Original Research Article

Impact of Acute Kidney Injury pRIFLE Criteria Application on Critically Ill Children

ABSTRACT

Aims: The aim of the study to assess the impact of using pRIFLE criteria to define the incidence, the main causes, outcome and associated morbidity of AKI at SQUH pediatric ICU. Also, we aim to implement a guideline for early detection and management of AKI in critically sick Omani children.

Study design: A retrospective study included Omani children, less than 14 years, admitted to Pediatric intensive care, with Acute kidney injury.

Place and Duration of Study: The study conducted between 2016-2017 in Sultan Qaboos University Hospital, PICU.

Methodology: AKI diagnosis and staging were based on pRIFLE criteria. Serum creatinine level and Urine output (UOP) were enrolled for all patients. Estimated Creatinine Clearance (eCrCL) was calculated using the Schwartz formula. Data was compiled using SPSS software using chi square test and fisher's exact test.

Results: Out of 499 cases, 469 cases were included while 30 cases were excluded. Incidence of AKI was 43 (9.17%). Stage 'Risk (R)', 'Injury (I)' and 'Failure (F)' constituted 32.6% (14), 27.9% (12) and 39.5% (17) respectively. Children below five years were more developing AKI with frequency of 79.07% (p= 0.80). UOP and serum creatinine classification were matching in 42.11%. Ventilator had the highest frequency (88.4%), Hypotension (65.1%), Sepsis (58.1%) followed nephrotoxic drug (14.50%) as a common primary cause. The logistic regression model was statistically significant. Prerenal causes constituted 88.47% and renal 11.63%.

Conclusion: pRIFLE criteria is easy tool for early identification and stratification of AKI. Higher incidence of AKI patients was in failure stage on admission with preventable and treatable Pre-renal causes. Ventilation is still the main concern of AKI in critical children. Nevertheless, Hypotension, sepsis and drugs are the main risk factor contributing to AKI.

Keywords: Acute Kidney Injury; PICU; SQUH; pRIFLE; Oman

1. INTRODUCTION

Acute Kidney Injury (AKI) is a frequent and sometimes devastating syndrome, with high costs to patients and healthcare systems. [1] AKI is a sudden

reduction of a kidney function in which there is a significant decrease in glomerular filtration rate (GFR) [2]. The most consequence of AKI are increase serum creatinine (or cystatin c), retention of nitrogenous waste and inability to regulate electrolyte and fluid hemostasis [2,3]. Serum creatinine elevation is the most characteristic marker that is used for diagnosis of AKI. However, Serum creatinine level does not reflect the kidney function accurately because it is delayed on those individuals with unstable state of kidney function. Moreover, it is influenced by many non-renal factors, such as nutritional and hydration status of the child [2,4]. So, serum creatinine cannot be used alone to describe an abrupt decline of renal function. Ideal AKI staging criteria should be simple, sensitive, specific, low cost and good correlation between stage and outcome. [1] Therefore, standardized definitions for pediatric AKI appear to be multidimensional, which depends on staging and accurate assessment using pRIFLE criteria "Pediatric Risk, Injury, Failure, Loss, End-Stage Renal Disease", which depends on serum creatinine and urine output [1,5].

Unfortunately, the incidence of AKI increases globally with simultaneous increase in mortality and morbidity. A world meta-analysis, showed that 13.3 million people develop AKI, out of which 1.7 million die every year [6]. In addition, incidence of AKI is 33.7% in children, when compared to 21% in adults [6]. AKI is considered as major cause that increase mortality pediatric patients [7]. The incidence of AKI is varying from one region to another in the same period of time. Many studies approve that AKI has various burden between the developing countries and developed countries. Moreover, the younger age patients in developing countries are more susceptible to develop AKI and infection considered the main cause [8]. Among the infection causes, sepsis was found the most prevalent cause of AKI followed by acute gastroenteritis [9].

Careful history, physical examination, and investigations are essential to determine the cause of AKI [9,10]. The etiological classification of AKI are divided to three main categories; Pre-renal injury, Intrinsic renal disease and Obstructive uropathy. The main causes of Pre-renal injury are reducing intravascular volume (true or effective intravascular volume). While there are several etiologies for intrinsic renal injuries such as acute tubular necrosis, Uric acid nephropathy, Toxin mediated, Drug induced and vascular lesions. However, it can be Idiopathic in many cases. Whereas, bilateral ureteral obstruction, ureteral Obstruction in a solitary kidney and Urethral obstruction are the main causes of Obstructive uropathy [10].

