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ORIGINAL ARTICLE

Etiology and outcome of acute kidney injury in children

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Abstract The aim of this prospective, multicenter study was to define the etiology and clinical features of acute kidney injury (AKI) in a pediatric patient cohort and to determine prognostic factors. Pediatric-modified RIFLE (pRIFLE) criteria were used to classify AKI. The patient cohort comprised 472 pediatric patients (264 males, 208 females), of whom 32.6% were newborns (median age 3 days, range 1–24 days), and 67.4% were children aged >1 month (median 2.99 years, range 1 month–18 years). The most common medical conditions were prematurity (42.2%) and congenital heart disease (CHD, 11.7%) in newborns, and malignancy (12.9%) and CHD (12.3%) in children aged>1 month. Hypoxic/ischemic injury and sepsis were the leading causes of AKI in both age groups. Dialysis was performed in 30.3% of newborns and 33.6% of children aged>1 month. Mortality was higher in the newborns (42.6 vs. 27.9%; $p<0.005$). Stepwise multiple regression analysis revealed the major independent risk factors to be mechanical ventilation [relative risk (RR) 17.31, 95% confidence interval (95% CI) 4.88–61.42], hypervolemia (RR 12.90, 95% CI 1.97–84.37), CHD (RR 9.85, 95% CI 2.08–46.60), and metabolic acidosis (RR 7.64, 95% CI 2.90–20.15) in newborns and mechanical ventilation (RR 8.73, 95% CI 3.95–19.29), hypoxia (RR 5.35, 95% CI 2.26–12.67), and intrinsic AKI (RR 4.91, 95% CI 2.04–11.78) in children aged >1 month.

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Introduction

Acute kidney injury (AKI) is a medical condition commonly encountered by pediatricians, nephrologists, and intensivists. However, only a limited number of studies on the epidemiology of AKI in children have been performed to date. Flynn drew attention to the variation in the etiology of AKI that was present not only between centers from developing and developed countries, but also between different centers from only developing countries [1]. Socio-economical status, availability of health facilities, and environmental factors may affect the etiology and outcome of AKI. In a recent study from Nigeria, for example, gastroenteritis was reported to be the leading cause (28.9%) of AKI, while malaria constituted 13.7% of all reported AKI cases [2]. In comparison, in developed countries, malignancies, cardiac surgery, sepsis, and nephrotoxicity are the leading causes [3–6]. Despite significant developments in the management of AKI, the overall mortality rate of patients with AKI has not improved dramatically [7].

Data on the epidemiology of AKI in Turkey are limited. Single-center experiences from tertiary centers in the 1980s revealed that acute gastroenteritis (58%), sepsis (21%), and acute glomerulonephritis (6%) were the leading causes, with malignancy (1.4%) and perinatal asphyxia (0.5%) being only rarely associated with AKI [8, 9]. Bircan et al. reported a relatively recent series over a 5-year period (between 1994–1998) involving 106 children aged 2 months to 14 years in which AKI was defined as persistently high values of serum creatinine >1.5 mg/dl. Among these children, acute glomerulonephritis (49%), urinary stones (20%), and acute tubular necrosis (16%) were the leading causes of AKI; hemolytic uremic syndrome (HUS) was causally related in only 2% of cases [10].

Turkey has achieved remarkable results in recent decades in terms of improving the socio-economical status of its citizens, availability of health facilities, and parameters of child health. In the prospective study reported here, our aim was to determine the demographics, clinical characteristics, and outcome of AKI among a Turkish pediatric patient cohort and to identify risk factors for mortality.

Given similar changes in health care availability and technology in other areas of the world, the data reported here on AKI in children are likely to be reflective of changing patterns being seen in other developing countries also benefitting from improvements in the socioeconomic status of their citizens and being able to offer improved critical care services to ill children.

Patients and methods

Out of the 24 pediatric nephrology centers (teaching hospitals with intensive care units) in Turkey, 17 centers and 472 pediatric patients with AKI participated in this study. These patients were enrolled prospectively between 1 May 2006 and 30 April 2007. The majority of patients were from urban areas, which is in agreement with the demographic distribution of the population within Turkey.

