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Acute kidney injury in children with cancer admitted in an intensive care unit

Lesão renal aguda em crianças com câncer internadas em unidade de terapia intensiva

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ABSTRACT

Objective: Evaluating the association between acute kidney injury and death in critically ill children with oncological diseases admitted in an intensive care unit (ICU). **Material and Methods:** Unicentric cohort study, evolving children with cancer admitted in the ICU of a pediatrics referral hospital. The patients were divided according to the presence or absence of acute kidney injury. Patients with a history of urogenital disease, nephrectomy or chronic kidney disease were excluded. The acute kidney injury was defined by the Kidney Disease Improving Global Outcomes (KDIGO) classification. The main outcome was death. **Results:** The sample was composed of 84 patients, in which 46.4% were diagnosed with hematologic neoplasm, 29.8% evolved with febrile neutropenia, 11.9% had a history of bone marrow transplant, and 27.3% deceased. Acute kidney injury occurred in 51.2% of the sample, 53.6% used furosemide, 38% showed fluid overload, and 8.3% had renal replacement therapy. The main variables related to kidney dysfunction were admission due to hemodynamic shock, pediatric risk of mortality score 2 ≥5%, bone marrow transplant, volume overload and multiple organ dysfunction syndrome. More advanced stages of acute kidney injury were associated with renal replacement therapy (p<0.001), longer stay in the ICU (p=0.006), and death (p=0.003). **Conclusion:** Children with cancer showed many risk factors of acute kidney injury, and this complication is associated with higher death rate.

Keywords: Acute kidney injury; Pediatric intensive care units; Medical oncology; Child; Multiple organ failure.

RESUMO

Objetivo: Avaliar a associação entre lesão renal aguda e óbito em crianças com doenças oncológicas criticamente enfermas internadas em uma unidade de terapia intensiva (UTI). **Material e Métodos:** Estudo de coorte unicêntrico, envolvendo crianças com câncer internadas na UTI de um hospital de referência em pediatria. Os pacientes foram divididos de acordo com a presença ou ausência de lesão renal aguda. Pacientes com história de doença urogenital, nefrectomia ou doença renal crônica foram excluídos. A lesão renal aguda foi definida pela classificação do *Kidney Disease Improving Global Outcomes* (*KDIGO*). O desfecho principal foi a morte. **Resultados:** A amostra foi composta por 84 pacientes, em que 46,4% foram diagnosticados com neoplasia hematológica, 29,8% evoluíram com neutropenia febril, 11,9% tinham histórico de transplante de medula óssea e 27,3% foram a óbito. A lesão renal aguda ocorreu em 51,2% da amostra, 53,6% usaram furosemida, 38% apresentaram sobrecarga hídrica e 8,3% fizeram terapia renal substitutiva. As principais variáveis relacionadas à disfunção renal foram admissão por choque hemodinâmico, escore *pediatric risk of mortality 2* ≥5%, transplante de medula óssea, sobrecarga de volume e síndrome de disfunção de múltiplos órgãos. Estágios mais avançados de lesão renal aguda foram associados à terapia renal substitutiva (*p*<0,001), maior permanência na UTI (*p*=0,006) e óbito (*p*=0,003). **Conclusão:** Crianças com câncer apresentaram muitos fatores de risco de lesão renal aguda, e esta complicação está associada a uma maior taxa de mortalidade.

Palavras-chave: Lesão renal aguda; Unidades de Terapia Intensiva Pediátrica; Oncologia médica; Criança; Falência de múltiplos órgãos.

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INTRODUCTION

Acute kidney injury (AKI) is a frequent complication found in children with oncological disease, being associated with chronic kidney disease and increase of death risk.[1] Many risk factors are related with AKI in patients with cancer, such as tumor lysis syndrome, vascular obstruction, and malignant cell infiltration in the urogenital system. The use of nephrotoxic drugs, such as antimicrobials, chemotherapy and iodinated contrast also predispose to the development of the problem.[2] Besides that, the use of more aggressive therapy for the cancer treatment can result in prolonged immunosuppressive conditions, predisposing to the development of infections, septic shock and, consequently, kidney dysfunction due to organic hypoperfusion.[3]

