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Acute kidney injury: A pediatric experience over 10 years at a tertiary care center

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ABSTRACT

Background: The etiology of acute kidney injury (AKI) varies in different countries. In addition, the etiology of AKI in hospitalized children is multifactorial. The importance of diagnosing AKI is not only because of short-term high morbidity and mortality rate, but also for its effect on developing chronic kidney disease.

Objectives: we studied retrospectively AKIs of children who were hospitalized over 10 years in a University hospital.

Materials and Methods: A retrospective analysis of the medical recorded data of 180 children less than 18 years treated for AKI in Alzahra Hospital, Isfahan, Iran, were performed during the period of March 2001 to February 2011. For each patient, demographic and anthropometric data, laboratory data, electrocardiographic findings, ultrasound results, etiology of AKI and short-term outcomes were recorded.

Results: The male to female ratio was 1.57 to 1. Mean age was 5.28 ± 6.3 (SD) years and the median was 1.8 years. The more frequent age group was children less than 2 years. The mortality rate was 22.2% (40 patients). The mortality was not correlated with age (p= 0.74). Renal replacement therapy was recommended for 62 patients (34.4%). Mean of the first and last glomerular filtration rate (GFR) were 18.33± 1.12 ml/min/1.73 m^2 and 52.53 ± 2.98 ml/min/1.73 m^2, respectively. The most common urinary sediment finding in approximately 70% of the patients was either renal epithelial cell or renal cell cast. Increased kidney echogenicity was the most common ultrasound finding (48%). Using ANOVA regression analysis, the etiology of disease was the only predictor of mortality (p=0.0001).

Conclusions: We concluded that the mortality is still high in AKI. Furthermore, the poor outcome (defined as low GFR) are higher among patients with low levels of first GFR and higher RIFLE score.

Implication for health policy/practice/research/medical education:
The etiology of acute kidney injury (AKI) varies in different countries. In a retrospective analysis data of 180 children less than 18 years treated for AKI was studied. We concluded that the mortality is still high in AKI. The poor outcome (defined as low GFR) are higher among patients with low levels of first GFR and higher RIFLE score.

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Original Article

1. Background

Acute kidney injury (AKI) is defined as reversible inability of kidney in secreting nitrogenous waste products, balancing fluid and electrolytes that occurs during hours or days (1). The exact incidence of AKI is not clear in pediatric population; however, an increase in its incidence in hospitalized neonates and children has been reported recently (1-4). The etiology of AKI varies in different countries (5-7). In addition, the etiology of AKI in hospitalized children is multifactorial (1). Among the causes of AKI, diseases resulted in acute tubular necrosis such as sepsis, nephrotoxic medication and ischemia were more prevalent (8). The importance of diagnosed AKI is not only because of short-term high morbidity and mortality rate, but also for its effect on developing chronic kidney disease (9). Finding the etiologies and outcomes of AKI, help the health system to decrease the incidence and improve outcome.

2. Objectives

We studied retrospectively AKIs in children, who were hospitalized over 10 years in a University Medical center, Alzahra Hospital, Isfahan, Iran. This study will analyze the underlying diseases leading to AKI, the short-term outcome, laboratory and ultrasound findings in addition to some variables associated with mortality and short-term outcome in children with AKI.

3. Materials and Methods

3.1. Patients

In a retrospective analysis, medical recorded data of children less than 18 years who were treated for AKI at Alzahra Hospital, Isfahan, Iran, during the period of March 2001 until February 2011 were studied. The study did not include neonates (age less than 28 days). All children were diagnosed with AKI based on the RIFLE criteria (table 1) (10). A total of 180 eligible cases were collected. Patients were divided into 4 groups according to the age: one month to less than 2 years, 2-5 years, 5-10 years and 10-18 years. For each patient, demographic and anthropometric data (age, sex, height, weight, and blood pressure), laboratory data (serum urea, serum creatinine, serum electrolytes and urine analysis with sediment), electrocardiographic findings, ultrasound results, etiology of AKI and short-term outcome were recorded.

3. 2. Calculation of glomerular filtration rate(GFR)

Glomerular filtration rate was calculated based on Schwartz formula (11). The first GFR (at the time of hospitalization) and the last GFR (up to 7 days of discharging from hospital) were also recorded.

