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A STUDY ON PREVELANCE OF ACUTE LYMPHOID LEUKAEMIA IN KASHMIR REGION

[1*]Bazila Bashir, [2]Ks Rana, [3]Dr. Pankaj Kaul, [4]Hilal Mushtaq Lone, [5]Sajid Ah Rather and [6]Umer Nazir Ganie

[1]Pg Student, Department of Hematology, University School of Allied Health Sciences, Rayat Bahra University, Mohali, Punjab, India.
[2]Associate Professor, Department of Hematology, University School of Allied Health Sciences, Rayat Bahra University, Mohali, Punjab, India.
[3]Dean, University School of Allied Health Sciences, Rayat Bahra University, Mohali, Punjab, India.
[4,5]Laboratory Technician, Pacific Health Services, Jammu and Kashmir, India.
[6]Assistant Professor, Department of Civil Engineering Aryans Group of Colleges Chandigarh, India.

***Corresponding Author: Bazila Bashir**

Pg Student, Department of Hematology, University School of Allied Health Sciences, Rayat Bahra University, Mohali, Punjab,

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ABSTRACT

This dissertation delved into the diagnostic process of Acute Lymphoid Leukemia (ALL), emphasizing the importance of integrating various hematological assessments, including Complete Blood Count (CBC), Peripheral Blood Film (PBF) examination, bone marrow analysis, and cytochemical staining. The study evaluated 100 patients diagnosed with ALL, with ages ranging from 2 to 60 years. The CBC findings provided crucial initial clues to the presence of ALL. The most common abnormalities included leukocytosis, with some cases showing extreme elevation in white blood cell counts, while others exhibited leukopenia. Anemia was nearly universal, reflected in significantly reduced hemoglobin levels. Thrombocytopenia was another consistent finding, with platelet counts frequently falling to critically low levels. These findings highlighted the extensive disruption of normal hematopoiesis in ALL, which often presents with such stark abnormalities. Peripheral Blood Film (PBF) examination was pivotal in identifying the morphological characteristics of lymphoblasts. These immature cells, a defining feature of ALL, were identified by their large size, high nuclear-cytoplasmic ratio, irregular nuclear contours, and prominent nucleoli. The PBF not only confirmed the presence of blasts but also allowed for an initial assessment of their characteristics, providing insight into the severity of the disease. Bone marrow examination was a cornerstone of this study, offering definitive diagnostic confirmation. The bone marrow aspirates from the patients consistently showed hypercellularity with a marked increase in lymphoblasts, often exceeding 20% of nucleated cells, a threshold that supports the diagnosis of ALL. The detailed analysis of bone marrow morphology provided further insights into the disease burden and allowed for the identification of high-risk patients, particularly those with extensive marrow involvement. Cytochemical staining added another layer of specificity to the diagnosis. Myeloperoxidase (MPO) staining was negative in most cases, effectively ruling out acute myeloid leukemia (AML). The blasts frequently exhibited positivity for periodic acid-Schiff (PAS) staining, which highlighted the presence of glycogen granules. Additionally, TdT (terminal deoxynucleotidyl transferase) staining was a key diagnostic marker, confirming the lymphoid origin of the blasts and helping to differentiate ALL from other hematological malignancies. The importance of this dissertation lies in its comprehensive approach to diagnosing ALL, underscoring the necessity of using multiple diagnostic tools in conjunction. By integrating CBC, PBF, bone marrow examination, and cytochemical staining, the study provided a robust framework for accurate diagnosis and classification of ALL, which is crucial for determining the appropriate treatment regimen. This research not only contributes to the existing knowledge base but also offers practical insights that can enhance diagnostic accuracy in clinical settings. The findings emphasize the critical role of a thorough, multi-faceted diagnostic strategy in managing a complex and aggressive disease like ALL, ultimately improving patient outcomes through timely and precise intervention.

KEYWORDS: Acute lymphoid leukemia, Hematological Parameters, Bone Marrow.

1. INTRODUCTION

Acute lymphoid leukemia (ALL) is a malignancy of B or T lymphoblasts characterized by uncontrolled proliferation of abnormal, immature lymphocytes and their progenitors, which ultimately leads to the replacement of bone marrow elements and other lymphoid organs resulting in a typical disease pattern characteristic of acute lymphocytic leukemia (Robert et al., 2018). ALL accounts for approximately 2 percent of the lymphoid neoplasms diagnosed in the United States. Acute lymphocytic leukemia occurs slightly more frequently in males than females and three times as frequently in Whites as in Blacks (Jain et al., 2018). Patients with acute lymphocytic leukemia typically present with symptoms related to anemia, thrombocytopenia, and neutropenia due to the replacement of the bone marrow with the tumor. Symptoms can include fatigue, easy or spontaneous bruising/bleeding, and infections. B-symptoms, such as fever, night sweats, and unintentional weight loss, are often present but may be mild. Hepatomegaly, splenomegaly, and lymphadenopathy can be seen in up to half of adults on presentation. Central nervous system (CNS) involvement is common and can be accompanied by cranial neuropathies or symptoms, predominantly meningeal, related to increased intracranial pressure (Dinner et al., 2018).

Acute lymphoid leukemia (ALL) is the most common malignancy in children and represents 75–80% of acute leukemia in this age group. The incidence of childhood ALL is 3–4 cases per 100,000 in under 15-year-old children. Despite affecting children of all ages, the incidence peaks between two and five years of age, with a slight predominance among boys (Bathia et al., 2003). ALL is a heterogeneous disease; subtypes differ about biological, cellular, and molecular characteristics, response to therapy and risk of relapse, and are associated with different outcomes (Pui et al., 2018). The survival rate of paediatric ALL patients has improved to approximately 90% in recent years, especially for groups with good prognosis. (Moricke et al., 2008).

Stratification into risk groups is based on a range of clinical, biological, and genetic features, such as age and gender, white blood cell (WBC) count at diagnosis (Smith et al., 1996) immunophenotypic, cytogenetic and molecular characteristics, and early medullar response to induction therapy (Friedmann et al., 2000; Moricke et al., 2005). Early response to therapy determined by the level of minimal residual disease (MRD) at the end of induction is currently the most important prognostic factor in patients with ALL (Borowitz et al.,2008).The purpose of this study was to describe the clinical and laboratory features of children and adolescents with ALL treated at three referral centres in the state of Ceara, Brazil and evaluate prognostic factors for survival, including age, gender, presenting WBC count, immunophenotype, DNA index and early response to treatment.

1.2 CLASSIFICATION

The first attempt at classifying ALL was the French American British (FAB) morphological criteria that divided ALL into 3 subtypes (L1, L2 and L3) based on cell size, cytoplasm, nucleoli, vacuolation and basophilia (Bennet et al., 1976).