AKI is usually treatable and preventable with few long-term health outcomes. High incidence of AKI in some countries means lack of receiving the early fundamental care. So, we need to raise awareness about AKI which includes early detection and appropriate management to prevent any complications. In addition, no studies regrettably were conducted in Oman related to AKI in pediatric. So, the observed data are important base for further studies of AKI in Oman. Our Study aims to assess the impact of using pRIFLE criteria to define the incidence, the main causes, outcome and associated morbidity of AKI in critically ill Omani children.

2. METHODOLOGY

2.1 STUDY DESIGN AND SUBJECTS

This retrospective observational study was conducted in Department of Child Health, Sultan Qaboos University Hospital (SQUH), in Muscat, Oman. Medical records of children admitted to Pediatric Intensive care Unit (PICU), in the period between January 2016 and December 2017, were obtained from SQUH electronic database. All children aged 1 month to 14 years old were enrolled for the study. Children with chronic kidney diseases were excluded.

2.2 DATA COLLECTION

All demographic characteristics which include age, gender, weight, height, geographical origin and disease duration were obtained. In addition, the cause of admission and clinical and laboratory investigation were recorded. However, AKI diagnosis and staging were based on pRIFLE (pediatric RIFLE) criteria (table1) [8]. Therefore, Urine output (ml/kg/hour) and Serum creatinine level also were recorded for each child diagnosed with AKI. Recording of serum creatinine was at diagnosis then after 6 hours, 12 hours and 24 hours of (6h,12h,24h). Baseline creatinine was determined by taking into consideration previous baseline readings, age-related creatinine range and lowest creatinine measurement during hospitalization. [1] In addition, estimated glomerular filtration rate (eGFR) was calculated by using Schwartz formula. Moreover, detailed clinical history was used to determine the risk factors, the main cause and outcome of AKI in diagnosed patients.

Table 1: pRIFLE criteria for classification of Acute Kidney Injury in children

Class	Serum creatinine/ GFR criteria	Urine output criteria
Risk	Serum creatinine *1.5 or GFR loss > 25%	0.5 < ml/kg/hour * > 6 hrs
Injury	Serum creatinine *2 or GFR loss > 50%	0.5 < ml/kg/hour * > 12 hrs
Failure	Serum creatinine *3 or GFR loss > 75%	0.3 < ml/kg/hour * > 24 hrs **Or** anuria > 12 hrs
Loss	Persistent failure of kidney function > 4 weeks	
End stage	Persistent failure of kidney function > 3 months	

Abbreviations: GFR = Glomerular Filtration Rate, hrs = hours.

2.3 STATISTICAL ANALYSIS

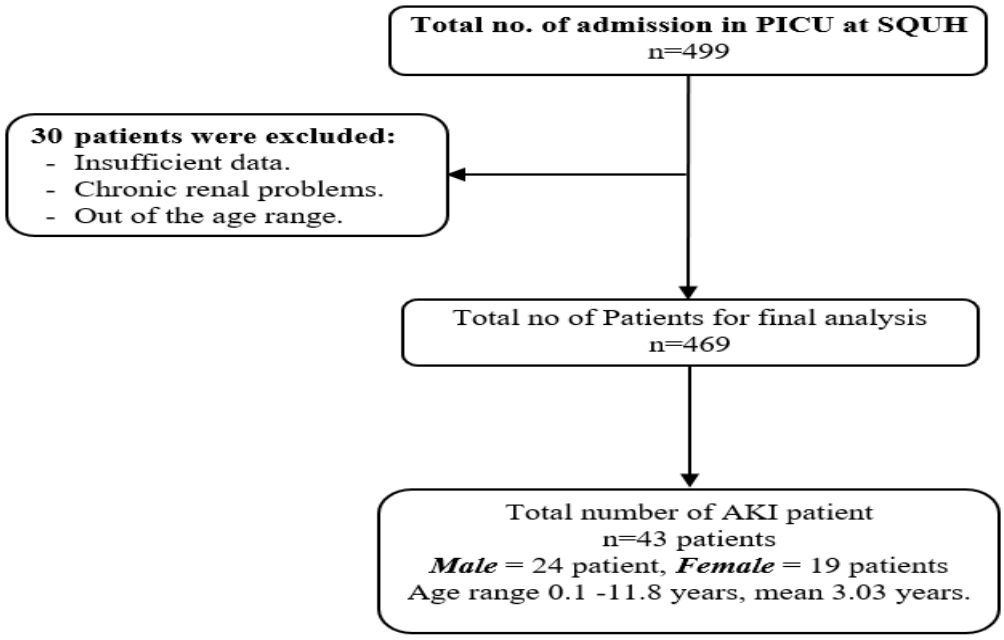
Data was analyzed utilizing SPSS (Statistical Package for Social Sciences) program 23, IBM, Chicago, Illinois, USA. Analysis included demographic features of the examined patients, Descriptive statistics were utilized including frequencies and percentages for categorical variables. in addition to mean (± standard deviation) for numerical variables. Comparison was made between patients using Chi-squared

