

The Incidence, Risk Factors, and Outcomes of Acute Kidney Injury in Pediatric Hematopoietic Stem Cell Transplant Recipients

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Introduction. Acute kidney injury (AKI) is a frequent complication after hematopoietic stem cell transplantation (HSCT), with reported incidences ranging from 20-70% within the first 100 days post-transplant. AKI can adversely impact outcomes and survival in this patient population.

Methods. This retrospective study evaluated 110 pediatric patients who underwent HSCT at Mofid Children's Hospital, affiliated with Shahid Beheshti University of Medical Sciences, Tehran, Iran, between 2016-2021. AKI was defined and staged according to the criteria for Kidney Disease Improving Global Outcomes (KDIGO).

Results. The cohort comprised 68 (61.8%) males and 42 (38.2%) females, with a mean age of 6.4 ± 4.1 years. Underlying disorders were malignant in 64 (58.1%) and non-malignant in 46 (41.9%) patients. Among the cohort, 84 (76.3%) patients underwent allogeneic HSCT, while 26 (23.7%) received autologous HSCT. Myeloablative and reduced-intensity conditioning regimens were used in 77 (70%) and 33 (30%) patients, respectively. AKI developed in 53 (48%) patients within 100 days post-transplant, with incidences of 38%, 40%, and 22% for stages 1, 2, and 3 AKI, respectively. AKI incidence was higher in allogeneic HSCT (52%) compared to autologous HSCT (17%; $P = 0.023$). Younger age ($P = 0.033$) and non-malignant disorders ($P = 0.033$) were associated with increased AKI risk. At the end of the study, 77 (70%) patients were alive, and 33 (30%) had deceased, with a significant positive correlation between AKI stage and mortality ($P = 0.004$).

Conclusion. This study highlights the high prevalence of AKI among pediatric HSCT recipients, particularly those undergoing allogeneic HSCT, at a younger age, and with non-malignant disorders. Regular post-transplant renal monitoring may improve survival in this population.

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INTRODUCTION

Hematopoietic stem cell transplantation (HSCT) is a potentially curative treatment for various malignant¹ and non-malignant disorders such as

primary immunodeficiencies, hemoglobinopathies, metabolic disorders (e.g., osteopetrosis),² and severe aplastic anemia but it carries a significant risk of acute kidney injury (AKI) in the early post-

transplant period. Previous studies have reported an incidence of AKI ranging from 20-70% within the first 100 days after HSCT. AKI requiring dialysis occurs in an estimated 1-19% of HSCT recipients.³⁻⁶

The development of AKI is a serious complication that can adversely impact outcomes and survival rates in this patient population. Several risk factors have been identified that may contribute to the development of AKI, including sepsis, acute graft-versus-host disease (aGVHD), exposure to nephrotoxic medications, veno-occlusive disease (VOD), total body irradiation (TBI), engraftment syndrome or cytokine storm, transplant-associated thrombotic microangiopathy (TA-TMA), and viral infections such as BK virus nephritis and adenovirus nephritis.⁷⁻¹¹

In adult HSCT recipients, previous studies have suggested that factors like myeloablative conditioning regimens,^{12,13} female sex, certain underlying diseases, and the development of aGVHD may increase the risk of AKI.^{8,14} However, these risk factors have not been consistently demonstrated in the pediatric HSCT population.^{3,15}

Importantly, children who develop stage III AKI (the most severe stage) after HSCT have been shown to have higher mortality rates.^{4,16} Additionally, overall survival rates in pediatric HSCT recipients decrease as the severity of AKI increases within the first 100 days post-transplant.^{3,16}

Several studies have evaluated AKI after pediatric HSCT using different standardized criteria for AKI definition.^{17,18} The KDIGO (Kidney Disease Improving Global Outcomes) criteria,¹⁹ and the pRIFLE (pediatric risk, injury, failure, loss, end-stage kidney disease) criteria,²⁰ are two standardized systems that have been utilized in some studies, but additional research using consistent criteria is needed to better elucidate the incidence, risk factors, and prognostic implications of AKI in this patient population.

