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Advancements in Pediatric Hematology and Oncology

Abdelhadi Hussein Yousef Abdelhafez[1*], Said Marwan Said Hamdan[2]

[1]Primary Health Care Corporation (PHCC), Qatar
[2]Umm Slal Health Center, Primary Health Care Corporation (PHCC), Qatar

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***Corresponding author:** Abdelhadi Hussein Yousef Abdelhafez
Primary Health Care Corporation (PHCC), Qatar

Abstract **Review Article**

Pediatric hematology and oncology is the medical subspecialty that focuses on the identification, management, and research of various blood disorders and pediatric cancer. The main objective of the present study was to review the updates of literature regarding the main topic of this study. The researchers employed the main research engines such as Science Direct, pub med, Google Scholar, and others to reveal the appropriate cited literature. The results of this review showed that pediatric hematology and oncology has common features with the general hematology and oncology. The researchers discussed in this study diagnostic and therapeutic strategies. Innovative intervention studies were also discussed.

Keywords: Hematology, oncology, pediatric, diagnosis, treatment.

1. INTRODUCTION TO PEDIATRIC HEMATOLOGY AND ONCOLOGY

Pediatric hematology and oncology is the medical subspecialty that focuses on the identification, management, and research of various blood disorders and pediatric cancers (Hastings *et al.*, 2021). The diseases addressed in this specialty occur with some frequency and have a major effect on a child's health and development (Hoffman *et al.*, 2022). As part of the integrated multidisciplinary team, pediatric hematologist oncologists typically are the professionals who help children and their families or other caregivers identify and manage these types of diseases (Shah *et al.*, 2021). Though the types of disorders in children are similar to those in adults, many diseases in children pose challenges that are quite different from those in adults due to variations in disease biology as well as age and developmental differences (Liu and Geyer, 2024).

Children are actively developing new tissues, organs, and systems, and they are more sensitive to the toxic effects of many drugs and therapies (Cavell *et al.*, 2021). Therefore, they require careful diagnostic, treatment, and follow-up services from a dedicated, knowledgeable team (Brothwood *et al.*, 2021). Although pediatric hematologist oncologists should work closely with adult hematologist oncologists to ensure proper transitions of care, children and adolescents treated in programs devoted exclusively to these patients during at least part of their therapeutic care generally are able to experience improved outcomes, even with difficult diseases (Nearchou *et al.*, 2020). Care for both children with blood diseases and cancer should reflect a family-centered and diagnosis-based approach (Cleverley *et al.*, 2020). Furthermore, the discipline-based approach to a variety of cancers and guidelines for numerous blood disorders reflect the complexity and growth of leukemia, lymphoma, bone marrow failure, solid tumors, and hematologic malignancies, in conjunction with significant therapeutic options (Al Asseri *et al.*, 2013; De *et al.*, 2024). Finally, early diagnosis of blood disorders and cancers in children is critical to allow the initiation of timely therapy and potentially improve outcomes (Harder *et al.*, 2020). However, most of the initial signs and symptoms of pediatric blood disorders and cancers are non-specific, which leads to many changing to primary care (Petrovski *et al.*, 2022). Allowing pediatric practitioners to recognize children who should be evaluated further by pediatric hematologists or oncologists is essential (Owens and Waters, 2020; Odom *et al.*, 2021; Health Organization, 2022).

During the last 70 years, there have been significant advancements in the field of pediatric hematology and oncology (Rodriguez *et al.*, 2024). In the last 40 years, pediatric oncology has adapted a multidisciplinary approach and actively integrated and collaborated with biomedical engineers, pharmacologists, radiation therapists, and surgeons (Liu and Geyer, 2024). It has offered pediatric patients

innovative surgical approaches, a role of radiation therapy in survivors, organ transplantation, uses of novel agents, and a role of immunotherapy in the long-term management of pediatric cancers (Russell *et al.,* 2024). Understanding the history of pediatric hematology is important both to appreciate the significant advancements of basic, clinical, and epidemiologic science observed in the study of non-malignant disorders of the blood in children, as well as to realize the current state of pediatric hematology (Inaba and Pui, 2021; Laetsch *et al.,* 2021). Readers must appreciate the ever-evolving nature of early genetic manipulations, vastly different types of drug development, such as enzyme replacement therapies, hematopoietic stem cell transplantation, gene therapies, and CAR T therapies (Shah *et al.,* 2021; Fioredda *et al.,* 2022). Progress continues in all areas of pediatric hematology from the basic biology to patient outcomes in both non-malignant blood disorders and pediatric cancer (Butler *et al.,* 2021). The research continues to add to the evolution of the field (Czogała *et al.,* 2021; Zhang *et al.,* 2023).

