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Prognosis of acute kidney injury based on pRIFLE criteria among patients admitted to pediatric intensive care unit in Northern Iran; a single center study

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ABSTRACT

Introduction: Acute kidney injury (AKI) is a frequent problem in pediatric intensive care units, while it is associated with significant mortality.
Objectives: The aim of this study was to determine the prevalence and prognosis of AKI based on pRIFLE (pediatric risk, injury, failure, loss, end-stage renal disease) criteria among children admitted to a pediatric intensive care unit
Patients and Methods: This research included 323 children from 1 month to 14 years old age, admitted to the pediatric intensive care unit. The pRIFLE was determined in patients along with urinary output and creatinine level. The pediatric risk of mortality (PRISM) score was also assessed.
Results: Mean PRISM III score was 34.66 ± 15.97 and 17.72 ± 6.06 respectively in children with and without AKI ($P=0.001$). It was found that variables of encephalopathy, PRISMIII score and gender were the only variables affecting the incidence of AKI.
Conclusion: While pRIFLE criteria are appropriate and efficient criteria for early diagnosis of AKI, their role alone as prognostic factors of mortality require further studies.

Original

Implication for health policy/practice/research/medical education:
The pRIFLE (pediatric risk, injury, failure, loss, end-stage renal disease) criteria adapted from the RIFLE criteria for use in children. This study was to determine the prevalence and prognosis of AKI based on pRIFLE criteria among children admitted to a pediatric intensive care unit. Although pRIFLE is appropriate and efficient criteria for early diagnosis of AKI to speed up treatment and reduce the incidence of AKI complications, its role alone as a prognostic factor of mortality requires further studies.

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Introduction

Acute kidney injury (AKI) is considered a complex syndrome that is characterized by a rapid decline (within a few hours to a few weeks) in glomerular filtration rate, resulting in retention of wastes metabolites such as creatinine and urea, dysregulation in fluid, electrolyte and acid-base homeostasis (1). This disease occurs in 2% to 3% of children referred to health centers and in about 8% of infants in the neonatal intensive care unit. It has a very diverse etiology. Usually, AKI is classified into categories of pre-renal failure associated with reduced renal blood flow for inappropriate cardiac output or intravascular volume, intrinsic renal disease caused by damage to renal parenchyma (such as artery ischemia, tubular or glomerular diseases) and post-renal failure (caused by urinary tract obstruction in one or both kidneys) (2-4). The main reason for AKI among pediatric population includes sepsis, use of drugs damaging kidney and renal ischemia. The incidence rate in hospitalized critically ill children has been reported between 20% and 30% (5). The exact incidence rate of this disease is not clearly identified in the pediatric population in Iran, however, recently it has been observed a growth in infants and children hospitalization (6). AKI is diagnosed commonly by slight increase in serum creatinine levels (7-10). Hence, pRIFLE (pediatric risk, injury, failure, loss, end-stage

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renal disease) criteria were defined finally for adults in 2004 after extensive studies. AKI in patients is detected by assessing changes in serum creatinine levels relative to baseline and sudden decrease in urine output (UOP). To define pRIFLE, first three grades indicate increasing AKI severity and two other show outcome variables. On the other hand, Akcan-Arikan et al provided a modified pediatric-RIFLE version (pRIFLE), based on a 12 months single center study where 150 critically ill children were prospectively analyzed (11).

Objectives

The aim of this study was to determine the prevalence and classification of patients admitted to the PICU based on the severity of the disease and pRIFLE criteria.

Patients and Methods

Study patients

In this study, patients admitted to the pediatric intensive care unit (PICU) at 17-Shahrivar hospital in Rasht, Iran, were enrolled in the study. Inclusion criteria were age over 29 days and less than 16 years, and presence over 24 hours. Exclusion criteria included patients with a history of chronic kidney disease, stage 5 (GFR <15 mL/min/1.73 m^2), bilirubin levels over 5 mg/dL and hospitalization less than 24 hours. Indication for admission to the PICU included decreased level of consciousness (Glasgow coma scale [GCS] <7).

Patients were categorized based on age, gender, prognosis of admission mortality risk rate (using PRISM III score; pediatric risk of mortality), grades of kidney damage (pRIFLE criteria) on admission and during hospitalization, requirement of mechanical ventilation (MV), requirement of vasoactive drugs (VD), exposure to nephrotoxic drugs (ND), requirement of renal replacement therapy (RRT), hospitalization duration in PICU (day) and hospital outcome (death or discharge).