($\chi 2$) test or fisher's exact test as appropriate. An a priori two-tailed level of significance was set at 0.05.

3. RESULTS AND DISCUSSION

At study period, total of 499 cases were admitted to PICU, with 30 cases met the exclusion criteria. 43 out of 469 patients developed AKI, with an incidence of 9.17% in age range 0.1-11.79 years, mean 3.03 years old. Boys were 24 while girls were 19. According to PRIFLE criteria, stage 'Risk' comprised maximum cases with 32.6% (14 cases), followed by 'Injury' comprised 27.9% (12 cases) and 'Failure' comprised 39.5% (17 cases). Out of 43 AKI patients, 30 (69.77%) patients had AKI at admission while 25.58% developed within 72 h.

FIGURE 1: Flowchart and demographics of children with Acute Kidney Injury (AKI)



Abbreviations: AKI = Acute Kidney Injury, PICU- Pediatric Intensive care unit, SQUH = Sultan Qaboos University Hospital, n = number, IQR= inter-quartile ratio

Serum creatinine criteria screened amongst all cases to classify AKI patients according pRIFLE criteria to risk, injury and failure stages. For serum creatinine criteria, 43 cases had AKI. Incidence of Risk stage (R) was 14 (32.56%), Injury stage (I) was 12 (27.9%) and Failure stage (F) was 17 (39.53%). Urine output criteria was only applied to 19 cases out of 43 cases of AKI. Among these 19 cases, Stage 'R', stage "I" and stage "F" cases were 6 (31.58%), 5(26.32%) and 8(42.12%) (Table2). There was matching between serum creatinine criteria and urine output criteria in 8 cases (42.11%). Matching rate in stage "R" was 16.67%, while there was 40.00 % matching in stage "I" and 62.50% in stage "F" (Table 3).

TABLE 1: Relation of creatinine, urine output criteria and incidence of Acute Kidney Injury

Stage	*Serum Creatinine Criteria*			*Urine Output Criteria*		
	No AKI	*AKI*	*Total*	*No AKI*	*AKI*	**Total**
No AKI	426(100%)	0(0%)	***426(90.83%)***	442(100%)	0(0%)	**450(95.95%)**
Risk	0(0%)	14(32.56%)	***14(2.99%)***	0(0%)	6(31.58%)	**6(1.28%)**
Injury	0(0%)	12(27.90%)	***12(2.56%)***	0(0%)	5(26.32%)	**5(1.07%)**
Failure	0(0%)	17(39.53%)	***17(3.62%)***	0(0%)	8(42.12%)	**8(1.70%)**
Total	***426(100%)***	***43(100%)***	***469(100%)***	***442(100%)***	***19(100%)***	***469(100%)***

P= 0.30 (kappa test)

TABLE 3: Pairing of creatinine criteria staging and urine output staging

Final RIFLE Stage		**Urine Output Stages (U)**			**Total**
		R(U)	**I(U)**	**F(U)**	
Serum Creatinine Stages	**R**	***1(16.67%)***	2(40.00%)	1(12.50%)	**4(21.05%)**
	I	3(50.00%)	***2(40.00%)***	2(25.00%)	**7(36.84%)**
	F	**2(33.33%)**	1(20.00%)	***5(62.50%)***	**8(42.11%)**
Total		**6(100%)**	**5(100%)**	**8(100%)**	**19(100%)**

Abbreviations: R = Risk, I = Injury, F = Failure, U = Urine.

