

## Acute Renal Failure in Neonates, Single Center Experience: Child's Central Teaching Hospital

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### ABSTRACT:

#### BACKGROUND:

Acute renal failure is an acute deterioration in the ability of the kidneys to maintain homeostasis of body fluids, electrolytes and is associated with acute decrease in the glomerular filtration rate that leads to retention of toxic metabolic end products. Its incidence in hospitalized neonates is 8-24%. The main causes of acute renal failure in neonates are pre-renal in nature, intrinsic and post-renal mechanisms of failure are much rarer conditions.

#### OBJECTIVE:

To evaluate; types, associated predisposing factors, and short term outcomes of renal failure in neonates of neonatal unit in Child's Central Teaching Hospital, and to compare the results with those reported in the literature.

#### PATIENTS AND METHODS:

A cross sectional study was carried out on 30 neonates with acute renal failure admitted to neonatal unit in Child's Central Teaching Hospital during the period from 1<sup>st</sup> of June 2012 to 30<sup>th</sup> of November 2012.

#### RESULTS:

There were 43 cases diagnosed as renal failure out of 927 hospitalized neonates (4.63%). Thirteen cases were excluded according to the inclusion criteria, so only 30 cases were enrolled in this study. Male to female ratio was 1.7:1. Most of patients were term (86.7%). The prevalence of pre-renal, renal and post renal causes of acute renal failure were 76.6%, 16.7% and 6.7% respectively. The most common predisposing factors for acute renal failure in this study were sepsis (80%), perinatal asphyxia (10%), heart failure (3, 4%). Most patients had more than one predisposing factor. Among admitted neonates with renal failure, mortality rate was 16.7% and it was significantly higher in patients with sepsis ( $P < 0.05$ ).

#### CONCLUSION:

Early recognition of risk factors such as sepsis, perinatal asphyxia or, heart failure, and rapid effective treatment of contributing conditions will decrease acute renal failure in the neonatal period.

**KEY WORDS:** renal failure, oliguria, neonatal sepsis.

### INTRODUCTION:

Acute renal failure (ARF) is defined as an acute deterioration in the ability of the kidneys to maintain homeostasis of body fluids, electrolytes and is associated with acute decrease in the glomerular filtration rate that leads to retention of toxic metabolic end products<sup>(1,2)</sup>. Most reports estimate the incidence of ARF in hospitalized neonates to be 8-24%<sup>(1,2,3)</sup>. Plasma creatinine (Pcr) concentration immediately after birth reflects the maternal creatinine concentration, and it's level gradually decreases from 1.1mg/dl in term infants (1.3mg/dl in preterm infants) to a mean value of 0.4mg/dl within the first two

weeks of life. Thus measuring glomerular filtration rate or following Pcr concentration over time is required to diagnose ARF in a newborn infant<sup>(1,2,3)</sup>. The main causes of ARF in the neonates are pre-renal, including; hypovolaemia, hypotension, and hypoxemia (more than 80% of cases). Intrinsic and post-renal mechanisms of failures include; acute tubular necrosis, renal vascular thrombosis, cortical necrosis, sepsis, and obstructive nephropathy are much rarer conditions (about 11% and 3% respectively)<sup>(4)</sup>. Normal urine output is found in approximately one-third of neonates with ARF, although low urine output may occurs in the absence of ARF. So, if urine output alone is used to assess the

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renal function, ARF may often be either overlooked or over diagnosed<sup>(5)</sup>. Management in the setting of pre renal type renal failure includes; treating and volume resuscitation implemented to restore renal perfusion. In post renal disease, obstruction may be relieved by primary surgical repair or via temporary drainage with an indwelling catheter<sup>(6,7,8)</sup>. When conservative measures fail to control the complications of ARF, renal replacement therapy is indicated including; peritoneal dialysis, hemodialysis, and hemofiltration with or without dialysis. The preferred method of dialysis in the neonatal period continues to be peritoneal dialysis<sup>(9)</sup>.

### AIM OF STUDY:

To evaluate the types, frequency of associated contributing conditions, and short term outcomes of ARF in neonates admitted to neonatal unit in Child's Central Teaching Hospital, and to compare the results with those reported in the literature.

### PATIENTS AND METHODS:

A small group cross sectional study was carried out on 30 neonates fulfilling the inclusion criteria of the study (age less than 28 days), presented with ARF, admitted to neonatal unit in Child's Central Teaching Hospital during period from 1<sup>st</sup> of June 2012 to 30<sup>th</sup> of November 2012.

