]. Large number of these neonates will suffer from renal dysfunction. Among oliguric survivors of AKI secondary to asphyxia, vascular

thrombosis, hypotension and toxins, 40% show persistently low creatinine clearance and Non-oliguric neonates with AKI have much better prognosis [3].

Even a mild increase in serum creatinine level by 10-24% results in a higher mortality and morbidity [5]. The lack of a uniform definition of AKI in neonates makes it difficult to study implications of AKI. Increasing serum creatinine level is usually considered as a marker for renal dysfunction however this is a complex issue in neonates as; postnatal serum creatinine level is a reflection of maternal serum creatinine level for the first 72 hours after birth. Moreover, GRF in neonates varies greatly with increasing postnatal age. Last but not the least; dramatic fluctuations in neonatal GFR are accompanied with negligible changes in serum creatinine level. Preterm neonates show lower GFR as compared with term neonates, therefore, the normal range can be wide. Hyperbilirubinemia can interfere with measurements of serum creatinine using Jaffee method requiring caution to interpret measured serum creatinine in the first days after birth [6].
Objective: In the present study neonates hospitalized in the NICU of a tertiary care hospital in Tehran were studied to determine the risk factors for mortality and prognosis of neonates with and without AKI.

Materials and Methods

Inclusion criteria: All newborns who were admitted in a tertiary care hospital were studied.
More than twofold increase in normal serum creatinine level >0.8 mg/dl (for infants > 4 days of age) or increase in serum creatinine (SCr) level of ≥0.3 mg/dl was defined as AKI. Neonates with incomplete data were excluded.
The two groups of neonates with and without AKI were compared and analyzed in terms of age, gender, weight, sepsis, mechanical ventilation, blood PH<7.2 ,serum potassium >6 mg/dl, serum potassium <4 mg/dl, leukopenia (WBC<3000),hemoglobin<10 mg/dl, positive blood culture, First minute Apgar score< 5, delivery type (NVD or C/S), blood sugar (BS)<50 mg/dl, serum calcium<8 mg/dl, Hyperbilirubinemia (Bili>5 mg/dl), HCO3<16, Pao2<50mmHg, PCO2>60 mmHg, duration of hospitalization more than a week, blood group type and RH.
Statistical analysis: SPSS version 15 was employed for data analysis. Chi-square, Fisher's exact test and T-test were used for qualitative, discrete quantitative and continuous quantitative variables analysis respectively. For multivariable analysis the odd ratio (OR) and confidence interval (CI) were calculated and ROC curve was plotted for determining specificity and sensitivity. P value<0.05 was considered as significant.

Results

Among 258 neonates included in the study, AKI occurred in 71(27.6%) neonates. The average age of hospitalization was 1.19±0.47 days (age range 1 to 17 days). Birth weight of neonates with AKI was 2656±873 g on average. The duration of hospitalization in NICU was 9.1±8.3 days (between 1 to 51 days). Sixty four percent of patients with AKI were male. Among AKI cases the mean SCr was 1.03 ±0.7, (range 0.9-1.7 mg/dl). Also 70% of AKI affected neonates suffered from prerenal failure (BUN/Cr>20).

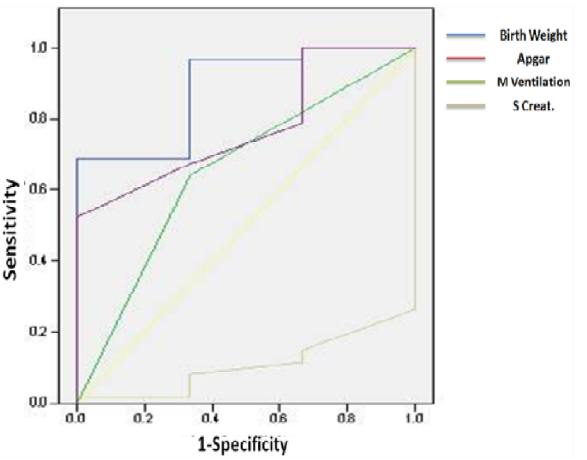

Figure 1. According to ROC curve, birth weight (AUC=0.885) showed the highest prognostic value in hospitalized neonates with AKI in NICU followed by low first minute Apgar score (AUC=0.776) and use of mechanical ventilation(M Ventilation) (AUC=0.653) and Serum Creatinine (S Creat.) in order

The following underlying diseases were found in the cases with AKI: Meconium aspiration:37 cases (14.3%), transient tachypnea of newborn:31 cases(12%), hyaline membrane disease (HMD): 155 cases(60.1%), septicemia: 3 cases(1.2%) and asphyxia: 1 case (0.4%). Overall mortality rate among 258 neonates hospitalized in the NICU was 4.3% and in those affected with AKI it was 4.5%. Comparing duration of hospitalization and mortality rate between neonates with and without

AKI revealed better prognosis for the non-AKI group (P<0.04).