Creatinine levels in patients were evaluated every 24 hours with modified Jaffe method using auto-analyzer. Creatinine clearance was then obtained according to Schwartz formula, and pRIFLE grade was determined in patients along with urinary output obtained based on below Table 1.

For patients with uncertain baseline renal function data, the creatinine clearance was considered 100 mL/1.73 m^2 of body area within 24 hours (based on Akcan-Arikan suggestion as the reference). Catheter or urine bag was placed and UOP was calculated every 8 hours.

Ethical issues

The study protocol was in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Guilan University of Medical Sciences (# IR.GUMS.REC.1397.420). Participants' parents gave their informed written consent to enter the study. This study extracted from Pediatrician thesis of Mahsa Jilani (Thesis# 798).

Statistical analysis

All variables were analyzed by SPSS 17 software. Descriptive statistical methods (frequency, percentage and mean ± SD) were used for the statistical evaluation. Logistic regression method, chi-square and Pearson's tests were applied for analytical evaluation and *P* value less than 0.05 was considered significant in the study.

Results

Total cases admitted in PICU during the study period and fulfilled the inclusion criteria were 323 (including 185 (57.3%) male). Male to female ratio was 1.34:1. Majority of cases included in this study were between 1-5 years of age (78.3%) while 21.7% of cases were above 5 years of age. At the time of PICU admission, 43 (13.3%) of patients had AKI according to the pRIFLE criteria. The mean age of children with AKI was equal to 3.45 ± 1.93 years, while it was 3.66 ± 2.32 years in children without AKI ($P=0.47$). Of 43 children who developed AKI, 31 (72%) were male and 12 (28%) were female. Our study shows significant statically difference in sex groups ($P=0.001$). The mean PRISM III score was respectively 34.66 ± 15.97 and 17.72± 6.06 in children with and without AKI ($P=0.001$). Table 2 shows the frequency distribution of patients based on PRISM III score between the groups with and without AKI.

In this study, out of 323 patients who admitted to PICU, 43 had AKI with an incidence of 13.3%. At diagnosis, 37.2% (16 cases) were 'risk' comprised, followed by 'injury' comprised 46.5% (20 cases) and 'failure' comprised 16.3% (7 cases) respectively.

Using logistic regression, various variables containing VD, hypertension, encephalopathy, thrombocytopenia, shock, renal underlying disease, ND, PRISM III score, age and gender were tested. We found that variables of encephalopathy, PRISM III score and gender were the only parameters affecting as dependent variables and AKI

Table 1. pRIFLE criteria

Classification	Estimated creatinine clearance (eCrCl)*	Urine output
Risk	Decreases by 25%	<0.5 mL/kg/h × 8 hours
Injury	Decreases by 50%	<0.5 mL/kg/h × 16 hours
Failure	Decreases by 75% or eCCL <35 mL/min/1.73 m^2	<0.5 mL/kg/h × 24 hours or anuric ×12 hours
Loss	Persistent failure >4/52 weeks	
End-stage	End-stage renal failure (persistent failure >3 months)	

incidence (Table 3).

In 31 male patients with acute renal failure, 25.5%, 32.6%, and 13.9% were in stages of 1, 2, and 3 (risk, injury, failure) while these values were in girls (11.6%) with risk, 6 (13.9%) with injury and 1 (2.5%) respectively. A significant statically difference was not seen between the AKI grades (pRIFLE criteria) and gender of patients ($P=0.29$). Additionally, according to age groups, majority of AKI cases in this study were at the ages between 2 to 5 years (46.5%). Likewise, at diagnosis, 18.6.3% of cases of AKI belonged to stage risk of pRIFLE Criteria, while 20.9% were stage injury and 6.9% were stage failure respectively. Moreover, in patients older than 5 years of age only 2 patients had acute renal failure at the risk stage and one patient at the injury stage. No statistically significant association was found among the patient status with AKI grades (pRIFLE criteria) and age groups ($P=0.36$) (Table 4).

To compare patients based on MV, most of the patients with acute renal failure were not mechanically ventilated (86.1% versus 13.9%). There was no statistically significant correlation between the intensity AKI (pRIFLE criteria) and need to MV ($P=0.205$).

Based on the presence or absence of shock during admission to PICU, 26 (60.2%) of the patients had acute renal failure in shock status. By considering the AKI grading, 9 patients (20.9 %) with risk, 10 patients (23.2 %) with injury and 7 patients (16.2%) with failure were observed in shock status. Statistically significant association was observed between the intensity of AKI (pRIFLE criteria) and the shock status ($P=0.002$).