Centers were asked to identify any patient with AKI (at the time of admission or during treatment at the hospital), also those who were acutely ill, and collect a wide range of data (age, gender, known medical disorders, such as prematurity, congenital heart disease, malignancy, urologic problems; signs and symptoms at diagnosis; laboratory test results; AKI-related problems; treatment modality; outcome) on all of these patients in real time. Data collection sheets were used to gather data prospectively.

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AKI was defined as an absolute increase in serum creatinine by either >0.3 mg/dl or an increase of ≥50% from baseline or a glomerular filtration rate (GFR; based on the Schwartz formula) decrease ≥25% from baseline, or a reduction in urine output (<0.5 ml/kg for more than 8 h). Pediatric-modified Risk, Injury, Failure, Loss, End-stage kidney disease (pRIFLE) criteria proposed by Akcan-Arikan et al. [6] were used to classify AKI. Both serum creatinine (SCr) and urine output (UO) were considered and the patients assigned to the appropriate pRIFLE strata if they fulfilled either the UO or SCr criterion or both: risk (R) was defined as an estimated (e) GFR decrease of 25% and/or UO<0.5 ml/kg/h × 8 h; injury (I) was defined as an eGFR decrease of 50% and/or UO<0.5 ml/kg/hour × 16 h; failure (F) was defined as an eGFR decrease of 75% and/or UO<0.3 ml/kg/h × 24 h or anuric for 24 h; loss (L) was defined as renal failure > 4 weeks; end-stage renal disease (E) was defined as renal failure>3 months. In the immediate newborn period newborns can be oliguric during the first 24 h of life and they may also reflect maternal creatinine values for the first few days; thus oligo-anuria was not accepted as a criterion for the first 24 h of life; in newborns, a decrease in eGFR or increase in serum creatinine level were used to filter out the reflection of maternal creatinine.

Oliguria was defined by a urine flow of <0.5 ml/kg/h in children <30 kg and <400 ml/day in children >30 kg. "Low fluid intake" was taken from information in the medical history of the patients with a diagnosis of AKI on admission (in patients with acute gastroenteritis, for example) and was based on the amount of fluid intake by the patients who developed AKI during their hospital stay.

Low fluid intake and prerenal, intrinsic, or obstructive AKI were defined by clinical assessment [11]. The category hypoxic/ischemic injury was defined to represent patients with hypoxia and/or hypotension/shock in the absence of sepsis. The categories low fluid intake and acute gastroenteritis were defined to include patients with presumed prerenal injury but no signs of hemodynamic compromise.

In infants and children, hyperkalemia was defined as a serum potassium level >5.5 mEq/l; in newborns, it was defined as a serum potassium level >7.5 mEq/l in the first day of life and >6.5 mEq/l in the remaining days for the category newborn. Hypertension was defined as systolic and/or diastolic blood pressure >95th percentile for age, gender, and length (for patients >1 year of age) [12–15]. Sepsis was defined as systemic inflammatory response plus a suspected or proven infection, and septic shock was defined as sepsis plus cardiovascular organ dysfunction [16, 17]. The degree of fluid overload was calculated using the method described by Goldstein et al.: (fluid in − fluid out) (l)/admission weight (kg) × 100; hypervolemia was defined as a fluid overload >7% [18, 19].

Statistical analysis

The results were analyzed using SPSS for Windows ver. 13.0 (SPSS, Chicago, IL), and descriptive statistics are presented as the mean ± standard deviation (SD) if equally distributed or as the median and range if unequally distributed. Univariate analyses for group comparisons were performed using independent samples *t* test or chi-square tests. Stepwise multiple regression analysis was performed to assess whether there were significantly independent predictors of mortality; variables with $p<0.20$ from univariate analysis were entered into the regression model, following analyses regarding co-linearity. The final model retained variables that were determined to be important predictors with less than 10% type-1 error level. A p value <0.05 was considered statistically significant.