In our study, frequency of children developing AKI below five years was abundant 79.07% (34 cases) but there was no association (p= 0.8). however, the percentage of patients of age (5-9 years) and (9-14 years) are 11.63% (5 cases), 9.3% (4 cases) respectively. The predominant causes of AKI in our studied group were the pre-renal causes which represented in 38 cases and percentage of 88.47% of AKI cases, while renal causes appeared in 11.63% only and no post-renal causes. Sepsis had the highest frequency as a primary cause in the studied group and it was present in 44.19% of AKI cases. Cardiopulmonary arrest and dehydration were the second most frequent cause of AKI and they were present in 18.6% of AKI cases (Table 4). Frequency of risk factors among AKI patients was vary. Patients with ventilator had the highest frequency which was 88.37%, then followed by hypotension then drug mediated AKI (Table 5). Sepsis, pneumonia, drug mediated and ventilator were the risk factors which get significant association with developing AKI. Among risk factors; ventilation, hypotension and sepsis had reliable association with developing AKI ($p<0.05$). However, nephrotoxic drug did not have reliable association with AKI ($p=0.57$) in our group study. (Table 6). Among AKI patients, the full recovery is the common outcome which occupied 55.81%, in contrast rate of mortality was 44.19%.

Table 4: Primary causes among AKI patients

	AKI cases	
	Frequency	**Percentage**
Dehydration	3	***18.60%***
Hypotension	1	***4.65%***
Sepsis	22	***44.19%***
Hemorrhage	1	***2.33%***
Metabolic Disease	3	***2.32%***
Hematologic Disease	1	***2.33%***
Respiratory Disease	2	***2.32%***
Drug mediated	1	***2.33%***
Epilepticus status	1	***2.33%***
Cardiopulmonary arrest	8	***18.60%***
Total	***43***	***100%***

Table 5: Corrlation of clinical variable in relation to incidence of AKI

Variables		**Final Rifle Stage**			
		AKI (43 Cases)	**NON-AKI (426 cases)**	**Total (469 cases)**	***P-Value***
Gender					
	Male	19 (44.2%)	188(44.1%)	**262(55.9%)**	***P=.559***
	Female	24 (55.8%)	238(55.9%)	**207(44.1)**	
Hypotension					
	Yes	28 (65.1%)	25 (5.9%)	**53(11.3%)**	***P<.0001***
	No	15(34.9%)	399(94.1%)	**414(88.7%)**	
Sepsis					
	Yes	25(58.1%)	52(12.2%)	**77(16.5%)**	***P<.0001***
	No	18(41.9%)	373(87.8%)	**391(83.5%)**	
Nephrotoxic Drug					
	Yes	20 (46.5%)	88 (20.7%)	**108 (23.1%)**	***P<.0001***
	No	23 (53.5%)	338 (79.34%)	**360 (76.9%)**	
Ventilator					
	Yes	38 (88.4%)	82 (19.2%)	**120 (25.6%)**	***P<.0001***
	No	5 (11.6%)	344 (80.7%)	**349 (74.4%)**	

Table 6: Assessment of the risk factors for development of AKI

Variable	**Logit coefficient**	**S.E**	**Wald**	**P Value**	**Adj. OR**	**95% C.I**	
						Lower	**Upper**
Hypotension	3.335	0.555	36.115	<0.0001	28.085	9.464	83.345
Sepsis	1.280	0.498	6.604	<0.01	3.597	1.355	9.550
Ventilation	3.520	0.606	33.685	<0.0001	33.783	10.291	110.902
Nephrotoxic Drug	0.283	0.503	0.317	0.573	1.328	0.495	3.558

AKI was defined in our study by using pRIFLE criteria. This was comparable to lots of studies which were done in this field. The cause of widely used pRIFLE criteria is simplicity and high sensitivity in Pediatric age group [11]. the Rustagi et al study showed higher incidence of AKI (14%) which may reflect inclusion of patient up to 18 years old [12]. In the other hand, incidence in our study was lower than other studies that was conducted in developing countries such as incidence of AKI is 26.1% in Bangalore, India where the Dengue spread [8]. Meanwhile, Gupta et al reported an incidence of 42.9% in Bikaner, India [10]. We must put in consideration that these two last studies are prospective studies, which can avoid the limitations of the retrospective studies. In addition, this variation can be explained by regional difference, heterogenicity of patients and sample size. Our incidence can markedly increase if we added the missed UOP criteria. Koeze et al concluded urine output criteria detect AKI earlier and double incidences in critically ill patients [13].