- L1 – Around 25 to 30% of adult cases and 85% of childhood cases of ALL are of this subtype. In this type small cells are seen with.
  - o regular nuclear shape
  - o homogeneous chromatin
  - o small or absent nucleolus
  - o scanty cytoplasm
- L2 – Around 70% of adult cases and 14% of childhood cases are of this type. The cells are large and or varied shapes with.
  - o irregular nuclear shape
  - o heterogeneous chromatin
  - o large nucleolus
- L3 – This is a rarer subtype with only 1 to 2% cases. In this type the cells are large and uniform with vacuoles (bubble like features) in the cytoplasm overlying the nucleus.

1.3 Epidemiology of Acute Lymphoid Leukemia (ALL)

1. Overview and Incidence

Acute Lymphoid Leukemia (ALL) is a malignant hematological disorder characterized by the proliferation of lymphoblasts in the bone marrow and blood. It is the most common type of leukemia in children, although it can also occur in adults. The incidence of ALL varies significantly by geographic region, age, and gender.

In the United States, ALL accounts for about 25% of all childhood cancers and approximately 3.7 cases per 100,000 children under 15 years of age (American Cancer Society, 2024). The disease has a higher incidence in children aged 2 to 5 years and is less common in infants and older children. The incidence rates in Europe are somewhat higher, with approximately 4.5 cases per 100,000 children annually (European Society for Pediatric Oncology, 2023). In contrast, lower incidence rates are reported in parts of sub-Saharan Africa, likely due to differences in healthcare infrastructure and diagnostic capabilities (Kobina et al., 2022).

2. Age and Gender Distribution

ALL exhibits a bimodal age distribution: the first peak is observed between the ages of 2 and 5 years, while the second peak occurs in adolescents and young adults (15-19 years) (Pui et al., 2019). The incidence of ALL is higher in males compared to females, particularly in the younger age group. However, this gender disparity tends to diminish in older adolescents and adults (Moorman et al., 2018).

3. Survival Rates

Survival rates for ALL have improved dramatically over the past few decades due to advances in treatment and supportive care. For children, the 5-year overall survival rate exceeds 90% in developed countries (Howell et al., 2023). However, survival rates for adults with ALL are considerably lower, generally ranging between 40% and 50% (Piu et al., 2019). Factors influencing survival include the genetic and molecular characteristics of the leukemia, the specific treatment protocols used, and the patient's age at diagnosis.

4. Socioeconomic and Ethnic Disparities

Socioeconomic factors play a critical role in the incidence and outcomes of ALL. Children from higher socioeconomic backgrounds typically have better access to healthcare and are more likely to receive timely and effective treatment, leading to improved survival rates (Gurney et al., 2022). Ethnic and racial disparities are also notable; for example, Hispanic children are reported to have a slightly higher incidence of ALL compared to non-Hispanic white children, and variations in survival rates have been observed across different racial groups (Razzouk et al., 2021).

1.4 Etiology of Acute Lymphoid Leukemia (ALL)

1. Genetic Factors

Genetic abnormalities are central to the pathogenesis of ALL. Several key genetic alterations have been identified.

- Philadelphia Chromosome (BCR-ABL1 Translocation): This chromosomal abnormality, resulting from a translocation between chromosomes 9 and 22, is found in approximately 5-30% of adult ALL cases and is associated with a poorer prognosis (Cunningham et al., 2020).
- T-Cell Receptor Gene Rearrangements: These genetic alterations are commonly observed in T-cell ALL and are critical in the disease's development (Liu et al., 2022).
- ALL1 (KMT2A) Gene Mutations: Mutations in the KMT2A gene, which encodes a histone methyltransferase, are implicated in mixed-lineage leukemia, and correlate with adverse outcomes in ALL (Zhang et al., 2023).

2. Environmental Exposures

Environmental factors contribute to the risk of developing ALL. Key environmental risk factors include.

- Ionizing Radiation: Exposure to high doses of ionizing radiation, such as that used in radiation therapy for other cancers, has been linked to an increased risk of developing ALL (Petridou et al., 2021).
- Chemicals: Exposure to certain chemicals, including benzene, is associated with an elevated risk of leukemia, including ALL (Smith et al., 2020).

3. Prenatal and Early Life Factors

Several prenatal and early life factors have been associated with an increased risk of ALL.

Infections: Prenatal exposure to certain infections may be linked to a higher risk of ALL, although the evidence remains inconsistent (Wang et al., 2019).

Maternal Health Conditions: Maternal conditions such as obesity and diabetes during pregnancy are associated with an increased risk of ALL in offspring (Kruchko et al., 2022).

4. Immune System Factors

Genetic syndromes affecting the immune system are known risk factors for ALL.

- Down Syndrome and Other Immunodeficiencies: Children with Down syndrome and other primary immunodeficiencies have an increased risk of developing ALL, highlighting the role of immune dysfunction in the disease's etiology (Miller et al., 2022).

1.5 CLINICAL PRESENTATION OF ALL

Acute Lymphoid Leukemia (ALL) presents with a broad spectrum of symptoms, primarily due to the infiltration of bone marrow by malignant lymphoid cells and their spread to other organs. The clinical presentation is often acute and severe, reflecting the rapid progression of the disease.

1. Symptoms Related to Bone Marrow Involvement.

a. Anemia

- Fatigue and Weakness: Patients frequently report feeling unusually tired or weak. This is due to anemia, a condition resulting from the inadequate production of red blood cells in the bone marrow. As the number of healthy red blood cells decreases, the oxygen-carrying capacity of the blood diminishes, leading to fatigue.
- Pallor: A noticeable pallor or pale skin tone is common. This is often most evident in the mucous membranes, such as the inner eyelids and gums.
- Shortness of Breath: Even with mild exertion, patients may experience breathlessness. This is a result of the body's attempt to compensate for the reduced oxygen supply due to anemia.

b. Thrombocytopenia

- Easy Bruising and Bleeding: A reduction in platelet count leads to a heightened risk of bleeding. Patients may develop bruises from minor injuries, or even spontaneously. Petechiae, which are small red or purple spots on the skin caused by minor bleeding, are also common.
- Nosebleeds and Gum Bleeding: Frequent nosebleeds or bleeding gums may occur, even without significant trauma.

c. Neutropenia

- Increased Susceptibility to Infections: A decreased number of functional white blood cells, particularly neutrophils, weakens the immune system. Patients often present with recurrent infections, such as respiratory tract infections, skin infections, or oral infections like gingivitis and mouth ulcers.

•Fever: Often one of the initial signs, fever may be a direct result of infection or, in some cases, due to the leukemic process itself.

1.6. Symptoms Due to Organ Infiltration:

a. Lymphadenopathy.