This retrospective cohort study aimed to determine the incidence and outcomes of AKI according to the KDIGO criteria in pediatric HSCT recipients. Additionally, the study sought to identify potential risk factors associated with the development of AKI in this population.

MATERIALS AND METHODS

Patient Population and Data Gathering

This retrospective cohort study included 110

pediatric patients aged ≤ 16 years who received hematopoietic stem cell transplantation (HSCT) at the pediatric transplantation ward of Mofid Children's Hospital, affiliated with Shahid Beheshti University of Medical Sciences, Tehran, Iran, between 2016-2021. The exclusion criteria for the study were medical history of kidney diseases. The number of autologous transplants was 26 (23.7%), while the number of allogeneic transplants was higher at 84 (76.3%). Patient data were extracted from the "Data Registry of Hematopoietic Stem Cell Transplantation in pediatrics group (0-18 years) in Shahid Beheshti University of Medical Sciences and allied centers", which contains medical records including date of transplant, sex, age at transplant, indication for HSCT (malignant or non-malignant underlying disorder), type of transplant (autologous or allogeneic), conditioning regimen (myeloablative or reduced-intensity), source of stem cells, donor type for allogeneic transplants (Match Sibling Donor (MSD), Match Related Donor (MRD), Mismatch Unrelated Donor, or Haploidentical), degree of HLA matching, and prophylaxis regimen for graft-versus-host disease (aGVHD). disease (aGVHD). However, it is important to note that the retrospective design of this registry limited the ability to control for certain confounding variables, and the dataset did not include sufficient data to apply other AKI definitions.

We also collected data on post-transplant complications, including aGVHD, infectious complications (viral infections and sepsis), medical complications (nephrotoxic compounds, thrombotic microangiopathy (TA-TMA), veno-occlusive disease (VOD)), and surgical complications (any surgical procedures performed during the transplantation process).

Initial patient assessment included reviewing medical histories to confirm the absence of pre-existing kidney diseases. Serum creatinine levels were measured at baseline (pre-transplantation), and then subsequently on the first, third-, and seventh-day post-transplantation, as well as from the second to fourteenth weeks. Glomerular filtration rate (GFR) was determined based on radioisotope (DTPA) scans, and patients were evaluated based on the KDIGO classification to determine the AKI stage and need for plasma exchange or dialysis, following transplantation.

The cohort was divided into two groups

based on the conditioning regimen received. The myeloablative conditioning (MAC) group consisted of patients who received higher doses of busulfan, cyclophosphamide, carboplatin, etoposide, fludarabine, and melphalan. In contrast, the reduced-intensity conditioning (RIC) group included patients whose dosage of agents was reduced by approximately 30%. Most patients in RIC group received fludarabine, melphalan, and rabbit anti-thymocyte globulin (R-ATG).

Definition and staging of AKI

The Kidney Disease Improving Global Outcomes (KDIGO) criteria¹⁹ were used to define and stage acute kidney injury (AKI). These criteria classify AKI into three stages based on changes in serum creatinine levels and urine output. The KDIGO staging system is as follows:

Stage 1: Serum creatinine 1.5-1.9 times baseline or ≥ 0.3 mg/dL (≥ 26.5 $\mu\text{mol/L}$) increase

Stage 2: Serum creatinine 2.0-2.9 times baseline

Stage 3: Serum creatinine 3.0 times baseline or increase to ≥ 4.0 mg/dL (≥ 353.6 $\mu\text{mol/L}$) or the initiation of renal replacement therapy or, in patients ≤ 18 years, a decrease in estimated glomerular filtration rate (eGFR) to ≤ 35 mL/min per 1.73 m².

Measurement of GFR

Glomerular filtration rate (GFR) was measured by using radioisotope (DTPA) scans for patients before transplantation. However, due to the inability to continue GFR measurements at different time points post-transplant and the potential overestimation of GFR based on the Schwartz formula, GFR values were not included in the analysis.²¹

Statistical Analysis

Patient and disease characteristics were summarized using descriptive statistics, including frequency and percentage for categorized data and mean and standard deviation for quantitative data. Analysis of variance and Chi-square or Fisher's exact tests were used to compare means and proportions, respectively. A multivariate Cox proportional hazards model was created to analyze time-to-event outcomes, with time as the dependent variable. Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated, adjusting for potential risk factors. Logistic regression with the stepwise method was used to estimate relative

risks and adjust for confounding factors. A *P*-value of $< .05$ was considered statistically significant. All statistical analyses were performed using SPSS software (version 26, IBM Corp., Armonk, NY, USA).