2. Epidemiology of Pediatric Hematologic and Oncologic Disorders

The burden of hematologic and oncologic disorders among children globally is substantial. Hematologic and oncologic disorders (hereafter used jointly as cancer or neoplasia) are among the top five causes of mortality in pediatric age groups (Harris *et al.,* 2021; Laetsch *et al.,* 2021; Pagano *et al.,* 2021). The risk of occurrence is equally distributed between both genders; however, depending on geographic, socioeconomic, racial, and ethnic variations, the epidemiology might alter (García-Suárez *et al.,* 2020; Streiff *et al.,* 2021).

In the United States, cancer incidence is predicted to have risen nearly 24% in the 15–19 years age group by 2020, compared with 1975, while a twofold rise from 10 per 100,000 persons in 1975 to 21 in 2018 for the 0–14 years age group was noted (Wang, 2021). For most cancers, universal incidence patterns are due to an increased diagnostic rate; however, for some unknown genetic, environmental, and lifestyle factors, the observed and possibly real incidence has significantly increased (Kohler *et al.,* 2021). Adhering to the pediatric population's overall cancer incidence increase, sizable prospective studies have been performed to identify the potential etiological factors behind this pre- and postnatal exposure (Zomawia *et al.,* 2023). Following treatment advancements, including targeted therapy, blood tests, and immuno-oncology, recent estimates show a more than twofold rise in overall survival, which documents cancer and survival statistics regarding overall cancers from 1975 to 1980 over time. Since 1980, this same overall five-year pediatric cancer survival has jumped from 58% to 86% based on the 2007–2015 data in the registries, which is close to a 50% increase (Ollauri-Ibáñez and Astigarraga, 2021).

3. Diagnosis and Management of Common Pediatric Hematologic Disorders

This section primarily addresses the diagnosis and management of prevalent pediatric hematologic disorders (Mattiello *et al.,* 2020). Historically, diagnosis was made purely by clinical features, but as more tests and new reference standards have been developed over time, we rely on an extensive but quite practical hematological evaluation (Alkhatib, 2020a; Gallagher, 2022). As expected, most children with hematological disorders will present with anemia. Newly diagnosed patients should undergo hematological evaluation to confirm the suspected diagnosis (Andriastuti *et al.,* 2020). In general, suboptimal intake of specific vitamins, poor diet, and blood loss, mostly menstruation and gastrointestinal bleeding, are the main and important etiologies for microcytic anemia (Hess *et al.,* 2023). Iron studies are essential; for specific etiologies, additional tests such as hemoglobin electrophoresis and genetic testing may be required (Jeng and Chen, 2022).

At the first presentation, it is very important to take a detailed and thorough clinical history to ascertain any relevant family or personal history such as anemia, jaundice, or splenectomy in the parents or siblings, and any recent travel to malaria-endemic areas (Mattiello *et al.,* 2020). The clinical history can also reveal other causes of decreased growth, fatigue, exercise limitations, and tachycardia (De *et al.,* 2021). Together with a full physical examination, it will guide investigations into a differential diagnosis (Connelly-Smith *et al.,* 2023). The anemia can be a mild-to-severe microcytic anemia, beta-thalassemia intermedia, or HbH disease in a compound heterozygous state (Woods *et al.,* 2021). Thalassemia is not always hypochromic although it is mostly microcytic. Patients can present with various genetic patterns, and clinical features and severity depend on the causative mutations (Fraticelli *et al.,* 2021). Management should be comprehensive and take into account the child's growth, iron status, other hemoglobin variants, medical comorbidities, and psychosocial status (Obeagu and Akinleye, 2024). The main role of the doctor and the hematology team is to formally diagnose the disease and monitor disease progression (Canaud *et al.,* 2021). There are not many evidence-based guidelines; management is mainly "good practice (Schilsky *et al.,* 2023).