In our study, 69.77% of patients developed AKI from admission while 25.58% developed AKI early in the course of PICU, in comparison with Gupta et al identifies 50% has AKI on admission and 40% develops AKI within 72h of PICU stay, emphasizing the importance of early diagnosis of AKI [10]. Also, grading of AKI according to pRIFLE criteria displayed that 32.6%, 27.9%, and 39.5% patients were in “R” stage, “I” stage, and “F” stage, respectively. This pattern of distribution is different from other studies for example, in Gupta et al AKI stratum R, I, F in diagnosed is 49.1%, 29.5%, 21.3% respectively [9] and these results are comparable to Srinivasa et al [6]. Regarding “F” stage in our study, 16 patients out of 17 having AKI in failure stage, had AKI from admission. This was an indication for importance of raising doctor's awareness about AKI Characteristics at primary and secondary health facilities before reaching our tertiary care facilities.

Serum creatinine and urine output are used in pediatric RIFLE criteria for AKI severity staging. In our study the matching between urine output classification and serum creatinine classification was 42.11%. In comparison with Srinivasa et al study where the matching between two criteria is 77% [7]. They applied urine output only to those patients who were catheterized so that increase the accuracy of urine output classification and the matching will be more accurate [7]. In our study, it was observed the matching between urine output and serum creatinine increased with AKI progression which explained by insertion of urinary catheter with progressive stages of AKI. Also, missing of documentation of accurate urine output in early stage of AKI.

The study showed that patients below five years occupied 77.83% of patients who developed AKI. However, there was no significant association between the age and developing AKI. However, this association is approved in Metha et al study which shows that younger children developing AKI more than others [6]. In addition, Srinivasa et al also shows patients who are below one year more likely to develop AKI [7].

Etiological spectrum of AKI was different from developing countries and developed countries [6]. Sepsis and glomerulonephritis are the common causes of AKI in developing countries. In contrast, nephrotoxic drugs, major surgery and

pulmonary failure are the predominant causes of AKI in developed countries [6]. In our study, the most common primary cause was sepsis (44.19%) followed by dehydration and cardiopulmonary arrest (18.60%). Sepsis had significant association with developing AKI and that was comparable to Sinha et al and other studies, where they also find that sepsis is the most common etiology associated with AKI [14,15]. Furthermore, hypotension and ventilator were associated with high incidence of AKI. The postulated mechanism was attributed to hemodynamic instability and, therefore, its predispose impairment of circulation and consequent reduction of renal blood flow, with risk of evolution to hypoxic-ischemic AKI [15].

It is observed that there were no post renal causes detected in the AKI patients. According Sinivasa et al where no post renal causes also detect and they explained that by the chronic course and progressive deterioration of renal function in post renal causes so the detection usually in pediatric ward than PICU [7]. In our study, prerenal causes were more predominant (88.47%). and they are usually preventable.We have potential limitations in our study. It is a retrospective observational study so we depend on medical record to obtain the information where there were some missing values and information. In addition, small sample size restricts the researcher in a certain range of findings.

4. CONCLUSION

Our study aimed to form basis and focus on burden of AKI in critically ill children. Higher incidence of AKI patients was in failure stage on admission which give an indication for importance of early identification of disease, by increasing awareness, adopting unified definition and staging of AKI to guide quick intervention. Pre-renal causes, which were usually preventable and treatable, were prevalent in AKI Patients. Elaborating preventable and non- preventable risk factors will improve the prognosis of AKI. Ventilator is still the main concern of AKI in a critically ill child in SQUH. Nevertheless, hypotension, sepsis and nephrotoxic medications are the main significant risk factors contributing to AKI. Such findings are worrisome, Pediatric intensivist should be alert, initiating measures to secure adequate renal perfusion. The Mortality rate were high in AKI patients, which requires raising awareness of AKI in health care community.