Results

The 472 patients (264 males, 208 females; male to female ratio 1.27) were categorized into the following age groups: newborn [32.6%; gestational age <30 weeks, 23.9%, median age 3 days, range 1–24 days; age <7 days, 84.4%], 2–12 months (23.7%), 13 months–5 years (13.1%), 6–10 years (14.5%), and 11–18 years (16.1%). The median age of children aged >1 month was 2.99 years (range 1 month–18 years). pRIFLE classification was available for 423 patients [risk group (R), 30.8%; injury group (I), 25.3%; failure group (F), 43.0%; loss group and end stage kidney disease, 0.9%], and there were no significant differences between newborns and children aged >1 month. The ratio of males among newborns was slightly higher than that among children aged > 1 month (60.0 vs. 53.7%, respectively), but the difference was not statistically significant ($p>0.05$).

Of the 472 patients, 63% had AKI on admission or within 24 h following admission, 23% developed AKI within 2–7 days, and 14% developed AKI 1 week after admission or later. The frequency of patients who developed AKI 24 h after hospitalization was higher in the newborn group than in children aged > 1 month (44.8 vs. 32.3%, respectively; $p<0.01$).

Known medical disorders

Known medical disorders were present prior to the diagnosis of AKI in 67.5 and 54.4% of newborns and children aged >1 month, respectively ($p=0.005$; Table 1). Fifty-seven patients had congenital heart disease, and AKI had developed in 17 patients (29.8%; median age 8 months, range 2 days–11 years) a mean of 2 days (range 0–4 days)

Table 1 Known medical disorders among the pediatric patients of the study cohort prior to the diagnosis of acute kidney injury (AKI) and etiology of AKI by age groups

Known medical disorders/AKI etiology	Age groups		
	Newborns (n=154)	>1 month (n=318)	Total (n=472)
Known medical disorders			
Prematurity	65 (42.2%)	1 (0.3%)	66 (14.0%)
Congenital heart disease	18 (11.7%)	39 (12.3%)	57 (12.1%)
Malignancy	–	41 (12.9%)	41 (8.7%)
Urologic disorders	7 (4.5%)	19 (6.0%)	26 (5.5%)
Mentally handicapped	–	16 (5.0%)	16 (3.4%)
Renal diseases	5 (3.2%)	12 (3.8%)	17 (3.6%)
Gastrointestinal disorders	3 (1.9%)	13 (4.1%)	16 (3.4%)
Respiratory disorders	–	9 (2.8%)	9 (1.9%)
Hematological disorders	–	5 (1.6%)	5 (1.1%)
Immunological disorders	–	4 (1.3%)	4 (0.8%)
Others	6 (3.9%)	14 (4.4%)	20 (4.2%)
None	50 (32.5%)	145 (45.6%)	195 (41.3%)
Etiology of AKI			
Hypoxic/ischemic injury	67 (43.5%)	65 (20.4%)	132 (28.0%)
Sepsis	37 (24.0%)	49 (15.5%)	86 (18.2%)
Low fluid intake without acute gastroenteritis[a]	24 (15.6%)	46 (14.5%)	70 (14.8%)
Acute gastroenteritis	1 (0.6%)	38 (11.9%)	39 (8.3%)
Renal dysplasia, cystic diseases	7 (4.5%)	1 (0.3%)	8 (1.7%)
Glomerular diseases	2 (1.3%)	49 (15.4%)	51 (10.8%)
Drug induced/exogenous toxins	1 (0.6%)	29 (9.1%)	30 (6.4%)
Acute tumor lysis syndrome	–	7 (2.2%)	7 (1.5%)
Pyelonephritis	1 (0.6%)	6 (1.9%)	7 (1.5%)
Urinary tract obstruction	5 (3.2%)	5 (1.6%)	10 (2.1%)
Other causes	9 (5.8%)	23 (7.2%)	32 (6.8%)

Values are given as the number (n) of patients, with the percentage given in parenthesis

[a] Inadequate fluid intake in the absence of acute gastroenteritis (for example poor sucking, mentally handicapped patients, vomiting, iatrogenic, among others)

after cardiac surgery. Malignancy was present in 41 patients (median age 8.3 years, range 2–18 years). Leading malignancies were leukemia [acute lymphocytic leukemia, n=12 (29.3%); acute myeloid leukemia, n=4 (9.8%)], central nervous system tumors (n=9, 22.0%), and non-Hodgkin lymphoma (n=4, 9.8%).