Park et al. (2019)[4] in their retrospective study with pediatric patients with cancer, observed the presence of AKI in 52.6% of the children in the first year of diagnosis.[4] The progressive worsening of the kidney function may require admittance in an intensive care unit (ICU), in consequence of the disease evolution or due to the complications resulting from the treatment. The coexistence of AKI with other organic dysfunctions, such as heart failure or liver failure makes the clinical handling of the child more complex, and it can evolve to anuria, volume overload, and severe metabolic acidosis.[5] Asperen et al. (2019)[6] identified that AKI with the need of continuous renal replacement therapy (RRT) increases 3.2 times the risk of death when compared to the patients that do not need this treatment.[6]

Despite the importance of the theme in the context of the pediatric patient with oncologic disease, there are few studies in the medical literature evaluating the interaction of AKI with multiple organ dysfunction syndrome. Besides that, few authors used standardized criteria of AKI, such as the Kidney Disease Improving Global Outcomes (KDIGO) classification system.[7] The main objective of this paper is to evaluate the association between kidney failure and death in children with oncological disease admitted in an intensive care unit.

MATERIAL AND METHODS

It is a retrospective cohort study involving children with cancer in a pediatric intensive care unit in a quaternary hospital that is a referral in pediatrics, with the capacity of 22 general beds between November of 2016 and January of 2019. The data were extracted from the electronic medical records and the study was approved by the Research Ethics Committee in the institution.

The inclusion criteria were being a carrier of oncologic disease, which were either solid or hematologic, length of stay in the ICU ≥ 24 hours and being between 1 month and 18 years old. The exclusion criteria were chronic nephropathy with estimated creatinine clearance <15ml/min/1,73m³, history of nephrectomy or urogenital disease.

All the patients of the sample were scanned as to the presence of AKI during the admittance in the ICU for a maximum period of 15 days. They were classified by the presence or absence of acute kidney injury. The main outcome was death in the ICU. Other analyzed variables were age, gender, pediatric risk of mortality 2 (PRISM) score, reason for admittance, kind of oncologic disease, history of autologous or allogeneic bone marrow transplant (BMT), use of recent chemotherapy, period between cancer diagnosis and admittance, multiple organ dysfunction syndrome, basal creatinine, stages of AKI, nephrotoxic drug (NTD), use of loop diuretics, volume overload, renal replacement therapy, and length of stay in the ICU.

Definitions

Acute kidney injury: classification of the Kidney Disease Improving Global Outcomes (KDIGO) initiative.[7] Patients with an increase in the creatinine (Cr) <0.3mg/dL or <1.5 times in relation to the basal serum level or urine flow rate (UFR) ≥0.5ml/kg/h were classified as without AKI. The patients with an increase of the Cr ≥0.3mg/dL or between 1.5-1.9 times in relation to the basal Cr or UFR <0.5ml/kg/h by 6-12 hours were classified as stage 1. Those with an increase of the Cr between 2-2.9 times or UFR <0.5ml/kg/h for more than 12 hours were classified as stage 2. Those with an increase of the Cr ≥3 times or UFR <0.3ml/kg/h for more than 24 hours or anuria for more than 12 hours were classified as stage 3. Basal creatinine was characterized as the creatinine within normal seeing the interval in the last 3 months identified in the electronic databank of the unit.

Nephrotoxic drugs: medication prescribed by the pediatric intensivist that presents a potential to cause AKI as an adverse event.[8] The following were characterized as NTD: acyclovir, amikacin, amphotericin B, captopril, cyclosporine, cidofovir, enalapril, foscarnet, ganciclovir, gentamicin, ibuprofen, lithium, mesalazine, sirolimus, sulfasalazine, tacrolimus, tobramycin, topiramate, trometamol, and vancomycin.

Volume overload: body fluid accumulation peak higher than 10% in any moment during ICU admittance, being calculated by the formule "[(administered fluids in liters - eliminated fluids in liters)/ weight at the ICU admission in kilograms] x 100".[9]

Multiple organ dysfunction syndrome (MODS): condition characterized by the failure of 2 or more organs or systems, including respiratory, cardiovascular, renal, hepatic, neurologic, and hematological dysfunctions.[10] Respiratory dysfunction was characterized by the need of invasive mechanical ventilation. Cardiovascular dysfunction was defined by the need of vasoactive drug use. Neurological dysfunction included the presence of anisocoria or focal motor deficit or Glasgow ≤8 or cranial computed tomography with a report suggestive of stroke made by a radiologist doctor.

Liver dysfunction was characterized by alanine aminotransferase higher than twice the abnormality rate or direct serum bilirubin ≥2mg/dL. Kidney dysfunction was defined as the presence of stage 2 or 3 AKI by the KDIGO classification. Hematologic dysfunction involved patients with thrombocytopenia < 100.000/mm³ or the international normalized ratio (INR) value ≥1.5.