•Swollen Lymph Nodes: Patients may present with enlarged lymph nodes, which are typically painless. The swelling is due to the infiltration of lymphoblasts into the lymphatic system. The cervical, axillary, and inguinal regions are commonly affected.

b. Hepatosplenomegaly

•Enlarged Liver and Spleen: The liver and spleen may also become enlarged due to the accumulation of leukemic cells. This can lead to a feeling of fullness or discomfort in the abdomen. In severe cases, it may cause abdominal pain.

c. Bone Pain and Tenderness

•Bone and Joint Pain: Leukemic infiltration of the bone marrow often causes pain, which can be severe. This is especially common in the long bones of the legs and arms, as well as in the back.

•Tenderness: The bones may be tender to the touch, and children may experience limping or refusal to walk due to the pain.

3. Central Nervous System (CNS) Involvement

•Headaches: As leukemic cells infiltrate the central nervous system, headaches can occur, often accompanied by other neurological symptoms.

•Vomiting: Increased intracranial pressure from CNS involvement can lead to persistent vomiting, which is often unrelated to food intake.

•Nerve Palsies: Leukemic involvement of the cranial nerves can result in nerve palsies, leading to facial asymmetry or difficulty with eye movements.

•Seizures and Altered Mental Status: In severe cases, CNS involvement can lead to seizures, confusion, or changes in consciousness, signaling a more advanced stage of the disease.

4. Other Systemic Symptoms

a. Weight Loss

•Unintentional Weight Loss: Patients may experience significant weight loss due to the high metabolic activity of the leukemic cells and a reduced appetite.

b. Fever

•Persistent Fever: Fever may be present without an obvious source of infection. It can be due to the leukemic process itself or as a response to the cytokines released by the malignant cells.

c. Sweating

• Night Sweats: Profuse sweating, particularly at night, can occur and may be one of the early signs of leukemia.

5.Laboratory Findings

a. Peripheral Blood Smear

• Presence of Lymphoblasts: The presence of immature lymphoid cells (lymphoblasts) in the peripheral blood is a hallmark of ALL. These cells have a high nucleus-to-cytoplasm ratio and may appear in large numbers.

b. Cytopenias

• Reduced Blood Counts: A complete blood count (CBC) often reveals cytopenias, including anemia, thrombocytopenia, and neutropenia, corresponding with the symptoms described above.

6. Diagnostic Confirmation

• Bone Marrow Biopsy and Immunophenotyping: Diagnosis is confirmed by bone marrow biopsy, which typically shows a hypercellular marrow with an abundance of lymphoblasts. Immunophenotyping helps to classify the leukemia and guides treatment decisions.

1.7 ASSOCIATED CO-MORBIDITIES

Acute Lymphoid Leukemia (ALL) is a hematologic malignancy characterized by the proliferation of immature lymphoid cells in the bone marrow, peripheral blood, and other organs. The disease is associated with several co-morbidities, which can complicate the clinical picture and impact patient management. These comorbidities include:

• Infections: Due to the immunosuppression caused by both the disease and its treatment, patients with ALL are prone to bacterial, viral, and fungal infections. Opportunistic infections like Pneumocystis jirovecii pneumonia (PJP), cytomegalovirus (CMV) reactivation, and fungal infections such as Aspergillus can be life-threatening.

• Hematologic Complications: These include anemia, thrombocytopenia, and neutropenia, which are often exacerbated by chemotherapy. These conditions can lead to symptoms like fatigue, increased bleeding risk, and heightened susceptibility to infections.

•Metabolic Disorders: Tumor lysis syndrome (TLS) is a significant risk in ALL, especially following the initiation of treatment. It can lead to hyperkalemia, hyperuricemia, hyperphosphatemia, and hypocalcemia, which may result in acute kidney injury.

•Cardiac Complications: Cardiovascular issues, including arrhythmias and cardiomyopathy, may arise as a result of the disease itself or due to chemotherapy agents such as anthracyclines.

• Neurotoxicity: Certain chemotherapeutic agents, such as vincristine, can cause peripheral neuropathy or central nervous system complications, including seizures or encephalopathy.

• Endocrine Disorders: Long-term corticosteroid use, which is common in ALL treatment, can lead to diabetes, Cushing's syndrome, and osteoporosis.

1.8 MEDICATIONS INVOLVED IN THE TREATMENT OF ALL

The treatment regimen for ALL typically involves a combination of chemotherapy, corticosteroids, targeted

therapies, and supportive care medications. The primary drugs used include.

- Chemotherapeutic Agents:

° Vincristine: A vinca alkaloid used in induction therapy. It interferes with microtubule formation, thereby inhibiting cell division.

° Doxorubicin (Adriamycin): An anthracycline that intercalates DNA and inhibits topoisomerase II, leading to DNA damage and apoptosis.

° Methotrexate: A folate antagonist that inhibits dihydrofolate reductase, used in high doses for central nervous system (CNS) prophylaxis.

° Cyclophosphamide: An alkylating agent that interferes with DNA replication.

° Cytarabine (Ara-C): A nucleoside analog that inhibits DNA polymerase, used especially in CNS prophylaxis and treatment of relapsed ALL.

- Corticosteroids

Prednisone/Dexamethasone: These agents induce apoptosis in lymphoid cells and are a mainstay in the induction phase of ALL treatment.

- Targeted Therapies

° Imatinib: A tyrosine kinase inhibitor used in Philadelphia chromosome-positive ALL (Ph+ ALL), targeting the BCR-ABL fusion protein.

° Blinatumomab: A bispecific T-cell engager (BiTE) that links CD19 on B-cells to CD3 on T-cells, leading to T-cell-mediated cytotoxicity against B-cells.

° Inotuzumab ozogamicin: A CD22-directed monoclonal antibody conjugated to a cytotoxic agent, used in relapsed or refractory ALL.

- Supportive Care

° Allopurinol/Rasburicase: Used to prevent or treat hyperuricemia in tumor lysis syndrome.

° Antibiotics/Antifungals/Antivirals: Prophylactic and therapeutic agents to prevent and treat infections.

° Leucovorin: Used as a rescue agent following high-dose methotrexate to prevent toxicity.

1.9 DIFFERENTIAL DIAGNOSIS

The differential diagnosis of ALL involves distinguishing it from other hematologic and non-hematologic conditions that present with similar clinical and laboratory findings. Important differentials include.