RESULTS

This study included 110 patients who received an HSCT, of which 68 (61.8%) were male and 42 (38.2%) were female, with a mean age of 6.4 (± 4.1) years. The demographic and clinical characteristics are shown in Table 1. The underlying disorders, that prompted the need for transplantation, were malignant in 64 (58.1%) patients and non-malignant in 46 (41.9%) patients. Most patients, 84 (76.3%), received allogeneic HSCT, while 26 (23.7%) underwent autologous HSCT.

In the allogeneic transplantation population, the majority of stem cells (78.5%) were sourced from peripheral blood, while a smaller proportion came from bone marrow (11.9%) and umbilical cord (9.5%). The following categories of donors were used in allogeneic transplants: haploidentical donors (2 cases), other family members (12 cases), unrelated donors (23 cases), and siblings (47 cases, or 55.9%).

In the Allogeneic transplant population, the degree of HLA matching was full in 73 (86.9%) cases and partial in 11 (13.1%) cases. A myeloablative conditioning regimen was administered to 77 (70%) patients, whereas 33 (30%) patients received a reduced-intensity conditioning regimen.

Acute kidney injury (AKI) was developed in 53 (48%) patients within the first 100 days post-transplant. The incidence of stage 1, 2, and 3 AKI was 38%, 40%, and 22%, respectively. Among 53 patients with AKI, 20 (37.7%) were in stage 1, 21 (39.7%) in stage 2, and 12 (22.6%) in stage 3 according to the KDIGO criteria (Table 2).

It was found that there was a greater risk of developing AKI in younger age groups (0-5 years, 62.3%; 5-10 years, 30.6%; 10-16 years, 42.9%; *P* = .012) and in cases where the underlying diseases were non-malignant (52.8% vs. 47.2% for malignant, *P* = .033). The incidence of AKI was significantly higher in allogeneic (52%) compared to autologous (17%) transplants (*P* = .023). However, the degree of HLA matching, whether partial or full, did not significantly influence the risk of AKI development (*P* = .554).

Table 1. Demographic and Clinical Characteristics of Patients Based on Development of Acute Kidney Injury (AKI)

Variables	All Study Participants (n=110)	Subjects with AKI (n=53)	Non-AKI Subjects (n=57)	P
sex, n (%)				
Male	68 (61.8%)	31 (58.5%)	37 (64.9%)	0.55
Female	42 (38.2%)	22 (41.5%)	20 (35.1%)	
Type of Transplantation				
Autologous	26 (23.6%)	9 (17%)	17 (29.8%)	0.02
Allogenic	84 (76.4%)	44 (83.0%)	40 (70.2%)	
Age at transplantation, y				
0-5	53 (48.1%)	33 (62.3%)	20 (37.7%)	0.01
5-10	36 (32.8%)	11 (30.6%)	25 (69.4%)	
10-16	21 (19.1%)	9 (42.9%)	12 (57.1%)	
Transplantation source				
PBSC	66 (78.6%)	33 (75.0%)	33 (82.5%)	0.40
CB	8 (9.5%)	6 (13.6%)	2 (5.0%)	
BM	10 (11.9%)	5 (11.4%)	5 (12.5%)	
HLA matching				
Full matched	73 (86.9%)	39 (88.6%)	34 (85.0%)	0.55
Partial matched	11 (13.1%)	5 (11.4%)	6 (15.0%)	
Transplantation source				
sibling	47 (56%)	27 (61.4%)	20 (50.0%)	0.40
Other family member	12 (14.3%)	6 (13.6%)	6 (15.0%)	
unrelated	23 (27.4%)	11 (25.0%)	12 (30.0%)	
Haploidentical	2 (2.40%)	0 (0.0%)	2 (5.0%)	
Conditioning Regimen				
RIC	33 (30.0%)	19 (35.8%)	14 (24.6%)	0.19
MAC	77 (70.0%)	34 (64.2%)	43 (75.4%)	