Table 1. Comparing AKI cases in terms of final prognosis (Survivors or Non-survivors)

variable	Non-survivors (%)	Survivors (%)	P value
Average age	1.00	1.094	0.78
Male **Female**	2 1	38 11	0.07
Sepsis	0	1(1.4)	0.45
HMD	2(66.6)	20(30.1)	0.03 (sig.)
Mechanical ventilation	2(66.6)	22(32.3)	0.041 (sig.)
Blood PH<7.2	2(66.6)	7(10.7)	0.15
Serum K>6	0	3(4.3)	0.3
Serum K<4	1(33.3)	2(2.8)	0.16
Serum Cr>1mg/dl	3(100)	24(34.7)	0.003 (sig.)
Leukopenia (WBC<3000)	0	0	0.8
Hgb<10	1(33.3)	4(5.7)	0.57
Positive blood culture	0	1(1.4)	0.82
Phototherapy	3(100)	52(75.3)	0.42
Use of Surfactant	1(33.3)	9(13.2)	0.04 (sig.)
Weight<2.5	3(100)	24(34.7)	0.003 (sig.)
Weight>4	0	1(1.4)	0.14
Apgar score<5	3(100)	6(8.6)	0.04 (sig.)
C/S	2(66.6)	46(66.6)	0.65
NVD	1(33.3)	19(27.5)	0.87
BS<50	2(66.6)	9(13.4)	0.74
Ca<8	1(33.3)	4(5.7)	0.88
Bill>5	1(33.3)	50(73.5)	0.52
HCo_3 < 16	1(33.3)	32(46.3)	0.98
Pao_2 < 50	1(33.3)	6(8.6)	0.38
$PaCo_2$ > 60	3(100)	4(5.7)	0.035 (sig.)
Average admission time> 1wk	1(33.3)	36(52.1)	0.16
Blood group: A	0	17(24.6)	0.32
Blood group: B	1(33.3)	16(23.5)	0.1
Blood group: O	1(33.3)	23(33.3)	0.54
Blood group: AB	1(33.3)	4(5.7)	0.36
Rh^-	1(33.3)	7(10.1)	0.33

The identified prognostic factors associated with higher mortality rate in AKI patients were hyaline membrane disease (P<0.03), use of mechanical ventilation P<0.041), use of surfactant (P<0.04), first minute APGAR score <5 (P<0.04), PCO2 >60 mmHg (P<0.035), birth weight < 2500 g (P<0.003) and SCr >1 (table 1). ROC curve was plotted to define the risk factors and revealed that low birth weight was the most significant risk factor for mortality of neonates with AKI admitted in the NICU(AUC=0.885), followed by low first minute Apgar score(AUC=0.776), and the need of mechanical ventilation(AUC=0.653) in order (Fig 1).

Discussion

The prognosis of neonates with AKI is different in various studies. In the present study mortality rate in neonates with AKI hospitalized in NICU generally was found to be 4.5% irrespective of being oliguric and non-oliguric and a significant difference was seen in the mortality rate between AKI and non-AKI neonates. The mortality rate owing to AKI were reported differently as 60, 24.4, 77 and 22% in studies done by Stepleten [3], Agras [7], AI-Idressy [8] and Simon [9] depending on the underlying medical condition and the cause of AKI. Generally, neonates with prerenal AKI, if immediately treated for kidney hypoperfusion, will show excellent prognosis. But in neonates with postnatal AKI owing to congenital urinary tract obstruction, the outcome is variable depending on the degree of renal dysplasia. Neonates with intrinsic AKI show a high rate of mortality and morbidity. In one study, the underlying cause of AKI determined the final outcome in which neonates with renal structural anomalies and ATN revealed mortality rates of 17 and 55% respectively [10]. In our study mortality rate of all newborns who were admitted in NICU and neonates with AKI were 4.3% and 4.5%, respectively. Comparing duration of hospitalization and mortality rate in newborns with and without AKI revealed better prognosis in the second group (P<0.04), confirming the other studied.

In a study by Mathur [11], mortality in septic cases affected with AKI was found to be significantly higher (P 0.001, 70.2% VS 25%). In another review on AKI, the mortality rate in AKI cases with oliguria and in comparison with congenital urinary tract anomalies or cardiac diseases was 60 and 86% respectively [3]. Prognostic factors for the neonates with AKI had been studied in

numerous studies. In the present study the identified prognostic factors associated with higher mortality rate in AKI cases were hyaline membrane disease, use of mechanical ventilation, use of surfactant, first minute Apgar score < 5,PCO2 > 60 mmHg ,birth weight < 2500 g and SCr >1 were indentified. In the study by Mathur [11], among affecting neonates with different prognostic factors including gestational age, weight, positive blood culture, meningitis ,asphyxia , concurrent shock and previous prescription of nephrotoxic drugs for sepsis, only shock was found to be as a significant predictor for mortality rate($P<0.001$). According to Chevalier [12], the lack of oliguria and presence of renal uptake on DMSA scan were found to be associated with a better prognosis. In contrast with our study, high SCr showed no correlation to mortality rate.

Multiorgan dysfunction has been recognized by most of the studies as having the worst outcome in AKI affected neonates regardless of the etiology [3, 13, 14, 15, and 16]. In the study by Tellier (17), age < 24 hours, underlying diseases, low urine output and multiorgan failure are shown as prognostic factors. In the study by Agras [7], intrinsic AKI, need for dialysis and mechanical ventilation were associated with higher mortality rates and no significant correlation was found between mortality rate and prematurity, serum BUN and Cr level and perinatal factors on the other hand. Early diagnosis of AKI in recent years using renal injury biomarkers such as NGAL, KIM-1, IL-18 and NHE3 [18] paves the way for rapid interventions like the use of theophylline in the neonates with asphyxia [19] which will improve the prognosis in AKI. We wish these interventions could reduce the mortality rate among our patients.

Conclusions

In the present study, neonates with low birth weight, prematurity, HMD, use of surfactant and asphyxia were shown as having the most paramount risk of mortality and therefore better management of these factors could culminate in an improved outcome for these neonates.

Given that some residual renal dysfunction exists in at least 40% of neonates, long term follow-up of neonates with AKI is highly recommended.

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Conflict of Interest

None declared

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None declared

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