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ORIGINAL ARTICLE

Frequency of acute renal injury in neonates with respiratory distress syndrome.

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ABSTRACT… Objective: To determine the frequency of acute kidney injury (AKI) in neonates with acute respiratory distress syndrome (RDS). **Study Design:** Cross-sectional study. **Setting:** Neonatal Intensive Care Unit (NICU) of National Institute of Child Health, Karachi, Pakistan. **Period:** January 2023 to June 2023. **Material & Methods:** A total of 118 neonates of both genders, born below 37 weeks of gestation and having RDS were analyzed. Demographic, clinical and laboratory parameters were noted. Frequency of AKI was determined while final outcome was noted in terms of discharged or mortality. **Results:** Of 118 neonates, 55.1% were girls. The mean gestational age: 33.11±1.76 weeks, mean admission age 8.30±9.0 hours, and mean birth weight 1.53±0.27 kg. AKI occurred in 50.8% of neonates with RDS. Mortality was reported in 46.6% cases. Factors associated with AKI included grunting at admission (63.3% vs. 43.1%, p=0.028), need for mechanical ventilation (35.0% vs. 12.1%, p=0.003), and platelet count on admission (p=0.042). Factors associated with mortality included lower Apgar score at minute 5 (p<0.001), resuscitation at delivery (p<0.001), grunting at admission (p=0.005), platelet count at admission (p=0.001), leukocyte count at admission (p=0.003), and the need for mechanical ventilation (p<0.001). **Conclusion:** Very high frequency of AKI (50.8%) in neonates with acute RDS was noted. Mortality was associated with lower Apgar scores, resuscitation at delivery, grunting at admission, low platelet and leukocyte counts, and the need for mechanical ventilation.

Key words: Acute Kidney Injury, Apgar Score, Mechanical Ventilation, Mortality, Respiratory Distress Syndrome.

INTRODUCTION

Respiratory distress syndrome (RDS) is considered to be the commonest factor causing respiratory failure among preterm babies, RDS is also known to be an important factor causing significant morbidity and mortlity.[1,2] Not much local data about the incidence of RDS is available but evidence from the developed world shows that the incidence ranges between 64.2-78.9 cases of RDS per 100,000.[3] RDS affects 50% of newborns having a birth weight (BW) of less than 1.5 kg, moreover, significant proportion of these babies develop acute kidney injury (AKI).[4] Among neonates, asphyxia and RDS are thought to be major risk factors for developing AKI in them.[5] In premature infants with RDS, poor adaptive mechanisms and immature tubular and glomerular function have been shown to be the main contributors to dysfunction of the kidneys and AKI.[6] Several potential causes have been suggested to explain the higher occurrence of renal failure in premature newborns. These factors include intrauterine infections, placental insufficiency, maternal drug exposure, hypovolemia, septicemia, drug-related toxicity, congenital anomalies, low birth weight, premature birth, the need for intubation at birth, respiratory distress syndrome (RDS), low Apgar scores, and the use of mechanical ventilation (MV).[7,8] According to reports, AKI affects between 18 and 52% of pediatric patients who are critically ill, and those who have it are more likely to have a poor prognosis.[9,10] One study showed that RDS (26.67%) and sepsis (53.3%) were the most frequent conditions in neonates who had AKI.[11]

Though, AKI secondary to respiratory distress syndrome has been reported in many international studies but few local studies and specially data in neonates is present so this study was planned. The objective of this study was to determine the

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frequency of AKI in neonates with acute RDS presenting to National Institute of Child Health, Karachi.

MATERIAL & METHODS

This was a cross-sectional study performed in the neonatal intensive care unit (NICU) of National Institute of Child Health, Karachi, Pakistan, from January 2023 to June 2023. A sample size of 118 was calculated using the confidence interval as 95%, the margin of error as 8%, and the anticipated prevalence of AKI in neonates as 26.67% with RDS. Written and informed and written consents were obtained from parents/guardians while approval from the "Institutional Ethical Committee" was acquired (IERB-13/2022).