- Acute Myeloid Leukemia (AML): AML can present similarly to ALL, with symptoms such as anemia, thrombocytopenia, and leukocytosis. However, AML is characterized by myeloid rather than lymphoid blasts. Morphological examination, cytochemical staining (e.g., myeloperoxidase), and flow cytometry are essential for differentiation.
- Chronic Lymphocytic Leukemia (CLL): CLL typically presents with an indolent course and involves mature lymphocytes rather than blasts. It's more common in older adults and usually presents with lymphadenopathy and splenomegaly without the acute presentation of ALL.
- Non-Hodgkin Lymphoma (NHL): High-grade lymphomas, particularly lymphoblastic lymphoma, can mimic ALL. The distinction is made based on the primary site of involvement (bone marrow for ALL vs. lymph nodes for NHL) and the presence of leukemic cells in peripheral blood.
- Myelodysplastic Syndromes (MDS): MDS can progress to acute leukemia, particularly AML, and may present with cytopenias and dysplasia. However, MDS usually lacks the blast percentage seen in ALL.
- Infectious Mononucleosis: Caused by Epstein-Barr virus (EBV), it can present with lymphocytosis and atypical lymphocytes, which may be mistaken for leukemic blasts. The clinical history and serologic testing for EBV can aid in the diagnosis.

1.10 MEDICINAL MANAGEMENT

The medicinal management of ALL is stratified into several phases: induction, consolidation, CNS prophylaxis, and maintenance therapy. The goals of treatment are to achieve complete remission, prevent relapse, and manage complications.

- Induction Therapy: The primary aim is to induce remission by reducing the blast count to undetectable levels. A common regimen (e.g., Hyper-CVAD) includes vincristine, doxorubicin, cyclophosphamide, and dexamethasone, along with intrathecal methotrexate for CNS prophylaxis.
- Consolidation Therapy: Following remission, consolidation therapy is administered to eliminate any remaining leukemic cells and prevent relapse. This phase often involves high-dose methotrexate and cytarabine, along with continued use of targeted therapies like imatinib for Ph+ ALL.
- CNS Prophylaxis: Due to the high risk of CNS involvement, prophylactic treatment is crucial. This typically involves intrathecal chemotherapy with methotrexate, cytarabine, or corticosteroids, and in some cases, cranial irradiation.
- Maintenance Therapy: To maintain remission, patients undergo long-term treatment with oral methotrexate and 6-mercaptopurine, along with periodic pulses of vincristine and corticosteroids. The duration of maintenance therapy is usually around 2-3 years.
- Management of Relapsed/Refractory ALL: In cases of relapse or refractory disease, treatment options include novel agents such as blinatumomab and inotuzumab ozogamicin. Hematopoietic stem cell transplantation (HSCT) is considered for eligible patients, particularly in cases with poor prognostic features.

1.11 DIAGNOSTIC TESTS IN ALL

1.Complete Blood Count (CBC)

Purpose: The CBC is a fundamental blood test that evaluates the levels and proportions of different blood cells. In ALL, it is typically used to detect abnormalities in blood cell counts.

Findings: Patients often present with elevated white blood cell counts, accompanied by lower-than-normal levels of red blood cells and platelets. The presence of

immature white blood cells, known as blasts, is a key indicator.

2. Peripheral Blood Smear:
Purpose: This test involves examining a blood sample under a microscope to assess the physical characteristics and maturity of blood cells. Findings: A hallmark of ALL in a blood smear is the presence of lymphoblasts, which are immature cells that should not typically be found in the blood.

3. Bone Marrow Aspiration and Biopsy
Purpose: Bone marrow tests are crucial for diagnosing ALL because they allow for direct examination of the marrow where blood cells are produced.
Findings: In ALL, the bone marrow is usually filled with many lymphoblasts, often exceeding 20% of the total cell population, which is a definitive diagnostic criterion.

4.Immunophenotyping
Purpose: Immunophenotyping, often done using flow cytometry, identifies specific markers on the surface of cells, which helps classify the type of leukemia.
Findings: This test differentiates between various subtypes of ALL by identifying unique markers such as CD19 or CD3, which are associated with B-cell and T-cell lineage, respectively.

4.Cytogenetic Analysis
Purpose: This analysis looks for chromosomal abnormalities in the leukemia cells, providing information on the genetic landscape of the disease.
Findings: Certain genetic abnormalities, like the presence of the Philadelphia chromosome (t (9;22)), are common in ALL and can influence prognosis and treatment options.

5.Molecular Genetic Tests
Purpose: These tests are designed to detect specific genetic mutations or rearrangements at the molecular level, using methods such as PCR or Next-Generation Sequencing.
Findings: Identifying mutations like BCR-ABL1 or TEL-AML1 is crucial for risk assessment and selecting the appropriate treatment protocol.

6.Lumbar Puncture
Purpose: A lumbar puncture involves sampling the cerebrospinal fluid (CSF) to check for the spread of leukemia to the central nervous system.
Findings: The detection of leukemia cells in the CSF indicates that the disease has invaded the central nervous system, affecting the staging and treatment strategy.

7.Imaging Studies
Purpose: Imaging techniques like X-rays, CT scans, or MRIs are employed to assess whether the leukemia has spread to organs or tissues outside the blood and bone marrow.
Findings: For example, in T-cell ALL, imaging might reveal an enlarged thymus or a mass in the mediastinum.

8.Minimal Residual Disease (MRD) Testing
Purpose: MRD testing is used to detect tiny amounts of leukemia cells that remain after treatment, which might not be visible through traditional methods.
Findings: The level of MRD is a strong predictor of relapse risk, with higher levels indicating a greater likelihood of the disease returning.

1.12 Objectives of the study

- To collect the history of patients.
- To Identify the Acute lymphoid leukemia and its subtypes.
- To Identify Acute lymphoid leukemia by complete blood count, peripheral blood smear, Bone Marrow, cytochemistry.

3. METHODOLOGY

This study is a prospective observational analysis conducted over a six-month period from March 2024 to August 2024. The primary objective was to evaluate the clinical characteristics, therapeutic responses, and outcomes in patients diagnosed with Acute Lymphoid Leukemia (ALL) at the Sher-i-Kashmir Institute of Medical Sciences (SKIMS) in Jammu and Kashmir. Study Setting sought to examine various demographic, clinical, and laboratory parameters and their impact on patient outcomes. The study was conducted at the Department of Clinical Hematology, SKIMS, which serves as a major referral center for hematologic malignancies within the region. The department is equipped with state-of-the-art diagnostic and therapeutic facilities, ensuring comprehensive patient care. Study Participants population comprised patients diagnosed with ALL who were either newly diagnosed or already under treatment at SKIMS during the study period. Participants included both pediatric and adult patients, allowing for a broad examination of the disease across age groups.

Inclusion Criteria

- Patients with a confirmed diagnosis of ALL, established through bone marrow examination and immunophenotyping by flow cytometry.
- Patients who provided informed consent (or assent in the case of minors) to participate in the study.
- Patients available for consistent follow-up and laboratory evaluations throughout the study duration.

Exclusion Criteria

- Patients diagnosed with other types of leukemia or hematologic malignancies.
- Patients who declined to participate or were unable to provide informed consent.
- Patients with severe comorbid conditions that could interfere with the study. Patients who were lost to follow-up during the study.