Schwartz formula: GFR (ml/min/1.73m^2) = k× height (cm)/serum creatinine

k= 0.55 for girls and children up to 7 years

k= 0.7 for boys older than 7 years.

Table 1: The RIFLE criteria (1)

	GFR Criteria	Urine output (UO) criteria
Risk	Increased creatinine ×1.5 or GFR decrease >25%	UO <0.5 ml/kg/h × 6 h
Injury	Increased creatinine ×2.0 or GFR decrease >50%	UO <0.5 ml/kg/h × 12 h
Failure	Increased creatinine×3.0 or GFR decreases > 75% or creatinine > 4 gm/dl	UO <0.5 ml/kg/h × 24h or Anuria ×12 h
Loss	Persistent ARF = complete loss of renal function > 4 weeks	
ESRD	End-stage renal disease	

Table 2: Etiologies of ARF based on the etiologies

Mechanism of ARF/Disease	Frequency	Percentage
Pre-renal		
Hypovolemia (gastroenteritis and heart failure)	27	15.0%
Intrinsic renal diseases		
Sepsis	65	36.1%
Hemolytic uremic syndrome	24	13.3%
Post-streptococcal glomerulonephritis	14	7.8%
Tumor lysis syndrome	10	5.6%
Rhabdomyolisis	6	3.3%
Nephrotoxic medications	5	2.8%
Scorpion bite (toxin)	5	2.8%
Rapidly progressive glomerulonephritis	3	1.6%
Systemic lupus erythematosus	2	1.1%
Henoch–Schönlein purpura	1	0.6%
Post bone- marrow transplantation	1	0.6
Post-renal		
Nephrolithiasis	8	4.4%
Posterior urethral valve	2	1.1%
unknown	6	3.3%

3.3. Statistical Analysis:

Data were analyzed using the SPSS ver. 18.0 (SPSS Inc, Chicago, IL, USA). The categorized data were reported as frequencies as well as percentages. Continuous data were reported as the mean ± SD. Pearson's correlation test was used to analyze correlations. ANOVA test was applied to determine predictor factors. P-value ≤ 0.05 was considered as significant.

4. Results

Of 180 participants, 110 were male (61.1%). The male to female ratio was 1.57 to 1. Mean age was 5.28 ± 6.3 (SD) years and the median was 1.8 years. The more frequent age group was children less than 2 years (57.2%) followed by 10-18 years (25.6%), 2-5 years (8.9%) and 5-10 years (8.3%). The mortality rate was 22.2% (40 patients). The mortality was not correlated with age (p= 0.74). The cause of death in 29 patients (72.5%) was Multi-Organ System Failure (MOSF) due to sepsis. However, 6 patients (15%) died due to severe fluid and electrolytes imbalance (hemolytic uremic syndrome and glomerular disease). Untreatable malignant diseases accompanied by tumor lysis syndrome were responsible for 5 cases of death (12.5%). Renal replacement therapy (RRT) such as hemodialysis and peritoneal dialysis was recommended for 62 patients (34.4%). 36 out of 62 patients (58%) underwent hemodialysis (HD). Considering the mechanism of ARF; pre-renal, renal and post-renal mechanism were reported in 15%, 76.2% and 5.5% of the patients respectively (Table 2).

Mean of the first and last GFR were 18.33 ± 1.12 ml/min/1.73 m^2 and 52.53± 2.98 ml/min/1.73m^2, respectively. Mean of some serum biochemical parameters is illustrated in table 3.

Renal epithelial cell and renal cell cast as the most common urinary sediment finding were seen

in approximately 70% of the patients. Red blood cell cast was reported in 31 patients (16.3%). The mechanism of ARF (intrinsic renal diseases), was the only predictor of the presence of RBC cast (p=0.0001). While microscopic hematuria was reported in 56 patients (30.3%), gross hematuria was only seen in 20.6%.

Increased kidney echogenicity was the most common ultrasound finding (48%). Large kidney was seen in 12 patients (6.6%). Hydronephrosis and hydroureter were reported in 12 (6.6%) and 8 (4.4%) patients, respectively. Increased bladder wall thickness was observed in only 2 patients (1.1%). However, dilated (spastic) bladder was not seen in any patient.