A detailed history was taken and complete physical examination was done to all patients enrolled in the study. The data included; demographic features, clinical 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, Acetylcholinesterase inhibitor, aminoglycosides, and vancomycin), congenital anomalies of the urinary tract system, and history of surgical operation.

Laboratory investigations were done, including; blood urea, serum creatinine, serum electrolytes, complete blood count (CBP), C-Reactive protein (CRP), Erythrocyte sedimentation rate (ESR), blood culture and sensitivity, abdominal ultrasound and others as indicated.

Regarding causes of renal failure they were divided to pre-renal, renal and post-renal depending on history and physical examination, and laboratory data whenever available in the hospital;

1- Abnormal renal function considered when: plasma creatinine level higher than 1.5 mg/dL, or a blood urea nitrogen (BUN) level higher than 20

mg/dL on two separate occasions at least twelve hours apart, while maternal kidney function was normal<sup>(10,11)</sup>.

2-Oliguria was defined as urinary output less than 1 mL/kg/hr.

3-Oliguric neonates without fluid overload were considered to have pre renal ARF and they rapidly responded to fluid challenge. The remaining patients were considered to have intrinsic renal failure if they did not respond to fluid challenge and their imaging studies were normal. After volume resuscitation, hypovolemic patients generally void within two hr.; failure to do so, that points toward the presence of intrinsic or post renal ARF<sup>(12)</sup>.

Response to fluid challenge was defined as resolving the oliguria after infusion of up to 3 doses of isotonic saline solution, 20 mL/kg, and restoration of creatinine level to less than 1.5 mg/dL.

4-Neonates who had obstruction in the urinary tract system based on imaging studies (ultrasonography or renal scintigraphy) were considered as post renal failure.

5-Sepsis was diagnosed in symptomatic patients on the basis of either positive blood culture for microorganisms or a positive sepsis screen (if two or more of the following criteria were present: high erythrocyte sedimentation rate for age, leukocyte count less than  $5 \times 10^9/L$ , and positive serum C-reactive protein)<sup>(13)</sup>.

6-The short-term outcome was determined by following the clinical course until discharge from hospital and was categorized into three groups; of "death", "discharge with normal kidney function", and "discharge with diminished kidney function".

7- In this cross sectional study; neonates who did not complete their investigations, those who died within the first 24 hours of admission, and those with maternal history of kidney failure were excluded.

Statistics: The collected data were analyzed by the SPSS software (Statistical Package for the Social Sciences, version14.0, 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 927 admitted neonates over 5 months period to the neonatal care unit, forty three patients were diagnosed with ARF (4.63%). Thirteen neonates were excluded based on the criteria determined

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for the study, and data of 30 patients, including 19 boys (63.34%) and 11 girls (36.66%) was studied. The male to female ratio was 1.7:1. Most of the patients with ARF were term (26 cases, 86.7%). Four cases (13.3%) were preterms and no post-term neonate was seen in this study as shown in table 1.

Demographic characteristics and renal function tests of newborn infants were summarized in table 2

Oliguric ARF was found in 21 cases (70%). The prevalence of pre-renal, renal and post-renal types of ARF were (23 cases, 76.6%), (5 cases, 16.7%) and (2 cases, 6.7%) respectively. Predisposing factors for ARF were sepsis in 80%, asphyxia in 10% and heart failure in 3.4%. There were more than one predisposing factor in most patients.

Congenital renal anomalies were documented in two patients, which included polycystic kidney in one case and obstructive uropathy was diagnosed

in the other patient. Peritoneal dialysis was done to seven (23%), and the other patients responded to conservative medical management. Five neonates (3 girls and 2 boys; 16.7%) died during their hospitalization (only one of them died with heart failure and had peritoneal dialysis, the remaining four patients died without doing peritoneal dialysis because their families refused doing it). Twenty one patients (70%) were oliguric, 23 (76.6%) were discharged with normal kidney function, and two (6.7%) had impaired renal function (one with infantile polycystic kidney and the other with obstructive uropathy) and were discharged with diminished renal function as shown in Table 3. Mortality among hospitalized neonates with ARF was 16.7% (5 cases). Girls were significantly more (3 of 11; 27.2%) than boys (2 of 19; 10.5%) among the dead cases ( $P = .003$ ). Sepsis was the most common cause of death (4 of 5, 80%) and one died from heart failure.