PBSC = peripheral blood stem cells, CB = cord blood, BM = bone marrow, RIC = reduced intensity conditioning, MAC = myeloablative conditioning, GvHD = graft-versus-host disease

Table 2. Association Between AKI Stages According to KDIGO Criteria and Mortality

Outcome of HSCT	AKI staging according to KDIGO (n=53)			P
	I (n=20)	II (n=21)	III (n=12)	
Alive	17 (85%)	9 (42.9%)	6 (50%)	0.004
Deceased	3 (15%)	12 (57.1%)	6 (50%)	

Sex ($P = .550$), HSCT source ($P = .404$), conditioning regimen ($P = .197$), aGVHD prophylaxis with methotrexate or Cellcept ($P = .134$), presence of aGVHD ($P = .436$), and complications like fungal infections ($P = .608$) and VOD ($P = .482$) did not significantly affect the incidence of AKI. The donor-patient relationship was statistically related to the timing of AKI development, with an adjusted hazard ratio of 0.63 (95% CI, $P = .01$) for non-relative donors compared to relative donors. However, patients without a relative donor experienced AKI earlier and more severely compared to those with a relative donor.

The degree of HLA matching ($P = .554$) or the presence of TA-TMA ($P = .194$) did not significantly

impact the incidence of AKI.

Patients diagnosed with sepsis had a significantly higher likelihood of developing AKI compared to those without sepsis (73.6% vs. 26.4%, $P = .030$) (Table 3). The incidence of cytomegalovirus viremia/infection was higher in patients with AKI compared to those without AKI (35.8% vs. 64.2%, $P = .014$). However, there was no significant difference in the incidence of BK virus viremia/infection between patients with and without AKI ($P = .800$) (Table 3).

At the end of the study, 77 (70%) patients were alive, and 33 (30%) patients were deceased. A statistically significant positive correlation was seen between the stages of AKI and mortality

Table 3. Post-Transplant Complications and Outcomes Based on AKI Status

Post-Transplant Complications	All study participants (n=110)	Subjects with AKI (n=53)	Non-AKI Subjects (n=57)	P
GvHD	43 (39.0%)	23 (43.4%)	20 (35.1%)	0.43
GvHD prophylaxis-Methotrexate	39 (46.4%)	17 (38.6%)	22 (55.0%)	0.18
GvHD prophylaxis-Cellcept	41 (48.8%)	25 (56.8%)	16 (40.0%)	0.13
GvHD prophylaxis-Cyclosporine	84 (76.4%)	44 (83.0%)	40 (70.2%)	0.19
VOD	1 (0.9%)	1 (1.9%)	0	0.48
HSCT-Associated TA-TMA	5 (5%)	4 (7.5%)	1 (1.8%)	0.19
Fungal Infections	18 (16.4%)	10 (18.9%)	8 (14.0%)	0.60
Sepsis	69 (62.7%)	39 (73.6%)	30 (52.6%)	0.03
BK Virus	20 (18.2%)	9 (17.0%)	11 (19.3%)	0.80
Adenovirus	2 (1.8%)	2 (3.8%)	0 (0.0%)	0.23
Cytomegalovirus	27 (24.5%)	19 (35.8%)	8 (14.0%)	0.01
Outcomes				
Alive	77 (70.0%)	32 (60.4%)	45 (78.9%)	0.03
Deceased	33 (30.0%)	21 (39.6%)	12 (21.1%)	

GvHD = graft-versus-host disease, VOD = veno-occlusive disease, TA-TMA = transplant-associated thrombotic microangiopathy, HSCT = hematopoietic stem cell transplantation

Table 4. Hemorrhagic Cystitis in Relation to Viral Infections and Cyclophosphamide Exposure

	Total	Hemorrhagic Cystitis		P
		No (n=73)	Yes (n=37)	
BK virus viremia/infection	20 (18.2%)	0	20 (54.1)	0.001
Adenovirus viremia/infection	2 (1.8%)	1 (1.4)	1 (2.7)	0.621
Cytomegalovirus viremia/infection	27 (24.5%)	16 (21.9)	11 (29.7)	0.482
Cyclophosphamide (CPM)	59 (53.6%)	32 (43.8)	27 (73)	0.004

($P = .004$), as indicated in Table 2; at the end of the trial, 85% of patients in stage 1, 42.9% in stage 2, and 50% in stage 3 remained alive.