Clinical features at presentation

Common clinical features (>10%) are shown in Table 2. Acute gastroenteritis and dehydration were more common in children aged >1 month. Low fluid intake was noted in 35% of cases (27.1% in newborns vs. 38.9% in children aged >1 month; $p<0.05$). Thirty-eight percent of patients were on mechanical ventilation (MV) before the diagnosis of AKI, and an additional 9.1% needed MV after the diagnosis of AKI; 10.4% of patients had recent surgery.

Etiology of AKI

AKI was prerenal, intrinsic, and obstructive in 23.9, 72.9, and 3.2% of newborns and in 40.0, 58.4, and 1.6% of children aged >1 month of life, respectively ($p<0.05$). Prerenal AKI was more frequent in the group who developed AKI on admission than in those who did not (43.4 vs. 25.2%, respectively; $p<0.001$).

The causes of AKI among our pediatric patient population are presented in Table 1. Hypoxic/ischemic injury and sepsis were the leading causes in both age groups, with the percentage of patients with hypoxic/ischemic injury being significantly higher in newborns than in children aged > 1 month (43.5 vs. 20.4%; $p<0.001$). Approximately 15% of patients in both groups had a low fluid intake in the absence of acute gastroenteritis (for example, poor sucking, mentally handicapped patients, vomiting, iatrogenic, among others)

Table 2 Common clinical features at diagnosis of AKI according to age groups

Features	Age groups			p^a
	All patients (n=472)	Newborns (n=154)	>1 month (n=318)	
Mechanical ventilation	181 (38.3%)	89 (57.8%)	92 (28.9%)	<0.001
Hypoxia	144 (30.5%)	79 (51.3%)	65 (20.4%)	<0.001
Hypotension	160 (33.9%)	60 (39.0%)	100 (31.4%)	0.120
Septic shock	83 (17.6%)	30 (19.5 %)	53 (16.7 %)	0.443
Heart failure	57 (12.1%)	15 (9.7%)	42 (13.2%)	0.296
Anuria	82 (17.4%)	21 (13.6%)	61 (19.2 %)	0.155
Oliguria	138 (29.3%)	38 (24.7%)	100 (31.5%)	0.132
Dehydration	128 (27.1%)	31 (20.1%)	97 (30.5%)	0.05
Acute gastroenteritis	66 (14.0%)	2 (1.3%)	64 (20.1%)	<0.001

Values are given as the number (n) of patients, with the percentage given in parenthesis

[a] Newborns vs. children aged >1 month

Glomerular diseases were the third most common cause of AKI (15.4%) in children aged >1 month (hemolytic uremic syndrome, n=18; acute post-streptococcal glomerulo-nephritis, n=7; membranoproliferative glomerulonephritis, n=4), followed by acute gastroenteritis (11.9%). AKI secondary to drugs/exogenous toxins was seen in 9.1% (29/318) of cases (acyclovir, n=5; amikacin, n=3; amphotericin B, n=2; cisplatin, n=4; cyclosporine A, n=2; radiocontrast agents, n=4).

Among the 41 patients with malignancy, sepsis (26.8%) and drug toxicity (26.8%) were the leading causes of AKI, followed by ischemic injury (17.1%) and acute tumor lysis syndrome (9.8%).

A total of 26 patients (median age 4 months; newborn–14 years) had AKI exacerbated chronic kidney disease (CKD); nine patients had glomerulonephritis, 17 patients had structural disease (cystic disease, hypo-dysplasia, posterio-urethral valve, among others).

AKI-related problems

Common problems and complications that arose during the course of AKI are shown in Table 3: oligo-anuria was the leading complication (55.7%), with oligo-anuria and hypervolemia being more common in children aged >1 month and metabolic acidosis being more common in newborns.

Dialysis

Dialysis was performed in 30.3% of newborns (93.3% peritoneal dialysis, 6.7% hemodialysis), and 33.6% of children aged >1 month (59.2% peritoneal dialysis, 40.8% hemodialysis). The ratio of hemodialysis was dramatically low in newborns (p<0.001).

Mortality and risk factors

Overall mortality was 32.8% (42.6% in newborns and 27.9% in patients aged >1 month; p<0.005) and was secondary to non-AKI related causes in 81.1% of cases. The mortality rate was higher in patients who developed AKI 24 h after admission than in those who did not, both in newborns (48.9 vs. 33.9%, p=0.07) and in children aged >1 month (52.8 vs. 12.2%; p<0.001). Median time to recovery among patients who survived was comparable between newborns and children aged >1 month of life [4.5 (range 1–37 days) vs. 5.0 (1–67 days); p>0.10].