**Table 1: Frequency distribution of neonates with acute renal failure according to sex and gestational age.**

		No. (30)	% (100%)
Gender	Male	19	63.34
	Female	11	36.66
Gestational age	Term	26	86.7
	Pre-term	4	13.3
	Post-term	0	0

**Table 2: Demographic characteristics and renal function tests of studied sample.**

	Mean $\pm$ SD	Minimum	Maximum
Age (days)	8.9 $\pm$ 7.2	2	27
Gestational age (wk)	38.7 $\pm$ 1.69	34	42
Weight (gr)	2945 $\pm$ 617.6	1600	4000
Plasma creatinine (mg/dl)	1.8 $\pm$ 0.58	1.5	3.8
BUN (mg/dl)	154.4 $\pm$ 47.3	120	300

**Table 3: Frequency distribution of neonates with acute renal failure according to the cause, predisposing factor, and outcome.**

		No. (30)	% (100%)
Cause	Pre-renal	23	76.6
	Renal	5	16.7
	Post-renal	2	6.7
Predisposing factors	Sepsis	24	80
	Asphyxia	3	10
	Heart failure	1	3.4
	Urological anomalies	2	6.6
Outcome	Good renal function	23	76.6
	Impaired renal function	2	6.7
	Died	5(2 male + 3 female)	16.7

### DISCUSSION:

The frequency of ARF in this study (4.63%) is lower than that reported in the Stapleton FB et al<sup>(5)</sup> (8-24%), but nearly similar to Mortazavi F et al<sup>(14)</sup> (2.7%) probably because we enrolled all admitted neonates (both in the neonatal intensive care unit and neonatal care unit) in the study. The ARF in boys was more than girls in this study (ratio 1.7:1) which is consistent with other studies; Airede A. et al<sup>(3)</sup> and Mortazavi et al<sup>(14)</sup> as both reported (2:1) ratio. The high frequency of ARF in boys may be due to the susceptibility of boys to some perinatal disorders such as sepsis. The premature patients with ARF in this study were 4 (13.3%), which is inconsistent with Agras et al<sup>(15)</sup> (31%), and Mortazavi et al<sup>(14)</sup> (25.2%). This may be because of small study group and relatively short duration of data collection. Neonatal ARF predominantly manifests with oliguria. In this study, 70% of patients were oliguric, which is similar to Pinna B, et al<sup>(16)</sup> (70%), and Mortazavi et al<sup>(14)</sup> (72.2%), but less in Gharehbaghi MM1 et al study<sup>(17)</sup> (32.8%) which had high prevalence of asphyxia in their patients that predisposed to non-oliguric ARF. The most common cause of ARF in this study was pre-renal cause (76, 6%), renal cause was (16.7%), post renal cause was (6.7%), which is similar to Hentschel R, et al study<sup>(4)</sup> (more than 80%, 11%, and 3% respectively). A wide variety of malformations or pre-natal, perinatal and post-natal events may cause ARF<sup>(4)</sup>. The most common predisposing factors of ARF in neonate in this study was sepsis (80%), asphyxia (10%), which is inconsistent with Mortazavi F et al (Iran)<sup>(14)</sup> who found that asphyxia 29.8% and sepsis 28.5%, but is consistent with Fahmi N et al (Iraq)<sup>(18)</sup> in which sepsis is the most common predisposing factor for ARF (56%) and 10% only for perinatal asphyxia. A variety of mechanisms, including shock, disseminated intravascular coagulation, haemorrhage, and cardiac failure may cause ARF in septic neonates. Mortality among hospitalised neonates was (16.7%) in this study which is consistent with Mortazavi F et al<sup>(14)</sup> (20.5%), this small difference is mostly due to early diagnosis and early treatment of ARF in our hospital. Sepsis was most common cause of death in this study 80%, which is consistent with Mathur et al<sup>(13)</sup> (50% to 78%) and Mortazavi F et al<sup>(14)</sup> (75%). Mortality was higher in female than male (27.2% vs. 10.5%), ( $P .003$ ) in this study which is consistent with Mortazavi F et al<sup>(14)</sup> and Fahmi N et al<sup>(18)</sup> (16.6% vs. 10.5%).

### CONCLUSION:

Acute renal failure constitute 4.6% of neonatal admissions and was more in males than females and the most common causes were pre-renal, of which sepsis was the commonest, and oliguria was the most common presentation.

Mortality was 16.7%, and the most common cause of death in neonatal ARF was sepsis, which was mainly amongst patients whom their families refused medical interference.

### Recommendations:

Identify neonates at high risk for renal failure and detection of oliguria immediately after predisposing events. Vital signs, electrolytes and renal function should be followed serially as one third of neonates with ARF have normal urine output.

If urinary tract anomalies are suspected, a complete urologic work up should be considered. In newborns with positive history of predisposing factors for ARF, correction of oxygenation, ventilation, cardiac output, blood pressure and early treatment of sepsis is needed for prevention and effective management of ARF.

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