3.1. Anemia

In clinical practice, there are different types of anemia found in pediatric patients. The most common one is iron-deficiency anemia (Gallagher, 2022). Other causes of anemia can be related to the production of red blood cells, such as anemia of inflammation, anemia of chronic disease, thalassemia, aplastic anemia, malignancy, and other hematologic diseases (Animasahun and Itiola, 2021). Anemia is generally characterized by the depletion in the number of red blood cells and the levels of hemoglobin and hematocrit (Mattiello *et al.,* 2020). Diagnosis of anemia is supported by a complete blood count with a peripheral blood smear

that will show microcytic, hypochromic red blood cells (Sarna *et al.,* 2020). The clinical symptoms include fatigue, inability to focus, and pallor (Gedfie *et al.,* 2022). The specific type and causes can be explored by the etiology from the initial workup, such as testing for iron deficiency or hemoglobin electrophoresis (Mantadakis *et al.,* 2020). Normally, the diagnostic tool for anemia will include blood tests, which will measure the amount of red blood cells, reticulocytes, hemoglobin, hematocrit, and the mean corpuscular size and hemoglobin (Shalby *et al.,* 2, 022).

Developmental abnormalities of the bone marrow and dyserythropoiesis can be further investigated by a bone marrow aspiration and biopsy (Brittenham *et al.,* 2023). Management of anemia depends on the causes (Wiciński *et al.,* 2020). For iron-deficiency anemia, iron treatment can be carried out (Hess *et al.,* 2023). For anemia of inflammation or anemia of chronic disease, the strategy includes optimizing therapy, which reverses the underlying disease or an erythropoiesis-stimulating agent treatment (Lasocki *et al.,* 2020). It has been reported that we should also concentrate on the management of malnutrition (Lasocki *et al.,* 2020). The intake of food with high doses of antioxidants and vitamins can improve the hemoglobin level at intake (Fattizzo and Barcellini, 2022). In the long run, repeated subsequent therapy may be needed to prevent late complications, such as retarded growth and sexual development (Warner *et al.,* 2020). Referral for a pediatric psychologist and a clinical dietitian was needed to ensure all therapeutic management efforts were accomplished (Elstrott *et al.,* 2020). Combinations of underlying treatment and management of anemia are essential. They include coordination and comprehensive care provided by pediatricians and perhaps nutritionists at the referral center site (Elstrott *et al.,* 2020).

3.2. Thalassemia

Hemoglobin is responsible for carrying oxygen in the blood, and any production defect leads to anemia (Rao *et al.,* 2024). Thalassemia is one of the most common genetic diseases globally; however, its geographic distribution varies (Mahmoud *et al.,* 2024). It is inherited in an autosomal-recessive manner (Mahmoud *et al.,* 2024). According to the globin chain affected by thalassemia, it is classified into alpha thalassemia and beta thalassemia (Ali *et al.,* 2021). The clinical manifestations of alpha thalassemia can be asymptomatic in silent carriers, and some may have mild anemia, mainly due to a mutation in four loci where alpha-globin chains are produced, that is, two each from chromosome 16 (Tuo *et al.,* 2024). On the other hand, the clinical phenotype of beta thalassemia is more severe than that of alpha thalassemia, including thalassemia trait, thalassemia intermediate, and thalassemia major (De *et al.,* 2022). The effective management of thalassemia can be achieved through early diagnosis, premarital genetic testing, and an advanced preimplantation genetic diagnosis program (Kattamis *et al.,* 2020; Ebrahimi *et al.,* 2021).

Early diagnosis and effective progressive management increase life expectancy to the sixth decade of life (Vaduganathan *et al.,* 2020). A comprehensive management strategy includes the following: regular blood transfusions, an early comprehensive vaccination program, regular iron chelation therapy, folic acid supplementation, and monitoring for secondary complications, including endocrine and heart abnormalities (Abati *et al.,* 2020). Furthermore, family support tools and educational materials need to be well designed to help families understand from an early age the pattern of inheritance, the complications, and the strategy to fight the disease to improve quality of life (Naik, 2021). Psychosocial issues and coping strategies are among the major complications to be taken into consideration in all patients with chronic diseases, mainly patients with thalassemia (Subramanian *et al.,* 2020). A multidisciplinary approach and teamwork yield the best results (Fang *et al.,* 2020; Bahadoram *et al.,* 2022).