For the statistical analysis, the Jamovi 1.6.23 software was used. In relation to the qualitative variables, frequencies and proportions were calculated. In relation to the quantitative variables, the average, standard deviation, median, quartiles, maximum and minimum amount were evaluated. For the analysis of categorical variables, the chi-square and Fisher's exact test were used. Quantitative variables of nonparametric distribution were analysed through the Kruskal-Wallis test and for the normal distribution data, the ANOVA test was used. The survival analysis was made through the log-rank test and Kaplan-Meier curves. The odds ratio (OR) was calculated with significance level of 5% ($p \leq 0.05$) and 95% confidence interval (95%CI). All the variables with $p \leq 0.05$ were evaluated by the logistic regression for the avoidance of possible confounders in the association between AKI and death.

RESULTS

The population of pediatric ICU admitted patients during the studied period was 810 children, excluding 726 children, resulting in a sample of 84 patients. In a decreasing order of frequency, 18 (21.4%) patients had acute lymphoid leukemia, 14 (16.7%) acute myeloid leukemia, 10 (11.9%) medulloblastoma, 9 (10.7%) glioma, 7 (8.3%) lymphoma, 5 (6%) neuroblastoma, 4 (4.7%) ependymoma, 4 (4.7%) rhabdomyosarcoma, 3 (3.6%) Ewing's sarcoma, 2 (2.4%) craniopharyngioma, 2 (2.4%) choroid plexus tumor, 1 (1.2%) adrenal carcinoma, 1 (1.2%) hepatocarcinoma, 1 (1.2%) osteosarcoma, 1 (1.2%) pleomorphic sarcoma, 1 (1.2%) teratoid rhabdoid tumor and 1 (1.2%) tongue tumor.

The sample showed a discrete male predominance (51.1%), with age medians and death expectation of 6.5 years and 1.9%, respectively. The main reason for the ICU admission was for monitoring, followed by hemodynamic shock, respiratory failure, and reduced level of awareness. Among the patients that were admitted for monitoring, 5 (12.2%) showed a risk of tumor lysis syndrome and 36 (87.8%) were in a post-surgical state. Fifty-three percent of the children had solid tumors, 39% had recently received the cancer diagnosis, 32.1% went through chemotherapy less than 4 weeks before ICU admission, 29.8% had febrile neutropenia, and 11.9% had a history of bone marrow transplant. The median of the ICU length of admittance was 5 days and 23 (27.3%) children died (Table 1).

Among the research subjects, 43 (51.2%) developed AKI, in which most of them were in the first 48 hours of admittance. Of these subjects, 12 (27.9%) were in stage 1, 17 (39.5%) stage 2 and 14 (32.6%) stage 3.

Table 1. Clinical profile of the studied sample (n=84).

Variables	General (%)
Age (year)[a]	6.5 (3-12)
Male	43 (51.1)
Reason for admission	
Monitoring	41 (48.8)
Respiratory failure	13 (15.5)
Hemodynamic shock	20 (23.8)
Reduced level of awareness	10 (11.9)
PRISM[a]	1.9 (0.8-4.2)
Type of neoplasm	
Hematological	39 (46.4)
Solid	45 (53.6)
Diagnosis time <2 months	33 (39.2)
Chemotherapy <4 weeks	27 (32.1)
Febrile neutropenia	
<1.500cel/mm³	25 (29.8)
<500cel/mm³	20 (23.8)
BMT	10 (11.9)
Basal creatinine (mg/dL)[a]	0.3 (0.2-0.4)
AKI	43 (51.2)
AKI stages	
Stage 1	12 (27.9)
Stage 2	17 (39.5)
Stage 3	14 (32.6)
AKI period since admission (days)[a]	2 (1-4)
Volume overload	32 (38)
NTD	41 (48.8)
MODS	48 (57.1)
RRT	7 (8.3)
Length of stay (days)[a]	5 (2-11)
Death	23 (27.3)

PRISM: Pediatric risk of mortality 2; BMT: Bone marrow transplant; AKI: Acute kidney injury; NTD: Nephrotoxic drug; MODS: Multiple organ dysfunction syndrome; RRT: Renal replacement therapy; a Values expressed in median (p25-p75).