Of the 37 patients who experienced hemorrhagic cystitis, 20 (54.1%) had BK virus infection, one (2.7%) had an adenovirus infection, and 11 (29.7%) had cytomegalovirus infection. BK virus infection showed a significant association with hemorrhagic cystitis ($P = .001$). In contrast, the associations between adenovirus and cytomegalovirus infections with hemorrhagic cystitis were not statistically significant ($P = .621$ and $P = .482$, respectively). The confounding effect of cyclophosphamide (CPM), a known cause of hemorrhagic cystitis in preparative regimens, was also examined. As expected, CPM exposure showed a significant association with hemorrhagic cystitis ($P = .004$), particularly with the early-onset type (Table 4).

DISCUSSION

Acute kidney injury (AKI) is a frequent complication following hematopoietic stem cell transplantation (HSCT), with a reported incidence

ranging from 20-70% in the first 100 days post-transplant.^{3,5,13} To the best of our knowledge, this is one of the few studies to comprehensively evaluate the incidence, risk factors, and outcomes of AKI in a pediatric HSCT population. In this retrospective study, we found an overall incidence of 48.2% for AKI among pediatric HSCT recipients, consistent with previous literature.^{22,23}

The incidence of AKI was significantly higher in allogeneic HSCT (52%) compared to autologous HSCT (17%). This finding aligns with several other studies.^{8,12,15} While our study did not find statistically significant associations between AKI and individual factors such as conditioning regimen or GVHD prophylaxis, the higher incidence in allogeneic HSCT may be attributed to the cumulative effect of various post-transplant factors. These could include a higher risk of complications such as infections, the potential for graft-versus-host disease (GVHD), and the overall intensity of the treatment protocol in allogeneic transplantation.

Younger age at transplantation was identified as a risk factor for developing AKI, with the highest

incidence (62.3%) observed in the 0-5-year age group. This contrasts with previous research in children^{15,24} that did not find age as a risk factor, but is consistent with the findings of Rajpal *et al.*²⁵ who reported older age as a predictor of AKI requiring dialysis. The discrepancies may be related to differences in sample sizes and study designs.

Patients with non-malignant underlying disorders had a higher risk of developing AKI compared to those with malignant disorders (52.8% vs. 47.2%, $P = .033$). While previous studies have examined AKI in pediatric HSCT recipients, our findings provide novel insights into the significant association between younger age at transplantation, non-malignant underlying disorders, and an increased risk of AKI development in this patient population. This finding requires further investigation to elucidate the potential mechanisms and underlying factors contributing to the increased risk in non-malignant conditions.

Sepsis was identified as a significant risk factor for AKI, with a higher incidence of AKI observed among patients with sepsis compared to those without (73.6% vs. 26.4%, $P = .030$). This is consistent with the established knowledge that sepsis is a major contributor to the development of AKI through various pathophysiological mechanisms, including hemodynamic changes, endothelial dysfunction, and inflammation.^{7,26}

The incidence of cytomegalovirus (CMV) viremia/infection was significantly higher in patients with AKI compared to those without AKI (35.8% vs. 64.2%, $P = .014$). This finding suggests a potential association between CMV infection and AKI, which may be attributed to the nephrotoxic effects of antiviral drugs or the direct effects of viral infection on renal cells. Notably, to the best of our knowledge, our study is among the first to report a correlation between cytomegalovirus infection and an elevated incidence of AKI in pediatric HSCT patients, suggesting a potential area for future mechanistic investigations. However, in this study, the incidence of BK virus and adenovirus infections did not differ significantly between patients with and without AKI.

Notably, the presence of hemorrhagic cystitis, a known complication of cyclophosphamide and certain viral infections, was not directly associated with AKI in this study. While BK virus infection was significantly related to hemorrhagic cystitis

($P = .001$), the contribution of adenovirus and CMV infections was not statistically significant. The effect of cyclophosphamide on early-onset hemorrhagic cystitis was significant ($P = .004$), as expected.