Evaluating electrocardiogram (ECG) showed that tall T-wave (hyperkalemic states) followed by prolonged PR interval was the most prevalent ECG findings in patients. Tall T-wave and prolonged PR interval were 21.7% and 6.7%, respectively.

The patient's outcome had reverse correlation with age and the first GFR. The worst outcome (The last GFR less than 50 ml/min/m^2) was seen in older patients (p = 0.009, r = -0.194) and in those with lower levels of the first GFR (p= 0.0001, r = -0.292). However, using ANOVA regression analysis, the etiology of the disease (intrinsic renal diseases, p= 0.002), the first GFR (p= 0.0001) and the RIFLE score (p= 0.0001) were the predictors of the last GFR less than 50 ml/min/m^2. Indeed, the lower levels of the last GFR were seen in patients with glomerulonephritis and rapid progressive glomerulonephritis (RPGN).

By applying ANOVA regression analysis, the etiology of disease was the only predictor of patient's death (p=0.0001).

According to the RIFLE criteria, most patients were placed in the failure category (table 1). The RIFLE criteria was the predictor of patients' outcome (p=0.0001).

5. Discussion

In this retrospective study, we evaluated AKI etiology, laboratory data, ultrasound findings and short –term outcome over 10 years of children who were admitted to a University Hospital, Alzahra Hospital, Isfahan, Iran. Considering the fact that the most children with AKI have been referred to this hospital (the only pediatric nephrology center in our province and a tertiary care center), the results of this study may show a nearly accurate evaluation of children with acute renal failure (ARF) over 10 years in the province. A preponderance ratio of male to female was found. In similar studies the male was the predominant gender (3, 5, 7, 12).

Table 3: Serum biochemical parameters of patients

Serum biochemical parameters	Minimum	Maximum	Mean± SD
First BUN (mg/dL)	1.6	270	86.19 ± 3.96
First creatinine (mg/dL)	1.4	20	4.12 ± 0.19
Last BUN (mg/dL)	3	225	38.18 ± 2.80
Last creatinine (mg/dL)	0.2	11	1.84 ± 0.13
Sodium (meq/L)	110	200	140.97 ± 1.31
Potassium(meq/L)	2.3	9.4	5.31 ± 0.11
Calcium (mg/dL)	5	12	8.13 ± 0.09
Phosphorus (mg/dL)	1	12	5.79 ± 0.14
Bicarbonate (mEq/L)	1.7	30	13.98 ± 0.94
PH	4.27	7.6	7.27 ± 0.03

It has been reported that the most common causes of AKI are secondary to sepsis, ischemia and nephrotoxic medications (8). Vachvanichsanong et al. indicated that sepsis (21.4%) followed by hypovolemia was the most prevalent causes of AKI (12), whereas different results were achieved by Shah et al. (7). According to their results, the prevalence of ischemic acute tubular necrosis (ATN) was higher than sepsis. This was in agreement with the results achieved by Hui-Stickle et al. who have revealed that the incidence of ischemia and nephrotoxic medications was higher (3). It is indicated that approximately 50% of our patients experienced sepsis or ischemia-hypovolemia as the etiology of AKI. However, nephrotoxic medication was not common in the studied patients (table 2). Regarding improving health care and appropriate treatment of streptococcal infections, the incidence of post streptococcal glomerulonephritis (PSGN) was not high (7.8%). However, PSGN is still a common cause of ARF in developing countries (5, 7). A high incidence of hemolytic uremic syndrome (HUS) has been reported in different studies (5, 7, 13). The incidence of HUS in our patients was higher than those reported by Shah et al, but was similar to the study reported by Ghani et al. (5, 7, 12). In tropical countries, infections (especially Malaria) were the most prevalent causes of AKI (14). Although Malaria infection has been reported in south of Iran, it was not seen in our province.

Ultrasound study is a non-invasive method in evaluating children with AKI. Among ultrasound findings, increased parenchymal echogenicity was the most frequent finding that was in agreement with Yamaguchi et al. (15).

