Chapter 1
The Changing Landscape of the Critical Care of Pediatric Immunocompromised Hematology and Oncology Patients

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Immunocompromised children and adolescent patients who have hematologic or oncologic diseases represent a small percentage of patients treated in pediatric intensive care units (PICUs) but have a disproportionately high mortality rate. A single-center study of 1278 patients admitted to a pediatric hematology-oncology service over an 11-year period found an admission rate of 4.2% with an overall PICU mortality rate of 38.9% [1]. Risk factors for PICU admission included older age, diagnosis of nonmalignant disease, and treatment with HCT. A more recent retrospective multicenter cohort analysis of almost 250,000 consecutive PICU admissions using the Virtual PICU Systems database identified 10,365 patients diagnosed with a malignancy who were admitted to PICUs for reasons other than perioperative admissions during the study period [2]. Children with cancer accounted for 11.4% of all PICU deaths and had mortality of 6.8% (43% in those who were mechanically ventilated) compared to 2.4% in patients without malignancy.

Outcome data regarding patients admitted to PICUs who have nonmalignant hematologic or immunologic diseases is limited, with the exception of those treated with hematopoietic cell transplantation (HCT). Far more is known about patients with oncologic diagnoses, and the literature is most robust regarding those treated with HCT. The survival of children with hematologic and oncologic diseases has improved in recent years despite remaining higher than those of other patients treated in the PICU (Table 1.1). A meta-analysis of mortality trends of children treated in the PICU after HCT over time showed a significant decrease in mortality associated with the year of inclusion as did a large single-center study comparing outcomes over time [3, 4]. However, interpreting comparisons of mortality across multiple

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Table 1.1 Published mortality of hematology, oncology, and HCT patients over time

Reference	Study period	Population	Number of PICU patients	PICU mortality (%)
Hayes et al. [5]	1987–1997	HCT	39	73
Hallahan et al. [6]	1987–1996	Oncology and HCT	150	27
Diaz De Heredia et al. [7]	1991–1995	HCT	31	45
Lamas et al. [8]	1991–2000	HCT	44	70
Kache et al. [9]	1992–2004	HCT	81	82 (1992–1999) 41 (2000–2004)
Cheuk et al. [10]	1992–2002	HCT	19	84
Diaz et al. [11]	1993–2001	HCT	42	69
Jacobe et al. [12]	1994–1998	HCT	40	44
Heying et al. [13]	1995–1999	Oncology (no HCT)	48	25
Tamburro et al. [4]	1996–2004	Oncology and HCT	329	41
Tomaske et al. [14]	1998–2001	HCT	26	58
Gonzalez-Vincent et al. [15]	1998–2002	HCT	36	53
Hassan et al. [16]	1998–2008	HCT	19	17
Faraci et al. [1]	1999–2010	Hematology/ oncology	54	39
Asperberro et al. [17]	2000–2006	HCT	53	51
Bartram et al. [18]	2000–2008	Sickle cell disease	46	7
Chima et al. [19]	2004–2010	HCT	155	37
Duncan et al. [20]	2005–2006	HCT	129	38
Zinter et al. [21]	2009–2012	HCT	1102	16.2
Zinter et al. [2]	2009–2012	Oncology	10,365	6.8
Rowan et al. [22]	2009–2014	HCT	222	60

HCT hematopoietic cell transplantation

studies must be done with caution. The published literature is comprised almost exclusively of retrospective studies, and the inclusion criteria are not consistent across studies. Some studies include only those felt to be at highest risk for worst outcome, specifically HCT patients supported with mechanical ventilation, whereas others include patients with all oncology diagnoses and admitted to the PICU for all indications. There are multiple reasons for the improved outcomes including scientific advances in critical care, hematology, oncology, and HCT. Equally important have been advances in supportive care and infectious disease management.

The severity of illness of immunocompromised hematology and oncology patients admitted to PICUs is broad including planned postoperative admissions, semi-urgent admissions of patients with worsening illness, and the emergent transfer of rapidly decompensating children. Equally broad are the reasons for critical

illness in this diverse population including infection, organ compromise, and complications of the primary disease. The management of critically ill immunocompromised children and adolescents must be guided by the primary disease and patient's treatment. General principles of the initial management and stabilization of critically ill hematology and oncology patients, in most cases, can follow practices applied to other children. Thereafter, the management is strongly influenced not only by the reason for the need for critical care, but by the unique features of the underlying disease as well. For example, the early care of a child with sickle cell anemia experiencing acute respiratory dysfunction may mirror that of a patient with acute lymphoblastic leukemia or one with severe combined immune deficiency. After the primary stabilization of the patient, an understanding of the underlying disease is key to the next steps of diagnosis and management. In the example, one may consider acute chest syndrome as the cause of the respiratory distress in the patient with sickle cell anemia. Clearly this would not be on the list of potential etiologies in a child with leukemia in whom infection may be a chief concern. The therapy that the child receives to treat the primary disease is important as the critical illness may be a direct result or influenced heavily by the treatment. A clear example is that of children undergoing HCT who may have organ compromise, bleeding, infection, graft-versus-host disease, and other toxicities related to the recent and past therapy in addition to underlying comorbidities.

A goal of this textbook is to provide an understanding of the specific aspects of different diagnoses and therapies that impact the critical care of immunocompromised hematology and oncology patients. It is unrealistic to expect PICU providers to have a comprehensive understanding of all the diseases and therapies used in this population and for hematologists-oncologists to fully understand advances in ICU care. This is particularly true given the rapidly changing landscape of pediatric hematologic and oncologic care. Recent years have seen the development and expanded use of molecularly targeted medications, chimeric antigen receptor T-cell (CAR-T) therapy, and gene therapy. Each of these and other emerging therapies carry unique risks. Because of the complexity of diagnoses and treatment, a collaborative relationship between the PICU and the disease-specific teams is important to the care of these patients. Different models for cooperative care are addressed later in this text.

Multiple research consortia including the Pediatric Acute Lung Injury and Sepsis Investigators and Pediatric Blood and Marrow Transplant Consortium have focused on the care of immunocompromised hematology and oncology patients. The work of these and other groups is important as the community works to improve the survival of these vulnerable patients.

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