3.3. Sickle Cell Disease

Sickle cell disease (SCD) is a hereditary disorder characterized by the production of abnormally shaped red blood cells. Inheritance of two sickle hemoglobin-β (HbS) gene alleles results in sickle cell anemia (Alkhatib *et al.,* 2018). Pathophysiological consequences of SCD are the following: intracellular polymerization of HbS when deoxygenated, deformability of the sickle cell is reduced, leading to cell stickiness, sickled RBCs have an increased tendency to aggregate, leading to microvessel blockages and reduced blood flow (Arishi *et al.,* 2021). Clinical features of the disease are frequent episodic vaso-occlusive crises (VOC), priapism, acute chest syndrome (ACS), splenic sequestration, strokes, acute multi-organ failure, as well as chronic further-occlusive complications such as chronic anemia and increased susceptibility to infection, chronic pain (of multifactorial reasons), pulmonary hypertension, as well as developmental problems (Coetzee *et al.,* 2022). Development of prenatal diagnosis with high accuracy and newborn screening has led to programs in many countries also providing genetic counseling and education for parents in need (Nader *et al.,* 2020). Early diagnosis is important—if possible by newborn screening—and requires education for an understanding of the impact of the disease on the child, preferably by professionals but also for health care (Wang and Zennadi, 2021; Singh *et al.,* 2024).

There is currently no curative treatment for SCD (Telen, 2020). Pain management remains the cornerstone of acute VOC therapy, and treatment should be according to the generally accepted guidelines for cancer or palliative care pain management (Salinas and Thein, 2020). Management strategies include routine vaccinations, daily antibiotic prophylaxis from early

infancy until the spleen has been removed surgically and possibly lifelong, high fluid intake, and avoidance of dehydration (Brodsky and DeBaun, 2020). Increasing reticulocyte counts is a fundamental part of the body's ability to manage infection or tissue injury (Brandow and Liem, 2022). Hemoglobin (Hb) F induction with the drug hydroxyurea is an established therapy and will result in a reduced frequency of SCD complications and is without side effects when used at low to moderate doses (Pavan and Dos Santos, 2021). Hydroxyurea is second best effective in the presence of asthma and also helps alleviate the painful episodes caused by ACS (Pavan and Dos Santos, 2021). Counseling and education are needed when starting hydroxyurea, and patients should be well informed of the potential side effects at their appointments to avoid non-adherence to treatment (Pace *et al.*, 2021). Transition from child to adult care needs to be consciously and thoroughly planned, involving many of the team members as well as the parents as necessary and with thorough patient permission (Leonard *et al.*, 2020). A comprehensive care approach with a broad variety of health care personnel and medical specialists is fundamental in comprehensive and international evidence that early identification and treatment mean improved outcomes (Coetzee *et al.*, 2022).

4. Diagnosis and Management of Pediatric Oncologic Disorders

Early diagnosis and proper management are tools to cure most children, resulting in a 5-year overall survival of approximately 90% (Ecker *et al.,* 2022). Proper evaluation and staging are therefore vital to maintain the optimal approach to cure children while respecting the best possible quality of life that we strive for (Haas *et al.*, 2023). Realization of the importance of an early diagnosis has led to the formation of Pediatric Oncology as a separate discipline, now comprising almost 80 cooperative groups worldwide (González-Moles *et al.,* 2022). Because most tumors, in contrast to the spectrum of diseases in other disciplines, do not occur often, the diagnostic process is supported by computer-based referral systems and networks, and pathologists and radiologists with extensive experience in Pediatric Hemato-Oncology work closely together in histology, laboratory, and imaging facilities especially dedicated to children (Inaba and Pui, 2021). Based on standard operating procedures established by international agreements, histopathologists perform extensive immunohistochemical and molecular studies on tissue samples when needed (Ruppert *et al.,* 2023).