The frequency of dialysis (38.5 vs. 32.1%; p>0.05) and mortality rate (23.1 vs. 34.1%; p>0.05) was comparable between CKD and non-CKD groups. Only one patient in the CKD group progressed to end-stage renal disease (3.8 vs. 0.7%; p>0.05)

Association between pRIFLE criteria at the diagnosis of AKI, dialysis and mortality according to age groups are presented in Table 4. In newborns, the dialysis rate was comparable between pRIFLE R (9.6%) and I (9.1%), and it was significantly lower than those with pRIFLE F (55.9%) (p<0.001). Mortality rates were higher in patients with pRIFLE I (51.5%) or F (48.5%) versus those with pRIFLE R (26.9%) (p<0.05). In children aged >1 month, dialysis rate was higher in patients with pRIFLE I (32.9%) or F (44.8%) than in those with pRIFLE R (11.5%) (p<0.001), but the differences between mortality rates (24.4, 30.2, and 24.1% between those with pRIFLE R, I and F, respectively; p>0.05) were not statistically significant.

Univariate analysis (variables were age group, known medical disorders, clinical features at diagnosis, problems and metabolic complications during AKI, type of AKI, MV, dialysis, and pRIFLE strata) revealed a significant increase

Table 3 Problems and metabolic complications during AKI according to age groups (data was available for 469 patients)

Problems and complications	Age groups			p^a
	All patients (n=469)	Newborns (n=154)	>1 month (n=315)	
Oligo-anuria	261 (55.7%)	74 (48.1%)	187 (59.4%)	<0.05
Hypertension	43 (9.2%)	8 (5.2%)	35 (11.1%)	<0.05
Hypervolemia	61 (13.0%)	13 (8.4%)	48 (15.2%)	<0.05
Heart failure	49 (10.4%)	13 (8.4%)	36 (11.4%)	0.422
Pulmonary edema	48 (10.2%)	13 (8.4%)	35 (11.1%)	0.420
Metabolic acidosis	247 (52.7%)	91 (59.1%)	156 (49.5%)	<0.05
Hypernatremia	88 (18.8%)	34 (22.1%)	54 (17.1%)	0.209
Hyponatremia	122 (26.0%)	41 (26.6%)	81 (25.7%)	0.824
Hyperkalemia	95 (20.3%)	24 (15.6%)	71 (22.5%)	0.087
Hypocalcemia	139 (29.6%)	48 (31.2%)	91 (28.9%)	0.667
Hyperphosphatemia	133 (28.4%)	38 (24.7%)	95 (30.2%)	0.232
Hyperuricemia	223 (47.5%)	68 (44.2%)	155 (49.2%)	0.326

Values are given as the number (n) of patients, with the percentage given in parenthesis

[a] Newborns vs. children aged >1 month

in mortality rate with certain parameters. The relative risk (RR) of mortality was highest in the presence of prematurity, hypoxia, MV, oligo-anuria, metabolic acidosis, hypervolemia, and dialysis in newborns; in children aged >1 month, the RR of mortality was highest in the presence of chronic heart disease (CHD), malignancy, hypoxia, septic shock, hypotension, heart failure, hypervolemia, pulmonary edema, intrinsic AKI, and dialysis. Stepwise multiple regression analysis revealed that in newborns the mortality risk increased independently 17.31-fold with MV, 12.90-fold with hypervolemia, and 9.85-fold with CHD (Table 5). In children aged >1 month, the mortality risk increased independently 8.73-fold with MV, 5.35-fold with hypoxia, and 4.91-fold with intrinsic AKI (Table 6).

Discussion

Previous studies of AKI in children from Turkey were single-center, retrospective studies. Although no patients from centers in the east and southeast Turkey were enrolled in our study, many patients from these regions were referred to centers in central and southern regions of Turkey that did participate. Consequently, more than 80% of all patients in pediatric nephrology centers in Turkey were evaluated in the above-mentioned 17 centers during the study period. As such, we believe our series well represents AKI in tertiary pediatric centers in Turkey.