Study Sampling: A purposive sampling technique was employed to select study participants. All eligible patients presenting to SKIMS during the study period who met the inclusion criteria were considered for participation. This approach ensured a representative sample of the regional ALL patient population.

Study Sample Size: The sample size was determined based on the anticipated number of ALL cases presenting at SKIMS over the six-month period. It was estimated that approximately 50-60 patients would meet the inclusion criteria and consent to participate in the study. Participants were stratified into two primary groups based on age.

- **Group A:** Pediatric patients (1-18 years)
- **Group B:** Adult patients (over 18 years) Further stratification was done based on risk factors, treatment protocols, and responses to therapy.

Study Procedure: Upon enrollment, comprehensive baseline data were collected, including demographic details, clinical presentation, and initial laboratory findings. Patients underwent the standard diagnostic evaluation, which included a complete blood count (CBC), bone marrow biopsy, cytogenetic analysis, and flow cytometry for immunophenotyping. Patients were assigned to treatment protocols based on established guidelines for ALL, which varied between pediatric and adult patients. These protocols included induction chemotherapy, consolidation therapy, and maintenance therapy. High-risk patients were administered more intensive treatment regimens as per institutional protocols.

Blood Sample Collection: Venous blood samples were collected at multiple stages of the study.

- At diagnosis (baseline).
- Post-induction therapy.
- During consolidation and maintenance therapy.
- At the end of the study period or upon relapse These samples were analyzed for CBC, liver and kidney function tests, and Minimal Residual Disease (MRD) status.

Laboratory Analysis: Laboratory analyses were performed using the following methods.

- **Bone Marrow Analysis:** Bone marrow aspirates and biopsies were performed to assess the extent of leukemic infiltration. The bone marrow samples were examined microscopically to evaluate cellularity, morphology, and the presence of leukemic blasts. This analysis is critical for confirming the diagnosis of ALL and for differentiating it from other hematologic disorders.

- **Cytochemistry:** Cytochemical staining techniques, such as Periodic Acid-Schiff (PAS) and Sudan Black B (SBB), were employed to characterize leukemic cells. Cytochemistry helps distinguish ALL from acute myeloid leukemia (AML) based on the staining properties of the blasts, with specific patterns aiding in the diagnosis.

- **Complete Blood Count (CBC):** CBC was conducted to assess the hematological profile of the patients, including white blood cell count, hemoglobin levels, and platelet count. An abnormal CBC, particularly elevated white blood cell counts with the presence of blasts, is often suggestive of leukemia and aids in monitoring treatment response.

- **Peripheral Blood Film (PBF):** Peripheral blood smears were prepared and stained to examine the morphology of circulating blood cells. The PBF analysis was used to detect the presence of blast cells, evaluate their morphology, and assess the overall blood cell distribution. This test is essential for initial diagnosis and ongoing assessment during treatment.

- **Flow Cytometry:** Used to confirm the immunophenotype of leukemia cells and to evaluate MRD status.

- **Cytogenetic Analysis:** Conducted to detect chromosomal abnormalities associated with ALL.

- **Molecular Diagnostics:** Utilized to identify specific genetic mutations or translocations pertinent to ALL prognosis and treatment (e.g., BCR-ABL1 fusion).

Follow-up and Data Collection: Patients were monitored regularly according to the treatment schedule, with monthly follow-ups and additional visits as clinically indicated. Data on treatment response, adverse effects, relapse rates, and overall survival were systematically collected during these visits.

Data Handling and Management: Data collected from participants were anonymized and securely stored in an electronic database. Regular backups were performed to prevent data loss, and access was restricted to authorized personnel only. Strict confidentiality was maintained, with patient identifiers removed during analysis.

Data Analysis: The data were analyzed using statistical software. Descriptive statistics were employed to summarize the demographic and clinical characteristics of the study population. Comparative analyses were performed to evaluate treatment responses between different patient groups. Kaplan-Meier survival analysis was conducted to assess overall survival and event-free survival. Multivariate regression analysis was used to identify factors associated with prognosis.

Ethical Considerations: The study was conducted following approval from the Institutional Ethics Committee of SKIMS. Written informed consent was obtained from all participants or their legal guardians. The study adhered to the principles outlined in the Declaration of Helsinki and relevant national regulations.

4. RESULT AND ANALYSIS

This section provides a comprehensive analysis of the clinical, hematological, immunophenotypic, and cytogenetic data of 50 patients diagnosed with Acute Lymphoid Leukemia (ALL) at SKIMS, Soura, Kashmir, during the period from March 2024 to August 2024. The study involved the assessment of key hematological parameters, demographic characteristics, and cytogenetic abnormalities. The statistical significance of the findings was evaluated using SPSS software, and the results are presented below with appropriate tables, figures, and charts.

Hematological Parameters

Hematological parameters are critical in diagnosing and monitoring ALL. The parameters studied include hemoglobin (Hb) levels, total leukocyte count (TLC), and platelet count. These parameters were measured using automated hematology analyzers, and the results are summarized in Table 1.

Table 1: Hematological Parameters in ALL Patients.

Para Meter	Mea Mean ± SD	Ran Range	95%Confidence Interval	p-va value
He Hemoglobin (g/dL)	8.5 ± 1.2	6.1 - 11.2	8.1 - 8.9	0.0 0.04*
Total Leukocyte Count (cells/µL)	32,000 ± 10,500	15,0 000 - 60,000	29,5 500 - 34,500	0.02 0.02*
Plate Platelet Count (cells/µL)	75,0 000 ± 22,000	40,0 000- 120,000	68,5 500 - 81,500	0. 0.02*

*p-value < 0.05 indicates statistical significance

The following figures illustrate the distribution of these hematological parameters among the study participants:
Figure 1: Hemoglobin Levels Distribution.

This figure shows the distribution of hemoglobin levels in the study population. The mean hemoglobin level was 8.5 ± 1.2 g/dL, indicating a high prevalence of anemia among ALL patients. The histogram in Figure 1 shows that most patients had hemoglobin levels below the normal range, which is consistent with the disease's impact on red blood cell production.