ETHICAL APPROVAL

Ethical approval was obtained from the Research and Ethics Committee, College of Medicine and Health Sciences, Sultan Qaboos University, Oman.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research

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REFERENCES

1. Thomas ME, Blaine C, Dawnay A, Devonald MA, Ftouh S, Laing C, Latchem S, Lewington A, Milford DV, Ostermann M. The definition of acute kidney injury and its use in practice. Kidney International 2015: 87, 62–73. doi:10.1038/ki.2014.328.

2. Mohd Ashraf, Naveed Shahzad, Mohd Irshad, Sheikh Quyoom Hussain, Parvez Ahmed. Pediatric acute kidney injury: A syndrome under paradigm shift. Indian J Crit Care Med 2014; 18(8): 518–526. doi: 10.4103/0972-5229.138156.

3. Khwaja, A. KDIGO Clinical Practice Guidelines for Acute Kidney Injury. Nephron Clin Pract 2012; 120(4): c179-84. DOI: 10.1159/000339789.

4. Shemesh, O, Golbetz, H, Kriss, J, Myers BD. Limitations of creatinine as a filtration marker in glomerulopathic patients. Kidney Int 1985; 28(5): 830-8. doi: 10.1038/ki.1985.205.

5. Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P, Acute Dialysis Quality Initiative workgroup. Acute renal failure - definition, outcome measures, animal models, fluid th erapy and information technology needs: The Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care 2004; 8(4): R204–12. doi: 10.1186/cc2872.

6. Mehta, R, Cerdá, J, Burdmann E, Tonelli M, García-García G, Jha, V et al. International Society of Nephrology's 0by25 initiative for acute kidney injury (zero preventable deaths by 2025): a human rights case for nephrology. Lancet 2015; 385(9987): 2616-43. doi.org/10.1016/S0140-6736(15)60126-X.

7. Gupta S, Sengar G, Meti P, Lahoti A, Beniwal M, Kumawat M. Acute kidney injury in pediatric intensive care unit: Incidence, risk factors, and outcome. Indian J Crit Care Med 2016; 20(9): 526. doi: 10.4103/0972-5229.190368.

8. Srinivasa, S, Reshmavathi V. Incidence and etiology of acute kidney injury in children admitted to PICU using pRIFLE criteria. Curr Pediatric Res 2016; 20(1-2): 1–6.

9. Maqbool, J, Mir A, Bhat N. Moona W. Incidence and etiology of acute kidney injury in children admitted to PICU using pRIFLE criteria. Int J of Contemp Pediatr 2018; 5(3): 917. doi: 10.18203/2349-3291.ijcp20181513
10. Akcay A, Turkmen K, Lee D, Edelstein CL. Update on the diagnosis and management of acute kidney injury. Int J Nephrol Renovasc Dis 2010; 3: 129. doi: 10.2147/IJNRD.S8641.

11. Srinivasa S, Reshmavathi V., Srividya S. A comparison of pRIFLE and AKIN criteria for acute kidney injury in pediatric intensive care unit patients. Int J Contemp Pediatrics 2016; 3(2): 398–402. doi: 10.18203/2349-3291.ijcp20161022.

12. Rustagi RS, Arora K, Das RR, Pooni PA, Singh D. Incidence, risk factors and outcome of acute kidney injury in critically ill children - a developing country perspective. Paediatr Int Child Health 2017; 37(1): 35-41. doi: 10.1080/20469047.2015.1120409.

13. J Koeze, F Keus, W Dieperink, I C C van der Horst, J G Zijlstra, M van Meurs. Incidence, timing and outcome of AKI in critically ill patients varies with the definition used and the addition of urine output criteria. BMC Nephrol 2017 Feb 20;18(1):70. doi: 10.1186/s12882-017-0487-8.

14. Mehta P, Sinha A, Sami A, Hari P, Kalaivami M, Gulati A et al. Incidence of acute kidney injury in hospitalized children. Indian pediatr 2012; 49(7): 537-42. doi: 10.1007/s13312-012-0121-6.

15. Louzada CF, Ferreira AR. Evaluation of the prevalence and factors associated with acute kidney injury in a pediatric intensive care unit. J Pediatr (Rio J) 2021;97(4):426-432. doi: 10.1016/j.jped.2020.08.003.