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A REVIEW ARTICLE ON ACUTE MYLOID LEUKEMIA A REVIEW OF DIAGNOSIS AND TREATMENT

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ABSTRACT

Acute Myeloid Leukemia (AML) is a fast-growing blood cancer that starts in the bone marrow when immature myeloid cells multiply uncontrollably and stop the production of healthy blood cells. This review discusses the main aspects of AML, including its causes, spread, symptoms, diagnosis, and the latest treatment options. Worldwide, leukemia makes up about 2.5% of all new cancer cases, and AML is the most common type of acute leukemia in adults. The disease usually develops due to genetic changes and chromosomal mutations which interfere with normal blood cell development and cause rapid cell growth. Common symptoms include tiredness, frequent infections, fever, pale skin, easy bleeding or bruising, and swelling of the liver, spleen, or lymph nodes. Diagnosis is confirmed through bone marrow testing, genetic and molecular studies, and identification of specific cell markers, following World Health Organization (WHO) guidelines. The standard treatment involves chemotherapy with cytarabine and anthracycline (known as the “7+3” regimen), often followed by stem cell transplantation to restore healthy bone marrow. However, relapse and resistance to treatment remain serious challenges. The article explains several important advanced therapies that are transforming the treatment of Acute Myeloid Leukemia (AML). These include targeted therapy, which attacks specific genetic mutations such as using drugs like midostaurin, gilteritinib, quizartinib, ivosidenib, and enasidenib. Another major advancement is venetoclax, a BCL-2(B-cell lymphoma2) inhibitor used especially in older or unfit patients. The article also discusses immunotherapy, including monoclonal antibodies that recognize leukemia-specific antigens and help the immune system destroy cancer cells. CAR-T cell therapy is highlighted as a major breakthrough in which a patient’s own immune cells are

modified to directly target leukemia cells. The article further mentions oncolytic virus therapy, where specially engineered viruses infect and kill cancer cells while stimulating an immune response. In addition, it includes the emerging strategy of targeting oxidative phosphorylation (OXPHOS), which many cancer cells depend on for energy and survival; blocking this pathway can weaken leukemia cells, especially those resistant to chemotherapy. Together, these advanced therapies aim to improve outcomes, reduce relapse rates, and offer options for patients who do not respond to standard chemotherapy.

KEYWORDS: Acute Myeloid Leukemia, Targeted Therapy, Immunotherapy, Stem Cell Transplantation, Cytogenetics, FLT3 Mutation, Molecular Diagnosis.

1. INTRODUCTION

Acute myeloid leukaemia (ACUTE MYELOID LEUKEMIA) is a clonal increase of myeloid progenitors (blasts) in the bone marrow and peripheral circulation. ACUTE MYELOID LEUKEMIA, which was formerly incurable, is now treated in around 35–40% of patients younger than 60 years old. For those who The prognosis is better but still gloomy for those over 60 years old. According to recent research, a sequence of recurring hematopoietic stem cell genetic abnormalities have accumulated to cause this illness with age. Deep sequencing techniques were used on primary and relapsed cancers, resulting in a phenomena known as both founding clones and fresh subclones have been identified in clonal evolution, affecting the treatment strategy. Despite our growing understanding of ACUTE MYELOID LEUKEMIA biology, we continue to make progress. The results of modifying the therapy technique have been poor. In this analysis, adults and children. Adults with the most prevalent form of acute lymphoblastic leukaemia, a kind of blood cancer, may respond to initial treatments only to have the disease recur, while others' tumours do not respond to treatment at all. These patients may now have another treatment option in the form of CAR T-cell therapy, a sort of immunotherapy.[1-6]

The FDA approved the CAR T-cell therapy brexucabtagene for people with B-cell precursor ALL who have not responded to treatment (refractory) or who have returned after treatment on October 1 (relapsed). Brexucabtagene is the first CAR T-cell treatment to be approved for people with ALL. The approval was based on the findiNext-Generation Sequencing of ZUMA-3, a modest phase ½ clinical research with more than 50 participants. Most individuals had side effects, including high rates of cytokine release syndrome, or CRS, and neurological issues, which were consistent with prior brexucabtagene investigations. An

unfavourable reaction to the treatment claimed the lives of two volunteers.[7]