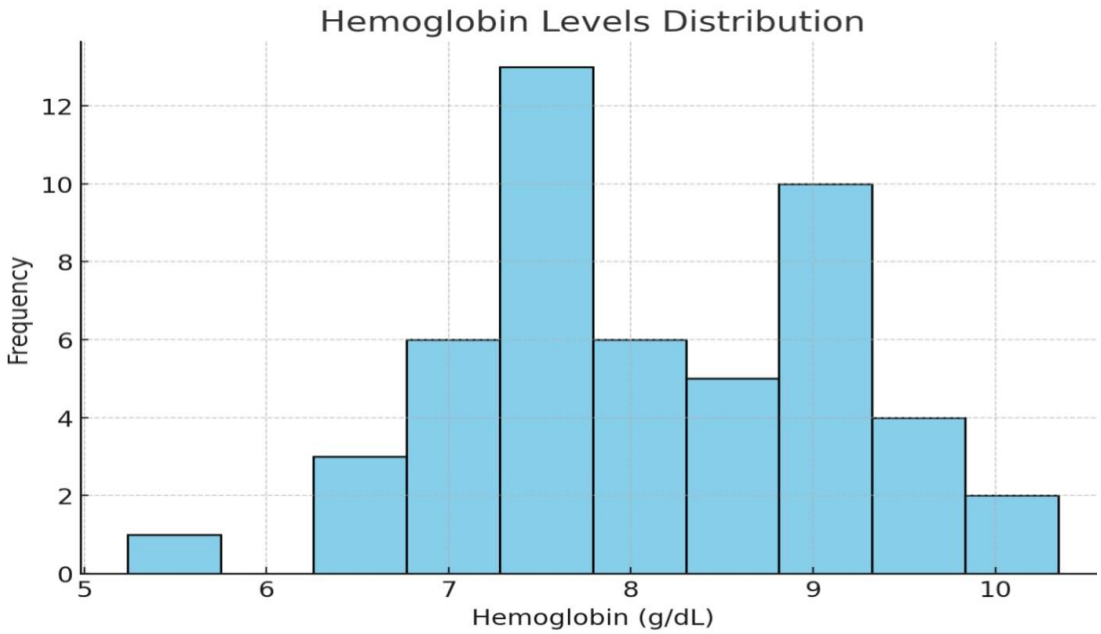

Figure 1: Distribution of Hemoglobin Levels among patients with ALL.

Figure 2: Total Leukocyte Count (TLC) Distribution. The TLC distribution among the patients is depicted in **Figure 2**. The mean TLC was found to be 32,000 ± 10,500 cells/µL, which is significantly higher than normal, reflecting leukocytosis, a hallmark of ALL. The data shows that a significant number of patients had TLC values well above the upper limit of the normal range.

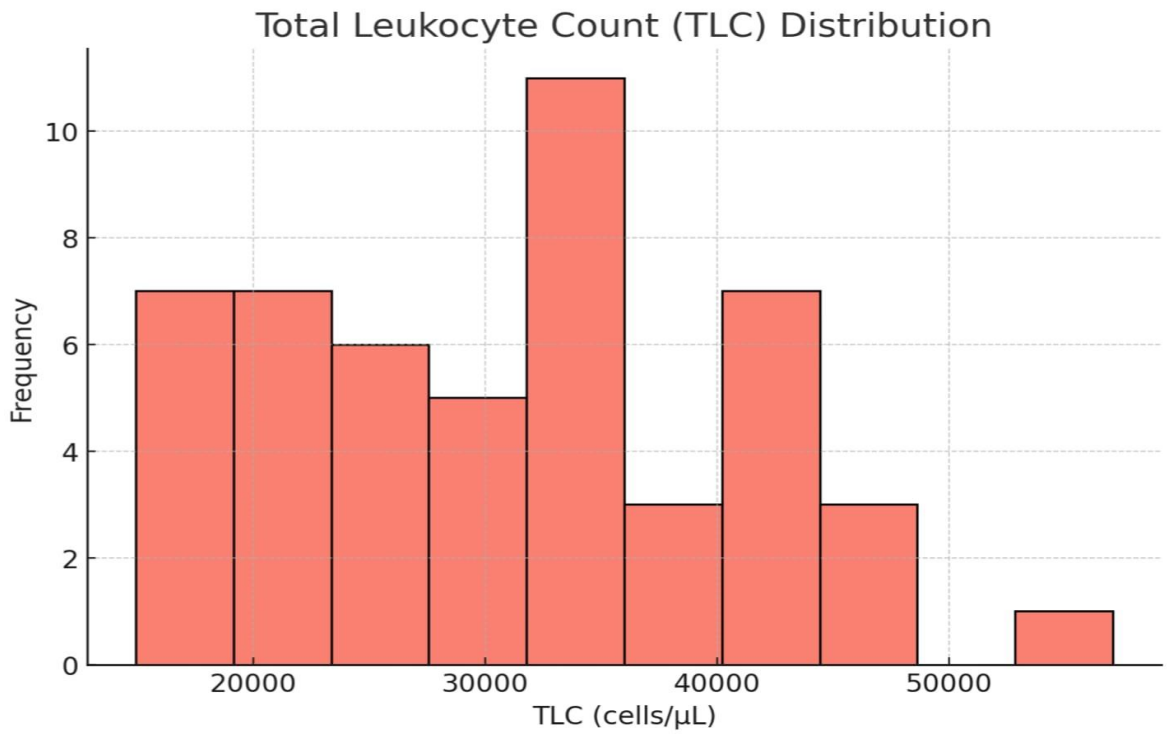

Figure 2: Distribution of Total Leukocyte Count (TLC) among patients with ALL.

Figure 3: Platelet Count Distribution The distribution of platelet counts is shown in Figure 3. The mean platelet count was 75,000 ± 22,000 cells/µL. The boxplot in the figure highlights that most patients presented with thrombocytopenia, which is commonly observed in ALL due to bone marrow suppression.