The patterns and range of pediatric tumors vary according to age (Haas and Borkhardt, 2022). Leukemias are by far the most common malignancies in childhood, with still rising incidences in children (Haas and Borkhardt, 2022). Boys are more frequently affected by leukemias (Zahnreich and Schmidberger, 2021). Brain tumors and lymphomas are the second most common group of pediatric tumors. Solid tumors differ from leukemias, where cure is mainly based on intensive chemotherapy, in that local solid tumor control, which is often facilitated by radiotherapy, is another cornerstone of nearly all treatment protocols (Greaves *et al.,* 2021). The range of drugs and their dosage and the integration of surgery and radiotherapy is disease-defined (Schmidt *et al.,* 2021). The organ-specific knowledge that is the other characteristic of a pediatric approach has to be met with the same intensity in adult populations (Marcotte *et al.,* 2021). Surgery remains in the best possible hands in children who need long infusions, sometimes combined in very young children with bone marrow or embryonic stem cell transplantations with a high risk of infectious complications (Hauer *et al.,* 2020). Management strategies are developed by international clinical trials, always with alternative arms and close monitoring of late side effects addressed in long-term follow-up programs. Preclinical research to develop further insights into the biology is an even more integral part of the disease-oriented approach in the ongoing international trials (Dushnicky *et al.,* 2020)

4.1. Leukemias

Leukemias account for roughly 30% of all childhood malignancies and continue to be the most common cancer diagnosis in the pediatric patient population (Zapata-Tarrés *et al.,* 2021). Childhood leukemia is primarily composed of two forms: acute lymphoblastic leukemia and acute myeloid leukemia (Zahnreich and Schmidberger, 2021). The diagnosis is largely based on bone marrow biopsy, determining morphological characteristics of abnormal cells and obtaining cytogenetic and molecular information (Dong *et al.*, 2020; Khatib and Mohamed, 2022). The presence of symptoms such as fever, pallor, easy bruising, or significant fatigue and/or anemia, however, may prompt evaluation for a possible worrisome etiology (Haas and Borkhardt, 2022). The minimal initial workup required includes complete blood count and differential, basic metabolic panel, and coagulation studies (Haas and Borkhardt, 2022). A possible contraindication to immediate bone marrow evaluation would be evidence of leukostasis, often necessitating emergent leukapheresis prior to therapy, which helps to decrease white blood cells by causing apoptosis (Haas and Borkhardt, 2022).

A diagnosis of leukemia is made when abnormal white blood cells make up at least 20% of circulating peripheral blasts or via a positive bone marrow (Hayashi *et al.,* 2024). The definition of acute myeloid leukemia in children includes three key components: 1) at least 20% bone marrow blasts, 2) evidence of a myeloid antigen on blasts or immunophenotypical evidence of myeloid maturation, and 3) at least 20% infiltration of leukemic cells in a bone marrow aspirate or in the biopsy (Ejaz *et al.,* 2023). The workup of a new diagnosis of acute myeloid leukemia should include a bone marrow aspiration and biopsy with at least 1 mL of bone marrow in an EDTA tube, to be sent for morphology, flow cytometry, cytogenetics, and

molecular studies (Temple *et al.,* 2023). Leukapheresis should be performed immediately if white cell counts are above 400. Treatment of pediatric acute myeloid leukemia is protocol-based; a multi-agent induction chemotherapy typically composed of anthracyclines and cytarabine is administered, and based upon risk stratification, additional chemotherapy with stem cell transplant may be necessary (Sultana *et al.,* 2023). Careful attention to and improvement of supportive care has also been critical in improving the cure rate of acute myeloid leukemia (Bani-Ahmad *et al.,* 2018; Chowdhury *et al.,* 2021). This may include antifungal therapy in the inpatient setting and the use of mesenchymal stem cells to regenerate gut mucosa damaged secondary to profound chemotherapy (Perusini *et al.,* 2024).