The study showed that most patients with acute renal failure did not receive ND. No statistically significant relationship between the AKI degree (pRIFLE criteria) and the use of ND was found ($P=0.412$)

According to AKI grades (pRIFLE criteria), 3 patients (21.4%) with no problem, 3 patients (21.4%) with risk and 4 patients (28.6%) with injury and also 4 patients (28.6%) with failure were recorded.

This study has shown that the majority of cases of most cases of acute renal failure occurred in patients who did receive VD (62.8 % versus 37.2%). To consider the grading of AKI, 9 patients (20.9 %) with risk, 12 patients (23.2 %) with injury and 6 patients (16.2%) with failure were observed in patients taking vasoactive medicines. There was a statistically significant correlation between the intensity of AKI and need to VD ($P=0.021$).

Out of 323 patients admitted to PICU, eleven patients (25.5%) had required RRT which included peritoneal dialysis in 7 cases and hemodialysis in 4 cases. Patients requiring RRT also had more severe AKI. There was a significant correlation between the intensity AKI and requirement to RRT ($P=0.002$) (Table 5).

Table 2. Frequency distribution of PRISM III score classes in two groups with and without AKI

PRISM III score	Groups						Statistical estimation
	Without AKI		With AKI		Total		
	No.	%	No.	%	No.	%	
0-9	14	5.4	0	0	14	3.4	P=0.001
10-15	74	28.6	5	7.8	79	24.5	
16-20	119	45.9	4	6.2	123	38.1	
21-25	41	15.8	13	20.3	54	16.7	
26-30	5	1.9	8	12.5	13	4	
Over 30	6	2.3	34	53.1	40	12.4	

Table 3. Role of different variables on admission to PICU in the incidence of AKI using logistic model

Variables in the Equation								
Variable	B	SE	Wald	*df*	*P* value	Exp(B)	95% CI for EXP(B)	
							Lower	Upper
Vasoactive drugs	0.652	1.063	0.377	1	0.539	1.920	0.239	15.421
Hypertension	6.510	4.094	0.08	1	1.000	67.749	0.39	3.32
Encephalopathy	6.436	1.893	11.55	1	0.001	62.039	15.27	2.550
Thrombocytopenia	18.94	7.795	2.8 7	1	0.998	1.697	0.86	2.94
Shock	-18.627	7.795	9.79	1	0.998	0.12	0.09	4.78
Underlying kidney disease	-20.546	1.729	1.94	1	0.999	0.09	0.34	3.68
Nephrotoxic drugs	-2.268	1.981	1.311	1	0.252	0.104	0.002	5.023
Prism score	0.257	0.039	42.68	1	0.09	1.294	1.197	1.398
Age	-0.026	0.092	0.083	1	0.773	0.974	0.814	1.166
Gender	1.172	0.445	6.934	1	0.008	3.229	1.349	7.725
Constant	8.021	8.889	0.023	1	1.000	3.045		

Table 4. Frequency distribution of acute kidney injury grades (pRIFLE criteria) in terms of PRISM III score

Prism score	AKI									
	No problem		Risk		Damage		Failure		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
0-9	0	0	0	0	0	0	0	0	0	0
10-15	2	40	1	20	2	40	0	0	5	100
16-20	2	50	2	50	0	0	0	0	4	100
21-25	5	38.5	4	30.8	3	23.1	1	707	13	100
26-30	2	25	3	37.5	3	37.5	0	0	8	100
Over 30	10	29.4	6	17.6	2	35.3	6	1736	34	100
Total	21	32.8	16	25	20	31.2	7	10.9	64	100

Table 5. Frequency distribution of AKI degrees based on pRIFLE criteria in children in terms of treatment outcome

Treatment outcome	Death		Discharge		Total		Statistical estimation
AKI degrees based on pRIFLE criteria	No.	%	No.	%	No.	%	
No problem	30	76.9	250	88	280	86.7	
With risk	3	7.7	13	4.6	16	5	
With injury	3	7.7	17	6	20	6.2	$P = 0.056$
With failure	3	7.7	4	1.4	7	2.2	
Total	39	100	284	100	323	100	

Discussion

AKI is a common side effect in patients hospitalized in intensive care unit that is associated with increased mortality, length of stay and high exploitation of financial resources (12-14). In this study, we tried to determine the prevalence rate of AKI in patients admitted to PICU at 17 Shahrivar hospital and study the risk factors related to mortality in patients.