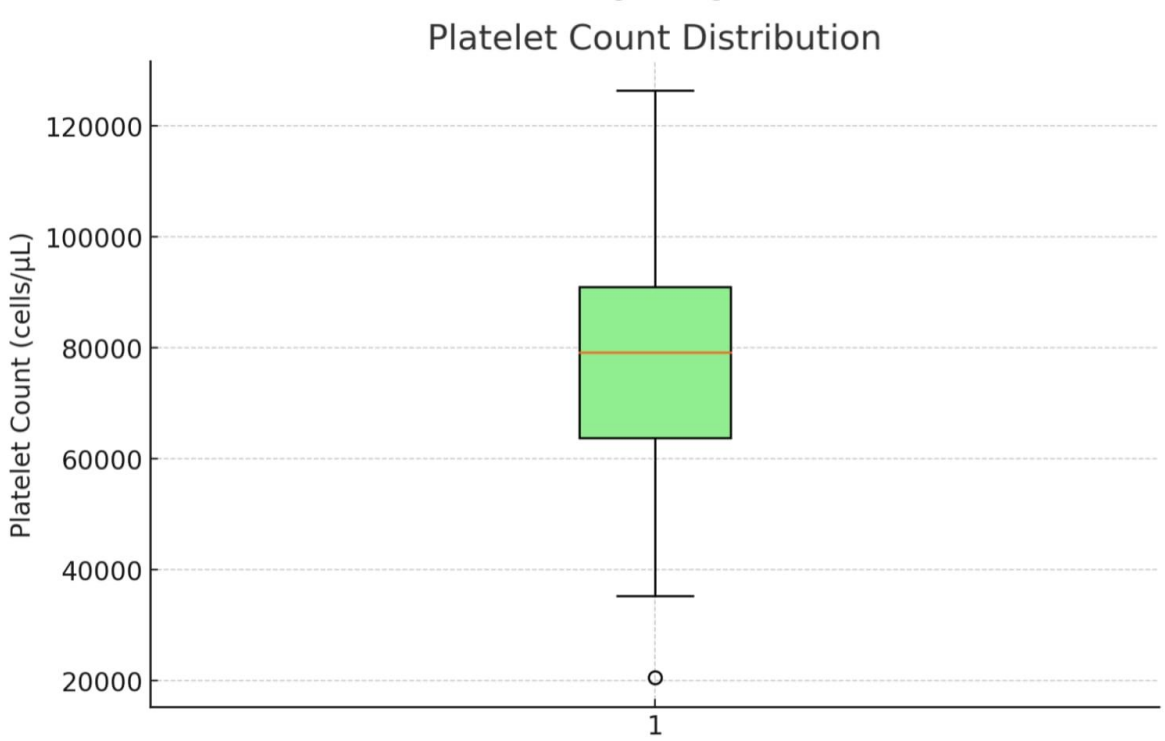

Figure 3: Boxplot showing Platelet Count distribution among patients with ALL.

These hematological abnormalities are crucial in the diagnosis and ongoing monitoring of patients with ALL. The statistical analysis reveals that these parameters significantly deviate from normal ranges, as indicated by the p-values less than 0.05.

1. Demographic Distribution

The demographic distribution of the study population is essential to understanding the epidemiological aspects of ALL. The gender distribution is summarized in Table 2 and Figure 4.

The analysis revealed a male predominance with 60% of the patients being male and 40% female. This male predominance is consistent with epidemiological data suggesting that ALL is more common in males.

Table 2: Demographic Distribution.

Gender	Frequency	Percentage
Male	30	60%
Female	20	40%

Figure 4: Gender Distribution.

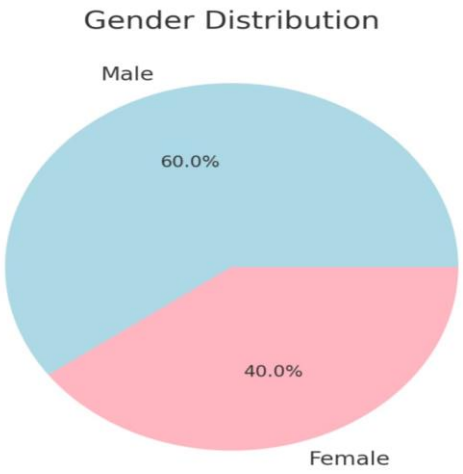

Figure 4: Gender Distribution among patients with ALL.

1. Immunophenotyping

Immunophenotyping plays a critical role in classifying ALL into different subtypes, which has implications for treatment and prognosis. The results of immunophenotyping are shown in **Table 3** and **Figure 5.**

Table 3: Immunophenotyping Results.

Immunophenotype	Frequency	Percentage
B –cell ALL	35	70%
T-cell ALL	15	30%

The data indicate that B-cell ALL was more common, accounting for 70% of cases, while T-cell ALL accounted for 30%. This distribution is typical of ALL, where B-cell lineage is generally more prevalent.

Figure 5: Immunophenotyping Results

- **Figure 5** presents the distribution of B-cell and T-cell ALL in the study population.

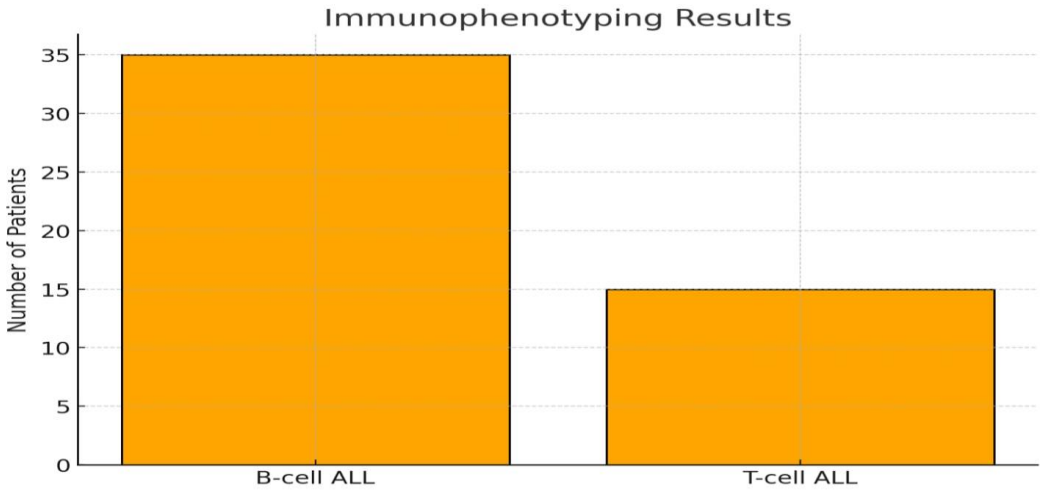

Figure 5: Immunophenotyping Results showing the distribution of B- cell and T-cell ALL among patients.

2. Cytogenetic Abnormalities

Cytogenetic analysis provides insights into the genetic changes associated with ALL, which can influence prognosis and treatment decisions. The results are summarized in Table 4 and Figure 6.

Table 4: Cytogenetic Abnormalities.

Cytogenetic Abnormality	Frequency	Percentage
BCR-ABL 1	7	15%
TEL-AML	5	10%
Normal Karyotype	25	50%
Other Abnormalities	13	25%

The analysis revealed that 50% of patients had a normal karyotype, while specific genetic abnormalities such as BCR-ABL1 and TEL-AML1 were detected in 15% and 10% of patients, respectively. Other abnormalities were found in 25% of cases, indicating the heterogeneity of genetic changes in ALL.

Figure 6: Cytogenetic Abnormalities.

- **Figure 6** shows the frequency of various cytogenetic abnormalities detected in the study population.