Compared to the results of a previous series from Turkey, the proportion of patients with acute gastroenteritis decreased from 58 to 8.3% in all age groups and that of

Table 4 Association between pRIFLE criteria at diagnosis of AKI, dialysis and mortality according to age groups (data was available for 423 patients)

pRIFLE	Age groups					
	All patients (n=423)		Newborns (n=153)		> 1 month (n=270)	
	Dialysis	Mortality	Dialysis	Mortality	Dialysis	Mortality
Risk (R)	14/130 (10.8%)	33/130 (25.4%)	5/52 (9.6%)	14/52 (26.9%)	9/78 (11.5%)	19/78 (24.4%)
Injury (I)	28/109 (25.7%)	40/109 (36.7%)	3/33 (9.1%)	17/33 (51.5%)**	25/76 (32.9%)***	23/76 (30.2%)
Failure (F)	90/184 (48.9%)	61/184 (33.2%)	38/68 (55.9%)*	33/68 (48.5%)**	52/116 (44.8%)***	28/116 (24.1%)
Total	132/423 (31.2%)	134/423 (31.7%)	46/153 (30.1%)	64/153 (41.8%)	86/270 (31.9%)	70/270 (25.9%)

pRIFLE, Pediatric-modified Risk, Injury, Failure, Loss, End-stage kidney disease criteria

*p<0.001 (F vs. R and I), **p<0.05 (F and I vs. R), ***p<0.001 (F and I vs. R)

Values are given as the number (n) of patients, with the percentage given in parenthesis

Table 5 Predictors of mortality in newborns by multivariate logistic regression

Predictors	*p*	RR	95% CI	
			Lower	Upper
Mechanical ventilation	< 0.001	17.313	4.880	61.422
Hypervolemia	0.008	12.901	1.973	84.366
Congenital heart disease	0.004	9.849	2.082	46.599
Metabolic acidosis	< 0.001	7.643	2.899	20.147
Prematurity	0.022	3.298	1.187	9.165
Hypocalcemia	0.028	3.110	1.132	8.541

RR, Relative risk; 95% CI, 95% confidence interval

acute glomerulonephritis decreased from 5.8–49% to 2.2% in children aged >1 month; however, the ratio of AKI secondary to malignancy and following cardiac surgery increased dramatically in our series. Improvement in sanitation and education, clean water, easier access to health facilities, early diagnosis and availability of oral rehydration solutions have probably resulted in a decline in the ratio of AKI secondary to acute gastroenteritis and acute glomerulonephritis. Similar experiences have also been reported from India and Thailand [20, 21].

Due to dissimilarities in the definition of AKI, study populations (i.e. special groups such as patients in intensive care units) and age groups of AKI, recent data on the epidemiology of AKI from different centers and countries are not easy to compare [2–5, 21–25]. However, our literature search revealed certain features: (1) underlying causes vary between developed and developing countries; (2) regionally, the male-to-female patient ratio is higher in developing countries; (3) there has been a change over time.

In the USA and Canada, cardiac surgery, hematological–oncological conditions, ischemia, and nephrotoxic drugs are the leading causes of AKI [3–5]. In developing countries, however, acute gastroenteritis and acute glomerulonephritis are more frequent causes of AKI, compared to developed countries [2, 21, 23–25]. The etiology of AKI in our series was similar to that reported in recent series from developed countries.

Table 6 Predictors of mortality in patients aged >1 month by multivariate logistic regression

Predictors	*p*	RR	95% CI	
			Lower	Upper
Mechanical ventilation	< 0.001	8.731	3.953	19.288
Hypoxia	< 0.001	5.346	2.257	12.666
Intrinsic AKI	< 0.001	4.907	2.044	11.776
Septic shock	0.006	3.411	1.412	8.238
Malignancy	0.066	2.437	0.942	6.303
Congenital heart disease	0.099	2.399	0.848	6.786
Dialysis	0.097	1.904	0.890	4.075

Among recently published series in the epidemiology of AKI in children, our series was unique in that it is the largest, prospective, and nationwide series reported to date, and the definition of AKI was based on pRIFLE classification. Only three series reported from Canada, Brazil, and Saudi Arabia were prospective; all were single-center experiences with a relatively small number of patients, and the series from Canada and Brazil involved patients from pediatric intensive care units [5, 22, 25]. In order to make consequential comparisons between the studies, a common definition of AKI is mandatory. pRIFLE criteria should be used and tested in future studies on the epidemiology of AKI in order to allow comparisons between different series.