The AKI diagnosis occurred through the urine flow rate in only 7.1% of the sample, being that most of it was made through the serum creatinine level. Besides that, 38% of it developed volume overload, 53.6% used furosemide and 8.3% needed renal replacement therapy. The most used classes of nephrotoxic drugs by the pediatric intensivist were antibiotics (39.3%), antivirals (9.5%) and nonsteroidal anti-inflammatory (4.8%). The variables that had a statistically significant association with the stages of acute kidney injury were bone marrow transplant (p=0.035), admission by hemodynamic shock (p=0.019), PRISM score (p= 0.036), volume overflow (p<0.001) and SDMO (p<0.001). More advanced stages of AKI were associated with RRT (p<0.001), longer ICU admission length (p=0.006) and death (p=0.003) (Table 2).

Table 2. Association of clinical-demographic variables with acute kidney injury (n=84).

Variables	Without AKI (%)	AKI 1 (%)	AKI 2 (%)	AKI 3 (%)	p
Age (year)[a]	7 (3-12)	3 (2-12)	6 (3-10)	8 (4.5-11)	0.57
Male	22 (51.2)	6 (14)	10 (23.3)	5 (11.6)	0.48
Basal creatinine[a]	0.4 (0.3-0.4)	0.2 (0.2-0.4)	0.3 (0.2-0.4)	0.3 (0.2-0.4)	0.3
PRISM[a]	1.3 (0.8-2.8)	2.1 (0.8-3.6)	2.8 (1.5-7.6)	3.1 (1.6-7.2)	0.036
Chemotherapy ≤4 weeks	10 (37)	6 (22.2)	6 (22.2)	5 (18.5)	0.27
Diagnosis <2 months	17 (51.5)	7 (21.2)	6 (18.2)	3 (9.1)	0.28
Hematologic neoplasm	14 (35.9)	8 (20.5)	10 (25.6)	7 (17.9)	0.08
Febrile neutropenia	9 (36)	5 (20)	8 (32)	3 (12)	0.34
BMT	2 (20)	1 (10)	4 (40)	3 (30)	0.035
Admission shock	6 (30)	1 (5)	8 (40)	5 (25)	0.019
NTD	16 (39)	7 (17.1)	10 (24.4)	8 (19.5)	0.11
Fluid overload	7 (21.9)	4 (12.5)	11 (34.4)	10 (31.3)	<0.001
MODS	13 (27.1)	8 (16.7)	16 (33.3)	11 (22.9)	<0.001
RRT	0 (0)	1 (14.3)	1 (14.3)	5 (71,4)	<0.001
Length of stay (days)[a]	2 (2-7)	7 (2.7-12.3)	10 (4-7)	6.5 (5.2-18)	0.006
Death	8 (34.8)	0 (0)	6 (26.1)	9 (39.1)	0.003

AKI: Acute kidney injury; PRISM: Pediatric risk of mortality 2; BMT: Bone marrow transplant; NTD: Nephrotoxic drug; MODS: Multiple organ dysfunction syndrome; RRT: Renal replacement therapy.[a] Values expressed in median (p25-p75).

The survival analysis identified the highest death risk among the patients with acute kidney injury stages 2 or 3 when compared to children without AKI or stage 1 (log-rank test, p=0.045) (Figure 1). The variables that showed a statistically significant association with death were hematologic neoplasm (p=0.009), PRISM score ≥5% (p= 0.008), febrile neutropenia (p=0.026), SDMO (p<0.001), and renal replacement therapy (p=0.006) (Table 3). After logistic regression, the only independent predictors of mortality were cardiovascular dysfunction (p=0.017) and neurological dysfunction (p=0.023).

It has been observed that all patients with up to 1 organic dysfunction were dismissed from the ICU. On the other hand, 33.3% of the children with 2 or 3 organic dysfunctions and 70.8% of patients with 4 or more organic dysfunctions evolved to death (p<0.001).