Tall T-wave, an ECG sign of hyperkalemia was the most common findings. Since after revealing tall T-wave, the vigorous treatment modalities were applied, no profound ECG finding (arrhythmia) was observed. Nevertheless, in at least 3 patients who died from fluid and electrolytes imbalance, severe hyperkalemia (serum potassium more than 8 meq/L) was also recorded.

The mortality rate of AKI has been reported from 10% in uncomplicated AKIs to 80% in those who required renal replacement therapy (RRT) (16,17). Irrespective of new treatment modalities in managing AKI, the mortality rate of patients with MOSFs was still high (60% to 100%). Even applying new treatment strategies such as continuous kidney replacement therapy, the mortality rate has not changed dramatically (18, 19). However, Williams et al. indicated a decrease in mortality rate in patients with MOSFs over the last years from 100% to 88% (20), while Ghani et al. reported an incidence of 44% of MOSFs in their patients (21). At this study, 22.2% patient mortality rate was shown. Not surprisingly, the most prevalent cause of mortality was MOSFs due to sepsis (72.5%). The difference between the mortality rates was possibly because of selected patients. Since we did not enroll newborns and neonatal intensive care unit (NICU) mortality rate was not entered in the study.

Rapidly progressive glomerulonephritis (RPGN), hemolytic uremic syndrome (HUS) and Henoch–Schönlein purpura may present as AKI. However, they may progress to chronic kidney disease as well (21). We found that children with the last GFR less than 50 ml/min/1.73 m^2 (Loss category of RIFLE criteria) were mostly had glomerular diseases (RPGN or HUS).

In the more recent decades, the use of acute peritoneal dialysis (PD) has decreased worldwide (20). Warady et al. described a trend of shifting from acute PD in favor of hemodialysis in AKI (22). However, Kendirli et al. reported that most of their patients underwent peritoneal dialysis (23). Ghani et al. reported dialysis in more than 70% of their patients and Hui-Stickle et al. indicated that 42% of the ICU patients are needed RRT (3, 5).

Approximately 34% of the studied patients

were required dialysis (PD and/or HD). Most of those who needed RRT underwent hemodialysis (58%). Nonetheless, the mortality rate was not significantly different between patients on PD or HD. However, it has been reported that early RRT may improve the chance of renal recovery (16). The differences among the incidences of RRT in various studies may be due to the different etiologies and mechanisms of AKI. In comparison to our study, Ghani et al. reported a higher incidence of sepsis and tumor lysis syndrome. Al Rohani et al. demonstrated that tropical infections with Malaria on the top were the most prevalent causes of AKI (15).

The younger age has been indicated as a predictor of death (7, 20, 24). Since most of the studies have recruited newborns, the higher mortality rate was seen in newborns and infants less than 1 year. Newborns were not enrolled to our work and therefore did not demonstrate a higher mortality rate in very young patients.

A rise in serum creatinine and a decrease in urine output have been used to verify AKI. Recently, RIFLE criteria have been developed to define AKI precisely (10, 25). According to the RIFLE criteria, most of our patients were placed in failure category. Olowu et al. reported high incidence of stage 3 AKI (60.7%) with a higher dialysis requirement by (26). However, loss category was not prevalent in our patients. Roughly, 13% of our patients were placed in this category.

Considering logistic regression analysis, we found that the etiology of the disease (intrinsic renal diseases), the first GFR and the higher RIFLE score were the independent predictors of the latest GFR less than 50 ml/min/m^2. Nevertheless, the etiology of disease was the only predictor of patient's death. Ghani et al. demonstrated that MOSFs and late referral to the nephrologist were the independent predictors of prognosis (5).

The main limitation of this study was its retrospective temperament, and the main strengths of the study were using RIFLE criteria, determining its role in short-term outcome and also including patients, hospitalized at a tertiary center over 10 years.

6. Conclusions

To conclude, the mortality is still high in AKI. Furthermore, the poor outcomes (defined as low GFR) are higher among patients with low levels of first GFR and higher RIFLE score.

Author's contributions

AG defined the aim of research and the study design. PM, AM and YM participated in the design of the study and performed the statistical analysis and wrote some parts of the draft. AG prepared the manuscript. All authors read and approved the final manuscript.

Conflict of interest

The author declared no competing interests.

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