The study did not find a significant association between AKI and factors such as sex source of HSCT, conditioning regimen, aGVHD prophylaxis, presence of aGVHD, fungal infections, veno-occlusive disease (VOD), or transplant-associated thrombotic microangiopathy (TA-TMA). However, it is important to note that the small sample size and heterogeneity of the study population may have contributed to the lack of statistical significance for some of these factors.

The severity of AKI, as defined by the KDIGO staging, showed a significant correlation with mortality ($P = .004$). Patients with stage 2 (57.1%) and stage 3 (50%) AKI had a higher mortality rate compared to those with stage 1 AKI (15%). This finding underscores the prognostic value of AKI stages and highlights the need for close monitoring and early intervention in patients with advanced stages of AKI, which is consistent with previous studies.^{4,16}

LIMITATIONS

The study's limitations included several key challenges. First, the retrospective design introduced potential selection bias and incomplete data retrieval from medical records. Prospective studies with standardized protocols could mitigate this limitation. Second, using the KDIGO criteria for the diagnosis and staging of AKI may have been less sensitive than pediatric-specific criteria like pRIFLE. Incorporating multiple AKI definitions could enhance the findings' robustness. Third, as a single-center study, the generalizability of results may be limited, necessitating larger multi-center collaborative studies for validation. Fourth, the inability to comprehensively adjust for potential confounders, such as conditioning regimens, immunosuppressive therapies, or comorbidities, due to original dataset limitations, may have influenced results. Advanced statistical modeling techniques are needed to address this limitation. Moreover, the lack of long-term follow-up data precluded evaluating chronic kidney disease outcomes in patients who developed AKI following transplantation. Longitudinal studies are

warranted to investigate potential long-term renal consequences. Despite these limitations, this study provides valuable insights into AKI incidence, risk factors, and outcomes in pediatric HSCT recipients, highlighting the need for regular post-transplant renal monitoring.

CONCLUSION

This study highlights the high prevalence of acute kidney injury (AKI) among pediatric patients who receive hematopoietic stem cell transplantation (HSCT), particularly in those undergoing allogeneic HSCT, at younger ages, and with non-malignant underlying disorders. The findings emphasize the prognostic significance of AKI stages and the importance of regular post-transplant renal monitoring to improve patient outcomes. While providing valuable insights, future prospective studies with larger cohorts and standardized AKI definitions are warranted to further elucidate risk factors, pathophysiology, and long-term renal consequences. Continued research that focuses on prevention and management strategies could potentially reduce AKI-associated morbidity and mortality in this vulnerable population.

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CONFLICT OF INTEREST

Authors declared no conflict of interest.

AUTHORS' CONTRIBUTIONS

Conceptualization, Reviewing, and Supervision by NM, BSS, and MM. Data curation, Writing-

Original draft preparation by AL, SK. Methodology by AS. Editing by MJ, and MA.