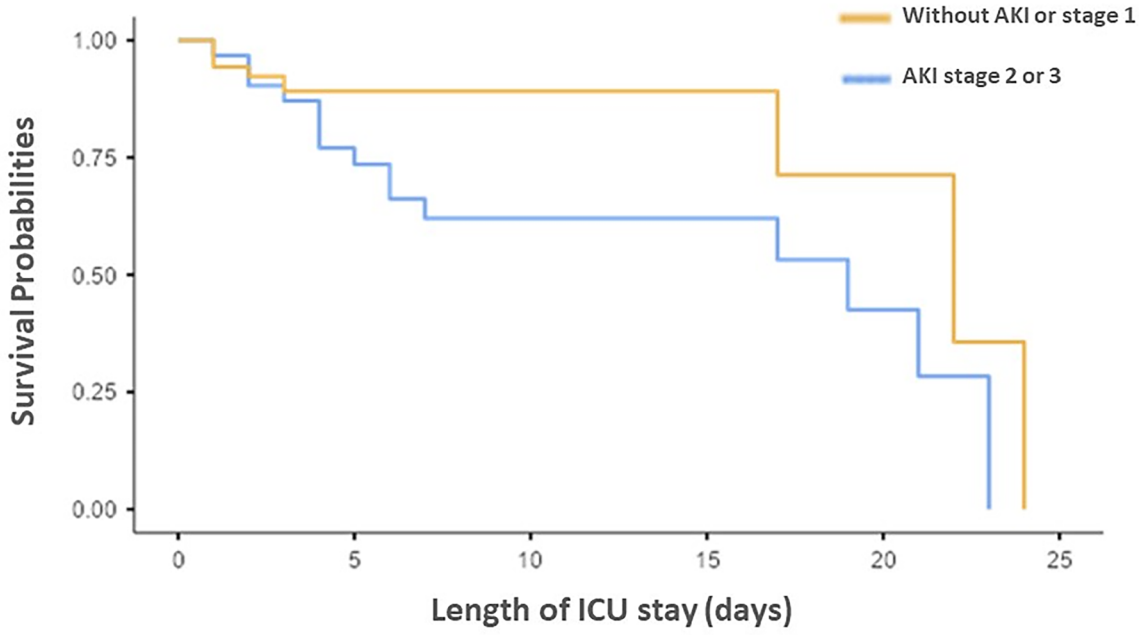

Figure 1. Survival analysis of patients with acute kidney injury
Kaplan-Meier curves representing the difference in survival between patients without acute kidney injury or stage 1 in relation to patients with acute kidney injury stages 2 or 3, log-rank test p = 0,045.

Table 3. Association of clinical-demographic variables with death (n=84).

Variables	Death					
	Yes (%)	No (%)	Total	OR	95%CI	p
Age						
Infant	2 (22.2)	7 (77.8)	9	0.57	0.09-3.27	0.53
Preschool	6 (25)	18 (75)	24	0.66	0.2-2.2	0.5
School	5 (23.8)	16 (76.2)	21	0.62	0.17-2.2	0.46
Teenager	10 (33.3)	20 (66.7)	30	1		
Gender						
Male	14 (32.6)	29 (67,4)	43	1.72	0.64-4.56	0.27
Female	9 (22)	32 (78)	41	1		
PRISM						
≥5%	9 (53)	8 (47)	17	4.26	1.39-13	0.008
<5%	14 (21)	53 (79)	67	1		
Type of neoplasm						
Hematological	16 (41)	23 (59)	39	3.78	1.35-10.6	0.009
Solid	7 (15.6)	38 (84.4)	45	1		
Chemotherapy ≤4 weeks						
Yes	11 (40.7)	16 (59.3)	27	2.58	0.95-6.99	0.059
No	12 (21.1)	45 (78.9)	57	1		
Febrile neutropenia						
Yes	11 (44)	14 (56)	25	3.08	1.12-8.47	0.026
No	12 (20.3)	47 (79.7)	59	1		
BMT						
Yes	5 (50)	5 (50)	10	3.11	0.8-12	0.087
No	18 (24.3)	56 (75.7)	74	1		
Respiratory dysfunction						
Yes	23 (50)	23 (50)	46	37	4.46-292	<0.001
No	1 (2.6)	37 (97.4)	38	1		
Cardiovascular dysfunction						
Yes	21 (63.6)	12 (36.4)	33	42.9	8.82-209	<0.001
No	2 (3.9)	49 (96.1)	51	1		
Kidney dysfunction						
Yes	15 (48.4)	16 (51.6)	31	5.27	1.88-14.8	<0.001
No	8 (15.1)	45 (84.9)	53	1		
Liver dysfunction						
Yes	10 (62.5)	6 (37.5)	16	7	2.17-22.9	<0.001
No	13 (19.1)	55 (80.9)	68	1		
Neurological dysfunction						
Yes	11 (55)	9 (45)	20	5.3	1.8-15.6	0.002
No	12 (18.8)	52 (81.3)	64	1		
Hematologic dysfunction						
Yes	16 (44.4)	20 (55.6)	36	4.69	1.66-13.2	0.002
No	7 (14.5)	41 (85.5)	48	1		
Fluid overload						
Yes	12 (37.5)	20 (62.5)	32	2.24	0.84-5.94	0.1
No	11 (21.2)	41 (78.8)	52	1		
RRT						
Yes	5 (71.4)	2 (28.6)	7	8.19	1.46-45.9	0.006
No	18 (23.4)	59 (76.6)	77	1		
Total	23 (27.3)	61 (72.7)	84			