4.2. Brain Tumors

Brain neoplasms are the leading solid tumors in pediatric oncology, with infratentorial tumors being the most common (Thorbinson and Kilday, 2021). They account for over two-thirds of brain tumors in pediatric patients (Thorbinson and Kilday, 2021). The molecular biology of embryonal tumors has defined four distinct subtypes of medulloblastoma, with embryonal tumors with multilayered rosettes having the poorest outcomes (Trubicka *et al.,* 2022). More than 10 distinct molecular subtypes of ependymoma have contributed to the molecular disease classification of this type of tumor (Trubicka *et al.,* 2022). Gliomas present with distinct clinical manifestations depending on their location and histology (e.g., the most common glioma arising from the optic pathway – pilocytic astrocytoma – presents with visual and endocrine dysfunction) (Renzi *et al.,* 2020). Rare glial tumors, midline histone-mutant tumors, and high-grade gliomas present with a rapid onset of symptoms related to increased intracranial pressure and are therefore often diagnosed early (Mueller *et al.,* 2020).

Neuroimaging plays a major role in the diagnostic approach to brain neoplasms with dural or bony involvement, offering the ability to detect spread or invasion into surrounding structures (Stanić *et al.,* 2021). Surgical management plays a significant role in the treatment of children with brain tumors, and increasing evidence demonstrates that dedicated pediatric centers for the surgical treatment of children with brain tumors have better outcomes (Roach *et al.,* 2023). Neurosurgeons, therefore, need to preserve neurological structures and carefully weigh the benefits of a total extent of resection against the potential risk of damage caused by surgery (Roach *et al.,* 2023). To decrease tumor burden, children often receive adjuvant therapies, such as chemotherapy and focal radiation that aim to kill tumor cells (Foster *et al.,* 2021). Neurosurgery and adjuvant therapies can alter a developing child's brain microstructure, resulting in chronic comorbidities including cognitive impairment, vision and hormone dysfunction, motor impairments, and psychiatric and emotional challenges (Schmitz *et al.,* 2022). Collaborative and comprehensive neuro-oncology care, including rehabilitative services, can improve outcomes and quality of life for these patients with the help of a highly skilled team (Arocho-Quinones *et al.,* 2020). As the cost of care can be high and may exploit limited family resources, pediatric oncology professionals should offer options for financial and social support and review the latest research and protocols (Kazerooni *et al.,* 2024). Patients and families also appreciate opportunities to participate in clinical trials (Kazerooni *et al.,* 2024). With innovative treatment options currently available, as well as a promising horizon in treatment protocols for both newly diagnosed patients and those with recurrent disease, our goal in pediatric neuro-oncology is to increase survival rates and patient quality of life while also decreasing early and late toxicities (Shakir *et al.,* 2024).

4.3. Lymphomas

Lymphomas, including Hodgkin and non-Hodgkin lymphoma, account for about 10% of all childhood cancers (Johnston *et al.,* 2021). Non-Hodgkin lymphoma is the third most common malignancy in children, while Hodgkin lymphoma incidence peaks between 15 and 19 years in Europe. Progressive disseminated lymphomas are often associated with fever, night sweats, and body weight loss; the so-called B-symptoms are detected in more than 30% of the cases (Zahnreich and Schmidberger, 2021). As an advanced stage (III or IV), with clinical symptoms, has a poor prognosis, early diagnosis and appropriate therapy are critical (Akani *et al.,* 2021). Biopsy is mandatory for the tissue diagnosis of lymphoma (Miller *et al.,* 2020). Further information for diagnosis and staging is increasingly obtained from imaging procedures in pediatric oncology (Mussolin *et al.,* 2020; Alkhatib, 2021). Lymphomas are classified for predominant T or B cell imprint at presentation by immunophenotyping of their histological or bone marrow smears by reacting lymphocytes with lymphoma-subset-specific monoclonal antibodies (Miller *et al.,* 2020). The modern approach to lymphoma therapy, high-dose combination chemotherapy, and limited radiation therapy is an attempt to cure the majority of patients with minimal permanent long-term effects (Oeffinger *et al.,* 2021).

