SUMMARY

Leukemia is the most common Childhood cancers; leukemia accounts for about one third of pediatric malignancies. Acute lymphoblastic leukemia (ALL) represents approximately 75% of all cases in children, and has a peak incidence at age of 4 years. Acute Myelogenous leukemia (AML) accounts for approximately 20% of leukemia, with a stable incidence from birth through age of 10 and increase slightly during the teenage years.

The cause of leukemia is unknown in the majority of patients. Several factors, however, associated with the development of leukemia. These factors are:

Environmental factors: Ionizing radiation and certain toxic chemical have a major role in development of leukemia.

Genetics factors: are presumed to play a significant role in the cause of acute leukemias. Evidence is based on several observations, including the association between various constitutional chromosomal abnormalities, the occurrence of familial leukemia, the high incidence in identical twins, and the demonstration of karyotypic abnormalities in leukemia cells.

Viral infection: The Epstein-Barr virus (EBV) has been linked to cases of endemic Burkitt's lymphoma and the L3 subtype of ALL.

Immunodeficiency: Several Immunodeficiency states have an associated increased risk for lymphoma and leukemia.

Leukemias have long been recognized to be morphologically heterogeneous. Recently have these observations been extended to a molecular genetic level. Multiple methods are available for characterizing leukemia these include standard morphologic

interpretation of specimens stained, in conjunction with cytochemistry, Karyotyping, Immunophenotyping and molecular genetics.

Beginning in 1976,the French-American-British (FAB) cooperative group proposed a classification system based primarily on morphologic and cytochemical features of the blast cells. ALL was classified into L1, L2& L3.AML was classified into M0 to M7.

Leukemia arises from the transformation of a hematopoietic cell, which gives rise to a clonal population of leukemic cells that eventually displace normal marrow elements and ultimately invade extramedullary tissues. A number of specific gene mutations that are thought to contribute to the pathogenesis of leukemia have now been identified.

The child with Leukemia may present with very few symptoms or, alternatively, the first signs of leukemia may be life threatening sepsis or hemorrhage. The presenting signs and symptoms usually reflect diminished production of red blood cells, granulocytes, and platelets, leading to anemia, infection, and hemorrhage.

The definitive diagnosis of leukemia is made by examination of the bone marrow aspirate. Wright-Giemsa and special histochemical stains of the aspirate provide a clear diagnosis in most patients.

In most cases, the bone marrow biopsy is hypercellular, with 30% to 100% blasts. The normal bone marrow contains less than 5% blast, a minimum of 25% Lymphoblasts on differential examination of the bone marrow aspirates is necessary for diagnosis of ALL. And more than 30% blasts for the diagnosis of AML

The morphology and histochemistry may fail to identify the type of acute leukemia in as many as 1 of every 5 patients. In these instances, the bone marrow cytogenetic and Immunophenotyping may help to differentiate between lymphoid and myeloid leukemia

Leukemias may be analyzed with a carefully selected panel of antibodies directed to both myeloid and lymphoid antigens in order to distinguish myeloid from lymphoid leukemias and to distinguish B cell from T cell ALL. Immunologic marker analysis has allowed for lineage assignment and often-maturational staging of the leukemias. And has offered some insight into the pathology of these diseases.

The identification of prognostic factors has become an essential element in the design and analysis of current therapeutic trials.

Prognostic characteristics of childhood leukemia include the initial leukocyte count, age at diagnosis, sex, race, cytogenetic, degree of organomegaly and lymphadenopathy, presence of a mediastinal mass, initial hemoglobin level. Initial platelet count, FAB morphologic classification, immunophenotype, expression of myeloid antigens on leukemic cells, serum immunoglobulin levels, CNS disease at diagnosis, the length of time to attainment of remission, Glucocorticoid receptor levels, and human Leukocyte antigen (HLA) type and nutritional status.

Extramedullary spread is a common features in leukemia especially ALL. Extramedullary disease is significant because it may cause morbidity at a localized site and because Extramedullary relapse frequently heralds a subsequent bone marrow relapse, presumably the result of "seeding" from the involved Extramedullary site to the bone marrow.

The goal of therapy in children with leukemia is to achieve a long-term remission while maintaining quality of life. Intensification of therapy along with improved supportive care has gradually improved the prognosis for children with leukemia.

The initial step required to prolong survival for patients with leukemia is to induce a complete remission. This is defined as the return of the marrow to a normal number of blasts (<5% blasts), return of normal peripheral blood counts, and resolution of signs of

extramedullary leukemic infiltration (e.g., Hepatosplenomegaly and lymphadenopathy).

After remission is achieved, the next objective is to prevent recurrence of leukemia. Several post-remission strategies have emerged in an effort to prevent relapse. These include consolidation or intensification chemotherapy, with or without maintenance, and marrow ablative therapy followed by allogeneic or autologous BMT.

The use of bone marrow transplantation as a therapeutic approach for patients with leukemia has increased in recent years. This approach, involves the administration of intensive cytoreductive therapy, usually employing total body irradiation and high-dose chemotherapy in doses lethal to normal bone marrow and subsequent hematopoietic "rescue" with intravenously infused bone marrow obtained from a compatible donor.