PRISM: Pediatric risk of mortality 2; BMT: Bone marrow transplant; RRT: Renal replacement therapy.

DISCUSSION

Our study identified that 51.2% of the sample developed some degree of acute kidney injury, being that more advanced stages of this complication showed a higher association with death. The incidence of renal dysfunction in severe pediatric patients may vary from 5% to 82% depending on the characteristics of the subjects studied.[11,12] The following must be taken into consideration: the underlying disease, the severity of the condition, the comorbidities, and the AKI definition that was used. Thus, children with cancer must be under constant care regarding this problem, as a result of the exposure to many risk factors.[5]

On the other hand, we noticed that the renal dysfunction does not compromise the body homeostasis of the critical patient in isolation. It is generally associated with other organic dysfunctions that, as a whole, result in a higher risk of death. That becomes clear when we observe that the only independent predictors of mortality in the study were cardiovascular and neurological dysfunctions, which were also found by other authors.[13] Dursun et al. (2009)[14] and Akhtar et al. (2011)[15] identified that sepsis, use of vasoactive drugs, and mechanical ventilation are variables that are most associated with death in this population.[14,15]

The cardiovascular dysfunction is characterized by the body's inability to supply the tissues with blood in a satisfactory way. This results in anaerobic metabolism, lactic acidosis and multiple organ dysfunction syndrome.[10,16] Prolonged and refractive hemodynamic shock increase the number of organic dysfunctions, which results in a higher risk of death. Haase et al. (2011)[17] identified a mortality rate of 9%, 36%, 44%, and 76% of the patients with 1, 2, 3, and 4 organic dysfunctions respectively in their study with 226 children in severe stages of cancer. Fiser et al. (2005)[18] and Ali et al. (2016)[19] also observed a higher rate of organic dysfunctions among children with septic shock that evolved to death (p=0.001). Our study showed similar results, and thus the identification and early treatment of the cardiovascular dysfunction is fundamental for the increase of the patients' survival especially those with a case of febrile neutropenia.[3,20] In an associated way, the indication of pediatric ICU admittance must not be postponed, since an elevated PRISM score is also associated with a worsened clinical evolution.[13,14]

Patients with a history of BMT may show additional risk factors for the development of AKI, such as graft-versus-host disease, thrombotic microangiopathy, immunosuppressive nephrotoxicity, and sinusoidal obstruction syndrome.[21,22] Our study identified that 80% of these patients showed some level of AKI. Koh et al. (2018)[23] reported that the incidence of renal dysfunction in patients with BMT may vary from 21 to 84%. Kizilbash et al. (2016)[24] noticed that AKI occurs early in patients with hematopoietic stem cell transplantation, regardless of whether the source is autologous or allogeneic.

Once the treatment of children with cancer involves the administration of large amounts of volume through the use of antimicrobials, hyperhydration, sedatives, chemotherapy, and transfusions, these patients show a higher risk of volume overload, especially in the presence of AKI with reduced urine flow rate.[25,26] Patients with positive cumulative fluid balance show longer mechanical ventilation time and greater need for RRT.[27] Raymakers-Janssen et al. (2019)[28] observed in their multicentric study with pediatric cancer patients that fluid overload (p=0.003) and a need for inotropic support at the beginning of the continuous renal replacement therapy (p=0.004) are independent predictors of death. Cortina et al. (2019)[29] verified that 77.8% of children with oncologic-hematologic disease that need renal replacement therapy in the ICU died (p< 0.001). We found similar results, since 71.4% of the patients that started this procedure evolved to death (p=0.006).