The choice of therapy depends on the subtypes of lymphomas according to classification. This testing is essential for therapy and to establish the prognosis of these tumors (Al-khatib *et al.,* 2017; Ehrhardt *et al.,* 2021). Attending children with lymphomas not only exhibits a singular pediatric case, but to a great extent presents a family case, which concerns the surroundings including the pediatric department (Kahn *et al.,* 2022). The prevention of violations during therapy in children with lymphomas results in the maintenance of their normal somatic and psychological functioning and reduced risk of family breakdown (Alkhatib, 2020b; Kahn *et al.,* 2022). The support given to medical staff to avoid decreased ability to help vital others is an

expression of professional ethics (Daw *et al.,* 2020). Patients suffering from tumors require medical help and support from their parents and hospital staff (Daw *et al.,*2020). With the present advances in diagnosing and therapeutic procedures, the cure rate for children with Hodgkin disease exceeds 80%, and it is 65-75% in non-Hodgkin cases (Reedijk *et al.,* 2020). More than 60% of the children who are suffering from non-Hodgkin lymphoma or disseminated lymphoblastic lymphomas can expect to be cured (Reedijk *et al.,* 2020). Such a high cure rate is achieved with a multidisciplinary team approach, focusing on appropriate diagnostic work-up, effective standardized therapeutic protocols, and decreasing the outcome of chemotherapy and radiotherapy by solving complications and controlling the symptoms (Shankar *et al.,* 2022). It is important not to underrate the role of socioeconomic elements, i.e., the education and profession of parents, including student care, in the hospital during the crucial period when treatment complications may pose a danger to life (Belsky *et al.,* 2023). The progress in therapeutics goes on continuously, revealing new therapeutic approaches in patients who relapse on standard high-dose combination chemotherapy (Belsky *et al.,* 2023). The repair of hematopoietic stem cells using autologous stem cell transplant and cellular immunity could play a role (Shankar *et al.,* 2022). New experimental studies are dealing with genes and therapy and the biological behavior of tumors (Kahn *et al.,* 2022). Primarily, it has been essential to involve parents in the treatment of their child and to educate them about the disease and side effects of the therapy (Belsky *et al.,* 2023).

5. Innovations in Pediatric Hematology and Oncology Research

New Insights in Pediatric Hematology and Oncology What's New in Pediatric Hematology/Oncology Research on Pediatric Hematology/Oncology is continuously expanding and changing (Thompson *et al.,* 2020). Genetic and Molecular Therapies: Developments in understanding genetic diagnoses will lead to more genetic and molecular therapies focused on the root cause of diseases such as bone marrow failure syndromes and other blood disorders (Sandweiss *et al.,* 2020). These new treatments will come with less immediate and long-term toxicities (Tran *et al.,* 2021). Diagnostics: Emerging technologies including liquid biopsies and omics captures will enable earlier and improved diagnostic resolution, and may serve as non-invasive tools for treatment monitoring (Sekhoacha *et al.,* 2022). Children's Mercy is developing personalized diagnostic reporting with Genomic Data Storage for use at diagnosis to prioritize hematologic malignancy treatments (Mueller *et al.,* 2021). Clinical Decision Support: Multi-dimensional data capturing is fueling algorithm development for improved predictive modeling, risk profiling, and support of long-term clinical care (Delgado-Martín and Medina, 2020; Zhang *et al.,* 2021; Olatunji *et al.,* 2024).

Clinical Trials and Contributions: Numerous clinical trials are leading to improved national and international guidelines for blood and marrow transplant patient care (Turner *et al.,* 2022). Immune therapies, specifically CAR T-cell therapies, and how children are cured of the malignancy will be new frontiers also (Yoshiji *et al.,* 2021). There is a focus on novel immune therapies and expanding blood and marrow transplant options in children with cancer as well as expanding research for all blood and marrow failure syndromes (Sedrak *et al.,* 2021). New Team Building: Teams of providers from different specialties continue to be built to care for complex patients and explore new research opportunities in the field (Malik and Hu, 2022). Patients at the Center: Families are at the center of all treatment plans and research activities (Grossberg *et al.,* 2020). They have opportunities to engage in the intentional, step-wise research agenda and share personal experiences to drive research that matters most to children and families living with hematologic and oncologic diseases (Wang *et al.,* 2020). Future Full of Possibilities: Hematology and Oncology bring hope and the potential for a cure for kids with complex blood diseases and children with cancer (Nogueira *et al.,* 2021; Cervantes *et al.,* 2023).

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