The overall mortality of children with AKI reported in recent series ranges from 20 to 41.5% [2–5, 21–25]. The etiology of AKI, underlying diseases, co-existing conditions, availabilities of dialysis resources, and transportation have an effect on the mortality rate.

Several risk factors, not always consistently, had been defined for mortality in previous series: younger age [3, 26], older age [21], extrarenal diseases [3, 22, 26–33], sepsis, septic shock, multiorgan failure [3, 26, 29, 31, 34–39], oligoanuria and/or anuria [22, 29, 40, 41], hypotension [32, 34, 37], use of pressor drugs [33], need for MV [22, 26, 32, 35, 36, 40], need for dialysis [22, 32, 35, 39, 40], and fluid overload [19, 42, 43]. A common major weaknesses to all of these studies were the relatively small size of the patient groups, the lack of a uniform definition of AKI, staging, and standardized treatment.

In our series, the need for MV was the most powerful predictor of mortality in newborns and children aged >1 month, increasing the mortality risk by a multiple of 17.31 and 8.73 in newborns and children aged >1 month, respectively. In the series reported by Gong et al. [26], the relative risk in patients on MV was smaller than that in our study (RR 9.96, 95%CI 1.82–19.50).

In their retrospective study, Foland et al. [19] showed that fluid overload was an independent risk factor for mortality (OR 1.37, 95%CI 0.97–1.94) in 113 children on continuous venovenous hemofiltration: median fluid overload level was 7.8% in survivors and 15.1% in non-survivors. In our series, hypervolemia (defined as fluid overload >7%) was an independent risk factor for mortality in newborns (RR 12.90; 95%CI 1.97–84.37), the most important risk factor after the need for MV. Timely follow-up of fluid status of the patient and active management of fluid overload can improve survival in newborns with AKI.

To the best of our knowledge, our study is the first to identify fluid overload as an independent risk factor for mortality in newborns.

In our series, among patients aged >1 month, the rate of hemodialysis was significantly higher in the AKI-failure group (45%) and injury group (33%) than in the risk group (11.5%). This pattern was not observed for mortality; AKI staging at diagnosis was not an independent risk factor of mortality. We should highlight, however, the fact that in our series and in many other series, the management of AKI was not standardized. Prospective studies with standardized management are needed to determine whether AKI staging has an impact on mortality.

AKI classification systems for newborns have not been developed and validated. Keeping in mind this fact; we have classified AKI in neonates according to pRIFLE criteria. We noted that the rate of dialysis was significantly higher in newborns in the AKI-failure group (56%) than in those in the injury (9%) and risk group (10%). Mortality was significantly higher in the AKI-failure group (48.5%) and injury group (51.5%) than in the risk group (26.9%). Similar to patients aged >1 month, AKI staging at diagnosis was not an independent risk factor of mortality. We once again would like to emphasize that in the immediate newborn period newborns may be acceptably oliguric during the first 24 h of life and that they may also reflect maternal creatinine values during the first few days.

In conclusion, our nationwide, prospective data show that pediatric nephrologists, intensivists, and pediatricians should focus on risk groups; prematurity, malignancy, CHD, and urologic disorders were predisposing conditions for AKI. The etiology of AKI in Turkey has greatly evolved during the last two decades, acute gastroenteritis and acute post-streptococcal glomerulonephritis has decreased significantly, and prematurity, malignancy, and CHD has increased. The etiology and mortality rates found in our study are similar to those of developed countries. Patients aged >1 month with AKI-failure and in the injury group needed dialysis more frequently than the risk group. Independent risk factors for mortality were MV, hypervolemia, CHD, metabolic acidosis, prematurity, and hypocalcemia in newborns, and mechanical ventilation, hypoxia, intrinsic AKI, septic shock, malignancy, CHD, and dialysis in patients >1 month of age. Prospective studies using pRIFLE classification with standardized management are needed to determine actual risk factors of AKI in children.

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