In our study, 19.8% of patients were diagnosed with AKI based on pRIFLE criteria, 32.8% with no kidney problems on admission, 25% in the risk stage, 31.2% in the damage stage and 10.9% in the failure stage. In a study by Ostermann and Chang (in the UK and Germany), 35.8% of patients were suffered from AKI, 17.2% in risk stage, 11% in the damage stage and 7.6% in the failure stage on admission (15).

Hui et al reported high AKI level (46%) in Hong Kong (16). Different statistics have been presented in other studies (17-21). The difference of these statistics with our study is justified considering the extent of study period and large sample size. For example in the studies by Ostermann and Chang et al conducted during ten years and the study by Hui et al during 2 years and a sample size of nearly 41 972 patients from 22 intensive care centers in two countries are the examples of the extent of study period and large sample size (15). In addition, other side factors including delayed referral, deficiencies in patient triage and lack of specialized forces such as children emergency medicine in our medical centers and limited PICU beds could not be ignored in the statistical differences.

Regression testing in our study indicated that high PRISM III score plays a role as an independent factor in the AKI incidence. Fereire et al found a statistical relationship between AKI and PIM II score with higher median and mean among the patients (19). However, Plötz et al demonstrated no differences for prognostic criteria in people with and without AKI (12).

In our study, there was no significant relationship among different AKI degrees based on pRIFLE criteria with PRISM III score, use of MV or shock and death. In addition, in our study no significant association among different AKI degrees based on pRIFLE criteria with taking VD or ND was seen, which is similar to the results of the study by Palmieri et al (20). However, in this study, intensification of AKI was associated with increased levels of VD and nephrotoxic, which may be due to the severity of underlying disease and sepsis. In our study, 9.4% of patients needed to RRT. We found a significant relationship between different AKI degrees based on pRIFLE criteria and the need for RRT. Other studies in this area have reported similar statistics (11.6% in the study by Fereire et al and 10% in the study by Plötz et al). All these studies and our study suggest that the requirement of RRT is proportional to the severity of AKI (7,19,22).

In the present study, a statistically significant association was found between death and different AKI degrees based on pRIFLE criteria. The results of our study differ with the studies by Gheissari et al, Hui et al, and Fereire et al who reported pRIFLE criteria alone predictor of mortality rate (6,16,19). The difference in the results suggests the idea that whether pRIFLE is a good criterion to determine patient prognosis in terms of mortality or not? Because AKI is a dynamic process, this means that patient with admission R stage may fall into F and I stages or may respond quickly to revive process and may be in the course of recovery (20). On the other hand, the assumption can be made that

the risk of death caused by high AKI degrees was reduced due to timely deal with the kidney status, and perhaps the patients died for reasons apart from the severity of kidney disease, for example, the severity of the underlying disease or multiple organ dysfunction, and the severity of AKI as an independent agent did not significantly associate with mortality rate. In the study of Ostermann and Chang, although the final outcome of the patients in the hospital (mortality rate) was significantly associated with the AKI degrees, the role of other independent factors such as age, high APACHE II (acute physiology and chronic health disease classification system II) score on admission, use of MV, previous underlying disease, multiple organ failure, admission after emergency surgery and non-surgical emergency admission was stronger and more prominent in the final outcome (hospital mortality rate) of these patients (7).

Conclusion

According to the obtained results, AKI seems still affects a large percentage of critically ill patients admitted to the PICU. The mortality rate is still high in patients with AKI. Although pRIFLE criteria are appropriate and efficient for early diagnosis of acute kidney injury to speed up treatment and reduce the incidence of AKI complications, their role alone as prognostic factors of mortality require further studies compared with other conventional methods used in the PICU. In addition, the use of this criterion seems to be suitable as a basis for assessing the effects of proper and quick treatment decisions, prognosis and follow-up of kidney status in the future.

Limitations/suggestions

Due to the increased risk of developing AKI in our patients, and considering prevention and reeducation of human morbidity and hospital outcomes and costs, further studies are recommended on the equipment of the centers in cities in terms of specialized personnel in emergency centers and early referral of patients when dispatching to the provincial equipped centers. Additionally, regarding better therapeutic management and the use of equipment including RRT, training and recruitment of subspecialties in emergency medicine, improvement of patient triage in emergency, the use of more accurate biomarkers in serum and urine for early diagnosis of AKI suggests. As a result, protective actions and faster treatment can reduce the incidence rate of the disease and relevant complications. This study is a single-center investigation requiring further evaluation by larger studies.

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Authors' contribution

ASA, MJ and SM contributed to design and conducted the research. MJ conducted data gathering and data interpretation. AS, AH analyzed the data. All authors prepared the manuscript read, revised, and approved the final manuscript.

Conflicts of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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