In view of these findings, avoiding advanced stages of AKI and its possible complications seem to be the most plausible strategy. The systematic monitoring of the renal function through the serum creatinine level and the urine flow rate must be the rule, so as to make an early diagnosis.[7] Arterial hypotension must not be tolerated, with indication of aggressive measures for the changing of the condition.[30] Besides that, adjusting the dose of medications according to the estimated glomerular filtration rate, maintaining a state of normovolemia, and avoiding the use of nephrotoxic drugs when possible is indicated.[31]

As positive points, our study was performed in a general ICU, reference in pediatrics, with a diverse sample of neoplasms and a research protocol with specific definitions. This allows us to generalize the data to other units. A holistic analysis of the critically ill patients, made it possible to minimize the risk of confusion bias in the association between AKI and death, when taking the multiple organ dysfunction syndrome into consideration. However, some limitations are shown. Firstly, the study is a retrospective study with a sample size that may be considered small when compared to other papers in the literature. Secondly, the iodinated contrast was not included in the list of nephrotoxic medications due to the absence of specification of types and their respective osmolarities. Thirdly, some risk factors such as graft-versus-host, thrombotic microangiopathy, and sinusoidal obstruction syndrome were not evaluated in this study. Finally, it was not possible to assess the dry weight of all the patients in the study, being opted in the use of the weight in the ICU admittance.

CONCLUSION

Children with oncological disease showed many risk factors of acute kidney injury, and this complication is associated with the increase of mortality rate, especially when associated with multiple organ dysfunction syndrome.

REFERENCES

1. Fragasso T, Ricci Z, Goldstein SL. Pediatric acute kidney injury. Contrib Nephrol. 2018;193:113-6.
2. Patzer L. Nephrotoxicity as a cause of acute kidney injury in children. Pediatr Nephrol. 2008 Dec;23(12):2159-73.
3. Berg ST, Loeffen EAH, Van de Wetering MDV, Martens DHJ, Van Ede CM, Kremer LCM, et al. Development of pediatric oncology supportive care indicators: evaluation of febrile neutropenia care in the north of the Netherlands. Pediatr Blood Cancer. 2019 Feb;66(2):e27504.
4. Park PG, Hong CR, Kang E, Park M, Lee H, Kang HJ, et al. Acute kidney injury in pediatric cancer patients. J Pediatr. 2019 May;208:243-50.e3.
5. Rosner MH, Perazella MA. Acute kidney injury in patients with cancer. N Engl J Med. 2017 May;377(5):1770-81.
6. Asperen RMWV, Van Gestel JPJ, Van Grotel M, Tschiedel E, Dohna-Schwake C, Valla FV, et al. PICU mortality of children with cancer admitted to pediatric intensive care unit a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2019 Oct;142:153-63.
7. Kellum JA, Lameire N, Aspelin P, Barsoum RS, Burdmann EA, Goldstein SL, et al. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group KDIGO clinical practice guideline for acute kidney injury. Kidney Int Suppl. 2012;2(1):1-138.
8. Goldstein SL, Kirkendall E, Ngouyen H, Schaffzin JK, Bucuvalas J, Bracke T, et al. Eletronic health record identification of nephrotoxin exposure and associated acute kidney injury. Pediatrics. 2013 Set;132(3):757-67.
9. Alobaidi R, Morgan C, Basu RK, Stenson E, Feathersone R, Majumdar SR, et al. Association between fluid balance and outcomes in critically ill children: a systematic review and meta-analysis. JAMA Pediatr. 2018;172(3):257-68.
10. Goldstein B, Giroir B, Randolph A; International Consensus Conference on Pediatric Sepsis. International pediatric sepsis consensus conference: definitions for sepsis and organ dysfunction in pediatrics. Pediatr Crit Care Med. 2005 Jan;6(1):2-8.
11. Kaddourah A, Basu RK, Bagshaw SM, Goldstein AL; AWARE Investigators. Epidemiology of acute kidney injury in critically ill children and young adults. N Engl J Med. 2017 Jan;376(1):11-20.
12. De Zan F, Amigoni A, Pozzato R, Pettenazzo A, Murer L, Vidal E. Acute kidney injury in critically ill children: a retrospective analysis of risk factors. Blood Purif. 2020;49(1-2):1-7.
13. Abraham RB, Toren A, Ono N, Weinbroum AA, Vardi A, Barzilay Z, et al. Predictors of outcome in the pediatric intensive care units of children with malignancies. J Pediatr Hematol Oncol. 2002 Jan;24(1):23-6.
14. Dursun O, Hazar V, Karasu GT, Uygun V, Tosun O, Yesilipek A. Prognostic factors in pediatric cancer patients admitted to the pediatric intensive care unit. J Pediatr Hematol Oncol. 2009 Jul;31(7):481–4.
15. Akhtar N, Fadoo Z, Panju S, Haque A. Outcome and prognostic factors seen in pediatric oncology patients admitted in PICU of a developing country. Indian J Pediatr. 2011 Aug;78(8):969-72.
16. Freire KMS, Bresolin NL, Farah ACF, Carvalho FLC, Góes JEC. Acute kidney injury in children: incidence and prognostic factors in critical ill patients. Rev Bras Ter Intensiva. 2010 Jun;22(2):166-74.
17. Haase R, Lieser U, Kramm C, Stiefel M, Vilser C, Bernig T, et al. Management of oncology patients admitted to the paediatric intensive care unit of a general children' s hospital – a single center analysis. Klin Padiatr. 2011 May;223(3):142-6.
18. Fiser RT, West NK, Bush AJ, Sillos EM, Schmidt JE, Tamburro RF. Outcome of severe sepsis in pediatric oncology patients. Pediatr Crit Care Med. 2005 Sep;6(5):531-6.
19. Ali AM, Sayed HA, Elzembely MM. The outcome of critically ill pediatric cancer patients admitted to the pediatric intensive care unit in a tertiary university oncology center in a developing country. J Pediatr Hematol Oncol. 2016 Jul;38(5):355-9.
20. Basu SK, Fernandez ID, Fisher SG, Asselin BL, Lyman GH. Length of stay and mortality associated with febrile neutropenia among children with cancer. J Clin Oncol. 2005 Nov;23(31):7958-66.
21. Lopes JA, Jorge S, Neves M. Acute kidney injury in HCT: an update. Bone Marrow Transplant. 2016 Jun;51(6):755-62.
22. Fernández-García M, Gonzalez-Vicent M, Mastro-Martinez I, Serrano A, Diaz MA. Intensive care unit admissions among children after hematopoietic stem cell transplantation: incidence, outcome, and prognostic factors. J Pediatr Hematol Oncol. 2015 Out;37(7):529-35.
23. Koh KN, Sunkara A, Kang G, Sooter A, Mulrooney DA, Triplett B, et al. Acute kidney injury in pediatric patients receiving allogeneic hematopoietic cell transplantation: incidence, risk factors, and outcomes. Biol Blood Marrow Transplant. 2018 Apr;24(4):758-64.
24. Kizilbash SJ, Kashtan CE, Chavers BM, Cao Q, Smith AR. Acute kidney injury and the risk of mortality in children undergoing hematopoietic stem cell transplantation. Biol Blood Marrow Transplant. 2016 Jul;22(7):1264-70.
25. Gist KM, Selewski DT, Brinton J, Menon S, Goldstein S, Basu RK. Assessment of the independent and synergistic effects of fluid overload and acute kidney injury on outcomes of critically ill children. Pediatr Crit Care Med. 2020 Feb;21(2):170-7.
26. Samaddar S, Sankar J, Kabra SK, Lodha R. Association of fluid overload with mortality in critically-ill mechanically ventilated children. Indian Pediatr. 2018 Nov;55(11):957-61.