REFERENCES

1. D'Souza, A., et al., Current use and trends in hematopoietic cell transplantation in the United States, 2017, Elsevier. p. 1417-1421.
2. Shamsian, B.S., et al., Allogeneic hematopoietic stem cell transplantation in an Iranian patient with osteopetrosis caused by carbonic anhydrase II deficiency: A case report. *Pediatric Transplantation*, 2024. 28(3): p. e14689.
3. Koh, K.-N., et al., Acute kidney injury in pediatric patients receiving allogeneic hematopoietic cell transplantation: incidence, risk factors, and outcomes. *Biology of Blood and Marrow Transplantation*, 2018. 24(4): p. 758-764.
4. Didsbury, M.S., F.E. Mackie, and S.E. Kennedy, A systematic review of acute kidney injury in pediatric allogeneic hematopoietic stem cell recipients. *Pediatric transplantation*, 2015. 19(5): p. 460-470.
5. Lopes, J. and S. Jorge, Acute kidney injury following HCT: incidence, risk factors and outcome. *Bone marrow transplantation*, 2011. 46(11): p. 1399-1408.
6. Hahn, T., et al., Acute renal failure requiring dialysis after allogeneic blood and marrow transplantation identifies very poor prognosis patients. *Bone marrow transplantation*, 2003. 32(4): p. 405-410.
7. Wanchoo, R., et al., Acute kidney injury in hematopoietic stem cell transplantation. *Current Opinion in Critical Care*, 2019. 25(6): p. 531-538.
8. Parikh, C.R., et al., Renal dysfunction in allogeneic hematopoietic cell transplantation. *Kidney international*, 2002. 62(2): p. 566-573.
9. Kogon, A. and S. Hingorani, Acute kidney injury in hematopoietic cell transplantation. in *Seminars in nephrology*. 2010. Elsevier.
10. Sawinski, D., The kidney effects of hematopoietic stem cell transplantation. *Advances in chronic kidney disease*, 2014. 21(1): p. 96-105.
11. Rondón, G., et al., Impact of fluid overload as new toxicity category on hematopoietic stem cell transplantation outcomes. *Biology of Blood and Marrow Transplantation*, 2017. 23(12): p. 2166-2171.
12. Parikh, C.R., et al., Comparison of ARF after myeloablative and nonmyeloablative hematopoietic cell transplantation. *American Journal of Kidney Diseases*, 2005. 45(3): p. 502-509.
13. Hingorani, S.R., et al., Acute renal failure after myeloablative hematopoietic cell transplant: incidence and risk factors. *Kidney international*, 2005. 67(1): p. 272-277.
14. Kersting, S., et al., Acute renal failure after allogeneic myeloablative stem cell transplantation: retrospective analysis of incidence, risk factors and survival. *Bone marrow transplantation*, 2007. 39(6): p. 359-365.
15. Kist-van Holthe, J.E., et al., Prospective study of renal insufficiency after bone marrow transplantation. *Pediatric Nephrology*, 2002. 17(12): p. 1032-1037.
16. Kizilbash, S.J., et al., Acute kidney injury and the risk of mortality in children undergoing hematopoietic stem

- cell transplantation. *Biology of Blood and Marrow Transplantation*, 2016. 22(7): p. 1264-1270.
17. Andronesi, A., et al., Incidence and risk factors for acute kidney injury after allogeneic stem cell transplantation: a prospective study. *Biomedicines*, 2022. 10(2): p. 262.
 18. Ando, M., et al., A comparative assessment of the RIFLE, AKIN and conventional criteria for acute kidney injury after hematopoietic SCT. *Bone marrow transplantation*, 2010. 45(9): p. 1427-1434.
 19. Khwaja, A., KDIGO clinical practice guidelines for acute kidney injury. *Nephron Clinical Practice*, 2012. 120(4): p. c179-c184.
 20. Akcan-Arikan, A., et al., Modified RIFLE criteria in critically ill children with acute kidney injury. *Kidney international*, 2007. 71(10): p. 1028-1035.
 21. Schwartz, G.J. and D.F. Work, Measurement and estimation of GFR in children and adolescents. *Clinical Journal of the American Society of Nephrology*, 2009. 4(11): p. 1832-1843.
 22. Avci, B., et al., Acute kidney injury and risk factors in pediatric patients undergoing hematopoietic stem cell transplantation. *Pediatric Nephrology*, 2024: p. 1-9.
 23. Hirano, D., et al., Independent risk factors and long-term outcomes for acute kidney injury in pediatric patients undergoing hematopoietic stem cell transplantation: a retrospective cohort study. *BMC nephrology*, 2020. 21: p. 1-7.
 24. Ileri, T., et al., Prospective evaluation of acute and chronic renal function in children following matched related donor hematopoietic stem cell transplantation. *Pediatric transplantation*, 2010. 14(1): p. 138-144.
 25. Rajpal, J.S., et al., Improved survival over the last decade in pediatric patients requiring dialysis after hematopoietic cell transplantation. *Biology of Blood and Marrow Transplantation*, 2013. 19(4): p. 661-665.
 26. Bagshaw, S.M., et al., Urinary biomarkers in septic acute kidney injury. *Intensive care medicine*, 2007. 33(7): p. 1285-1296.

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