Inclusion criteria were babies of either gender aged between 1 and 28 days, born below 37 weeks, and having RDS. Exclusion criteria were severe perinatal asphyxia (Apgar score at 5 minutes below 3), congenital malformations or genetic syndromes (as per clinical examination and medical record), or those having culture-proven septecimia. Babies born to mothers who had maternal history of renal dysfunction were also excluded. Children undergoing any kind of surgery were also not included in this study. "Acute respiratory distress syndrome (ARDS)" was characterized by the presence of hypoxia within seven days of a known injury or insult to the lungs. Clinical signs at birth included grunting, nasal flaring, intercostal and subcostal retractions, and cyanosis. Diagnosis was supported by specific radiological patterns, such as diffuse, symmetrical reticulo-granular patterns, a ground-glass appearance, and air bronchograms. ARDS is confirmed if there is a positive response to surfactant treatment, and other causes of respiratory distress syndrome (RDS) are excluded. Baseline demographic and medical information along with medical history were noted. Serum creatinine and urea were evaluated at 24 hours, 72 hours, after 1 week, and at the time of discharge. AKI was labeled as per KDIGO guidelines.[12] The final outcome was noted in terms of discharge or mortality.

The analysis of the entered data was performed using "Statistical Package for Social Sciences (SPSS)", version 26.0. The mean and standard deviation were calculated for quantitative variables such as age, duration of treatment, and weight (on a weighing scale). Qualitative variables, which included gender and AKI, were shown in terms of frequency and percentages. AKI was further stratified with respect to effect modifiers, and a post-stratification chi-square test was applied, taking $p \leq 0.05$ as significant.

RESULTS

In a total of 118 neonates, there were 65 (55.1%) girls. The mean gestational age, and age at the time of admission were 33.11±1.76 weeks and 8.30±9.0 hours respectively. The mean birth weight was 1.53±0.27 kg. The mean Apgar score at 1-minute and 5-minutes were 4.9±0.7 and 7.7±1.0 respectively. The mean platelets and white leukocytes were 207.68±67.78 x 10^9/L and 17.82±2.70 x 10^9/L respectively. Table-1 shows characteristics of neonates studied.

Characteristics		Frequency (%)
Gender	Boys	53 (44.9%)
	Girls	65 (55.1%)
Gestational Age	28-32	40 (33.9%)
	33-36	78 (66.1%)
Resuscitation needed at the time of birth		33 (28.0%)
Reluctant to feed		68 (57.6%)
Mechanical ventilation needed		28 (23.7%)
Grunting at the time of admission		63 (53.4%)

Table-I. Characteristics of neonates (n=118)

AKI as per operational definition was diagnosed in 60 (50.8%) neonates with RDS. In these 60 neonates, 58 had stage-1 AKI while remaining 2 had stage-2 AKI. Table-II is showing trends of urea and creatinine and significant variations were noted ($p<0.05$).

There were 63 (53.4%) neonates who were successfully discharged while remaining 55 (46.6%) died. Stratification of mortality with respect to effect modifiers is shown in table-3. Grunting at the time of admission (63.3% vs. 43.1%, $p=0.028$), need for MV (35.0% vs. 12.1%, $p=0.003$), and platelet count on admission ($p=0.042$) were significantly associated with the

occurrence of AKI (Table-III).

Relatively lower Apgar score at minute-5 (p<0.001), resuscitation required at the time of delivery (p<0.001), grunting at the time of admission (p=0.005), platelet count at the time of admission (p=0.001), Leukocytes count at the time of admission (p=0.003), and the need for MV (p<0.001) were significantly associated with death (Table-IV).

DISCUSSION

We investigated the frequency of AKI in newborns with acute RDS and explored its associations with various clinical parameters. Our findings provide valuable insights into the prevalence of AKI in this vulnerable population and its significant impact on neonatal outcomes.

	Urea	P-value	Creatinine	P-value
After 24 hours	62.03±46.94	<0.001	0.87±0.50	<0.001
After 72 hours	52.70±40.77		0.77±0.54	
After 1 week	36.39±29.16		0.51±0.41	
At Discharge	24.67±13.43		0.26±0.26	

Table-II. Patterns of urea and creatinine over the course of 7 days

Study Variables		AKI		P-Value
		Yes (n=60)	No (n=58)	
Gender	Boys	32 (53.3%)	21 (36.2%)	0.062
	Girls	28 (46.7%)	37 (63.8%)	
Age (hours)		7.55±6.06	9.09±11.31	0.363
Birth Weight (kg)		1.56±0.20	1.50±0.32	0.239
Gestational Age (weeks)		33.15±1.90	33.07±1.62	0.804
Apgar score at minute-1		4.79±0.84	5.00±6.51	0.225
Apgar score at minute-5		7.70±0.89	7.76±1.10	0.757
Resuscitation needed at the time of birth		21 (35.0%)	12 (20.7%)	0.083
Reluctant to feed		32 (53.3%)	36 (62.1%)	0.337
Mechanical ventilation needed		21 (35.0%)	7 (12.1%)	0.003
Grunting at the time of admission		38 (63.3%)	25 (43.1%)	0.028
Platelet count at admission (10^9/L)		220.27±79.66	194.88±50.62	0.042
Leukocytes count at admission (10^9/L)		17.92±2.92	17.71±2.49	0.681
Mortality		29 (48.3%)	26 (44.8%)	0.703