27. Lopes CLS, Piva JP. Fluid overload in children undergoing mechanical ventilation. Rev Bras Ter Intensiva. 2017 Jul/Sep;29(3):335-46.

28. Raymakers-Janssen PA, Lilien MR, Tibboel D, Kneyber MC, Dijkstra S, Van Woensel JB, et al. Epidemiology and outcome of critically Ill pediatric cancer and hematopoietic stem cell transplant patients requiring continuous renal replacement therapy: a retrospective nationwide cohort study. Crit Care Med. 2019 Nov;47(11):e893-e901.

29. Cortina G, McRae R, Hoq M, Donath S, Chiletti R, Arvandi M, et al. Mortality of critically ill children requiring continuous renal replacement therapy: effect of fluid overload, underlying disease, and timing of initiation. Pediatr Crit Care Med. 2019 Apr;20(4):314-22.

30. Weiss SL, Peters MJ, Alhazzani W, Agus MSD, Flori HR, David P, et al. Surviving sepsis campaign international guidelines for the management of septic shock and sepsis-associated organ dysfunction in children. Pediatr Crit Care Med. 2020 Feb;21(2):e52-e106.

31. Almeida JP, João PRD, Sylvestre LC. Impact of the use of nephrotoxic drugs in critically ill pediatric patients. Rev Bras Ter Intensiva. 2020;32(4):557-63.