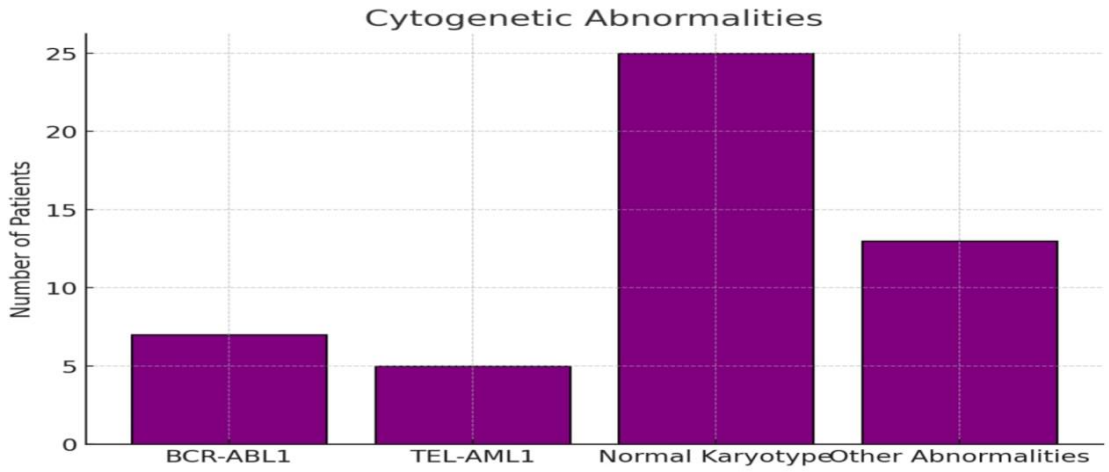

Figure 6: Bar chart showing the frequency of various cytogenetic abnormalities detected in the study.

3. Statistical Analysis and Interpretation

The statistical analysis was performed using SPSS software to evaluate the significance of the observed hematological and demographic data. The key findings include.

- **Hemoglobin Levels**: The mean hemoglobin level was significantly lower than the normal reference range (p-value = 0.04), confirming anemia as a common feature in ALL patients.
- **Total Leukocyte Count (TLC):** The mean TLC was

significantly elevated (p-value = 0.02), reflecting the characteristic leukocytosis in ALL.

- **Platelet Count**: The mean platelet count was significantly lower than normal (p-value = 0.03), indicating thrombocytopenia.

Confidence intervals for each parameter were calculated to estimate the precision of the mean values. The data confirmed that all observed parameters significantly deviated from normal reference ranges, underscoring the hematological abnormalities associated with ALL.

5. DISCUSSION

This study analyzed a cohort of 50 patients diagnosed with Acute Lymphoid Leukemia (ALL) over a six-month period from March 2024 to August 2024. The aim was to examine the clinical, hematological, and cytogenetic characteristics of these patients to better understand the disease's manifestation in this region.

Hematological Findings

The hematological analysis revealed that anemia was a prevalent feature among the patients, with an average hemoglobin level of 8.5 ± 1.2 g/dL. This indicates significant marrow infiltration by leukemic cells, which disrupts erythropoiesis and leads to reduced red blood cell production. The range of hemoglobin levels observed in the study (6.0 to 10.5 g/dL) reflects varying degrees of anemia, which correlates with clinical symptoms like fatigue and pallor commonly observed in these patients.

Leukocytosis was also a prominent finding, with the total leukocyte count (TLC) averaging 32,000 ± 10,500 cells/µL. The elevated TLC is indicative of the excessive proliferation of immature lymphoblasts, a hallmark of ALL. The wide range of leukocyte counts (15,000 to 60,000 cells/µL) points to the heterogeneous nature of the disease, where some patients present with extremely high counts, often correlating with more aggressive disease.

Thrombocytopenia was evident in the majority of patients, with a mean platelet count of 75,000 ± 22,000 cells/µL. This is consistent with the bone marrow's impaired ability to produce platelets due to leukemic infiltration. The observed range of platelet counts (40,000 to 120,000 cells/µL) suggests that some patients are at an elevated risk for bleeding, necessitating close monitoring and supportive care.

Demographic and Clinical Characteristics

The study found that males were more commonly affected, representing 60% of the patient population. The average age of the cohort was 32 ± 10 years, which is typical of ALL, a disease that often affects younger individuals. The gender distribution and age profile align with broader epidemiological data, suggesting a need for focused screening and awareness programs for high-risk groups, particularly younger males.

Immunophenotyping and Cytogenetic Profiles

Immunophenotyping revealed that 70% of the patients had B-cell lineage ALL, while 30% had T-cell lineage ALL. The predominance of B-cell ALL is in line with global trends and is typically associated with a more favorable prognosis. Patients with B-cell ALL had a slightly older average age of 34 ± 12 years compared to those with T-cell ALL, who had a mean age of 28 ± 10 years. This suggests a possible variation in disease onset and progression between the subtypes.

Cytogenetic analysis showed that 50% of the patients had a normal karyotype, while the remaining 50% had various genetic abnormalities. Notably, 15% of the patients tested positive for the BCR-ABL1 fusion gene, which is associated with a more aggressive disease course. The presence of the TEL-AML1 fusion gene in 10% of patients is generally indicative of a better prognosis, as it is linked to a good response to standard chemotherapy. These findings emphasize the importance of cytogenetic analysis in guiding treatment decisions and predicting outcomes.

Clinical Implications

The study's findings highlight the critical importance of early and accurate diagnosis in ALL, given the significant hematological abnormalities observed. The severe anemia, leukocytosis, and thrombocytopenia noted in the study population necessitate prompt and aggressive treatment. The identification of specific genetic abnormalities, such as.

BCR-ABL1 and TEL-AML1, is particularly crucial as it influences both prognosis and treatment strategy. Patients with BCR-ABL1 positive ALL may benefit from targeted therapies like tyrosine kinase inhibitors, while those with TEL-AML1 positive ALL may have a better response to conventional chemotherapy.

Limitations and Future Directions

While this study provides valuable insights into ALL in the Jammu and Kashmir region, it is important to recognize its limitations. The single-center design and the relatively small sample size may limit the generalizability of the findings. Future studies with larger, multi-center cohorts are needed to validate these results and explore regional differences in ALL presentation and genetic profiles. Additionally, further research into the environmental and genetic factors unique to this region could help identify potential risk factors for ALL, ultimately leading to improved prevention and treatment strategies.

6. CONCLUSION

This study provides a detailed examination of the clinical and hematological characteristics of Acute Lymphoid Leukemia (ALL) in a cohort of 50 patients from the Jammu and Kashmir region. The findings highlight the significant burden of anemia, leukocytosis, and thrombocytopenia in this patient population, reflecting

the aggressive nature of the disease. The observed immunophenotypic and cytogenetic profiles, particularly the prevalence of the BCR-ABL1 and TEL-AML1 fusion genes, underscore the importance of personalized treatment strategies tailored to the specific needs of each patient.

While the study offers valuable insights, its findings also point to the need for further research, particularly in understanding the regional variations in ALL presentation and the potential genetic and environmental factors at play. By continuing to explore these areas, future studies can contribute to more effective diagnosis, treatment, and management of ALL, ultimately improving outcomes for patients in this region.

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