Table-III. Stratification of acute kidney injury with respect to study variables N=118)

Study Variables		Outcome		P-Value
		Discharged (n=63)	Death (n=55)	
Gender	Boys	32 (50.8%)	21 (38.2%)	0.169
	Girls	31 (49.2%)	34 (61.8%)	
Age (hours)		8.92±7.62	7.58±10.43	0.424
Birth Weight (kg)		1.50±0.32	1.56±0.21	0.222
Gestational Age (weeks)		33.10±2.04	33.13±1.44	0.922
Apgar score at minute-1		4.93±0.78	4.82±0.78	0.525
Apgar score at minute-5		8.10±0.88	7.38±0.94	<0.001
Resuscitation needed at the time of birth		6 (9.5%)	27 (49.1%)	<0.001
Reluctant to feed		40 (63.5%)	28 (50.9%)	0.168
Mechanical ventilation needed		3 (4.8%)	25 (45.5%)	<0.001
Grunting at the time of admission		26 (41.3%)	37 (67.3%)	0.005
Platelet count at admission (10^9/L)		227.44±0.80.10	184.63±34.15	0.001
Leukocytes count at admission (10^9/L)		17.14±2.80	18.61±2.38	0.003
AKI		31 (49.2%)	29 (52.7%)	0.703

Table-IV. Distribution of outcome with respect to study variables (n=118)

We observed a substantial occurrence of AKI, with 50.8% of neonates meeting our operational definition criteria for AKI. This high prevalence underscores the importance of vigilant renal function monitoring in neonates presenting with RDS. Youssef et al revealed that 55.6% of neonates who developed AKI were having RDS.[13] Another study noted that out of 93 neonates who developed AKI, 82.8% had RDS.[14] A study by Momtaz HE et al noted RDS as the 3rd most common associated presentation with AKI (34.6%).[5] Our findings in terms of the high occurrence of AKI in RDS or the presence of RDS in neonates who develop AKI are consistent with the literature and highlight the clinical relevance of AKI in neonates with RDS. Our study also delves into the severity of AKI in these neonates. It is noteworthy that the majority of neonates with AKI exhibited stage-1 AKI (96.7%), while only a small proportion presented with stage-2 AKI (3.3%). This distribution suggests that AKI in the context of neonatal RDS tends to be predominantly mild to moderate in severity. The high mortality rate in the present study could be due to the fact that we only included children who were born preterms while the mean birth weight of the studied neonates was 1.53±0.27 kg.

To gain further insight, we identified several clinical factors that were significantly associated with the occurrence of AKI and neonatal mortality in our study population. Specifically, grunting at the time of admission, the need for MV, and the platelet count on admission were all found to be significantly associated with AKI. Likewise, lower Apgar scores at 5 minutes, resuscitation required at the time of delivery, grunting at admission, platelet count at admission, leukocyte count at admission, and the need for MV were all significantly associated with neonatal mortality. The associations we observed between these risk factors and AKI or mortality merit further consideration. For instance, the connection between grunting and AKI might be explained by the increased oxygen demand and potential hypoxemia associated with RDS, which could negatively impact renal perfusion.[16] MV, a common intervention in neonates with severe RDS, may contribute to renal injury through hemodynamic changes.[17,18] The associations with platelet count and leukocyte count may suggest that systemic inflammation plays a role in AKI and mortality in this population.[19,20]

Relatively small sample sizes and single-center study designs are some of the limitations of this study. We only noted a relatively short-term outcome for children presenting with AKI.

CONCLUSION

Very high frequency of AKI (50.8%) in neonates with acute RDS was noted. Mortality was associated with lower Apgar scores, resuscitation at delivery, grunting at admission, low platelet and leukocyte counts, and the need for MV. Timely identification and managing these risk factors can aid in early intervention and improved neonatal care for RDS patients, potentially reducing mortality rates.

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3	Hira Urooj	Literature review, Discussion.	
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