Blood cancer represents a large group of different malignancies. This group includes cancers of the bone marrow, blood, and lymphatic system, which includes lymph nodes, lymphatic vessels, tonsils, thymus, spleen, and digestive tract lymphoid tissue. Leukemia and myeloma, which start in the bone marrow, and lymphoma, which starts in the lymphatic system, are the most common types of blood cancer. What causes these cancers is not known. As leukemia and myeloma grow within the bone marrow, they can interfere with the bone marrow's ability to produce normal blood cells, including white blood cells, red blood cells, and platelets. Additionally, myelomas generate a substance that weakens bones and produce abnormal proteins that can cause symptoms in other parts of the body. Treatment of blood cancers has undergone substantial improvements, resulting in increased rates of remission and survival. Remission occurs when there is no sign of cancer. Today in the United States, almost 1 million people are alive with, or in remission from, blood cancer. People who have blood cancer can have problems with bleeding a infections. Blood cancer is a broad term that refers to a variety of cancers. Cancers of the bone marrow, blood, and lymphatic system, which includes lymph nodes, lymphatic vessels, tonsils, thymus, spleen, and lymphoid tissue of the digestive tract, are included in this category. Leukemia and myeloma are cancers that begin in the blood. The most prevalent cancers are bone marrow cancer and lymphoma, which begins in the lymphatic system. It is unknown what causes these cancers. As leukaemia and myeloma spread through the bone marrow, they might cause problems with the ability of the marrow to create normal blood cells, such as white blood cells, red blood cells, and platelets. This can lead to anaemia, recurrent infections, and easy bruising. Lymphoma is a type of cancer that affects the lymphatic system. Most commonly shown as lymph node hypertrophy, it can also obstruct the body's functions.[8-9]

2. LEUKEMIA

Leukemia is a malignancy that affects the blood cells. White blood cells are a type of blood cell. They aid the body's ability to fight infections. When a person is diagnosed with leukaemia, the condition is called leukaemia. The cells' DNA mutates, resulting in a significant number of immature white blood cells generated by the human body. Blasts are the name for these cells.

Leukemia can impact a variety of cells in the body.[11-13]

According to the cells they infect, blood and disease are divided into four categories. The

illness spreads as abnormal cells eventually take over the function of the bone marrow. The cells' DNA mutates, resulting in a significant number of immature white blood cells generated by the human body. Blasts are the name for these cells. Leukemia can impact a variety of cells in the body.[14- 15]

2.1 Types of Leukemia

a. Acute myeloblastic leukemia (ACUTE MYELOID LEUKEMIA-M1 and M2): Cancer in cells that become myeloid cells (neutrophils) with or without maturation.

b. Acute promyelocytic leukemia (APL or ACUTE MYELOID LEUKEMIA-M3): Cancer in immature white blood cells (promyelocytes) that prevents them from maturing. It is a specific subtype with a distinct treatment.

c. Acute myelomonocytic leukemia (AMML or ACUTE MYELOID LEUKEMIA-M4): Cancer that affects both myeloid and monocytic cells.

d. Acute monocytic leukemia (AMoL or ACUTE MYELOID LEUKEMIA-M5): Cancer in cells that would develop into monocytes, a type of white blood cell.

e. Acute megakaryoblastic leukemia (AMKL or ACUTE MYELOID LEUKEMIA-M7): Cancer of cells that are on the way to becoming megakaryocytes, which are the cells that produce platelets.[16-21]

3. Classification of Acute Myeloid Leukemia

1. **French–American–British (FAB) Classification (1970s)**

This early classification was based mainly on cell morphology and cytochemical staining. It defined eight major subtypes (M0–M7).

Table no. 1: classification of acute myeloid leukemia.[66]

FAB Type	Subtype Name	Description
M0	Minimally differentiated ACUTE MYELOID LEUKEMIA	Immature myeloblasts without granules
M1	ACUTE MYELOID LEUKEMIA without maturation	Myeloblasts predominate, minimal maturation
M2	ACUTE MYELOID LEUKEMIA with maturation	Myeloblasts show some maturation
M3	Acute promyelocytic leukemia (APL)	Presence of promyelocytes; associated with t(15;17)

M4	Acute myelomonocytic leukemia	Both granulocytic and monocytic cells
M5	Acute monocytic leukemia	Predominantly monoblasts
M6	Acute erythroid leukemia	Abnormal erythroid precursors
M7	Acute megakaryoblastic leukemia	Megakaryoblast proliferation

2. World Health Organization (WHO) Classification (Updated 2008, 2016, 2022)

The WHO classification integrates morphology, immunophenotype, cytogenetics, and molecular genetics.

It replaced the FAB system and includes additional entities based on genetic abnormalities, such as ACUTE MYELOID LEUKEMIA with recurrent genetic abnormalities, ACUTE MYELOID LEUKEMIA with myelodysplasia-related changes, therapy-related ACUTE MYELOID LEUKEMIA, and ACUTE MYELOID LEUKEMIA not otherwise specified (NOS).[22-24]

4. Epidemiology

In the year 2000, about 256,000 people around the world were diagnosed with leukemia, and approximately 209,000 died from it. This represented about 3% of all cancer deaths that year.

Globally, leukemia represents a significant portion of hematologic malignancies. According to Global Cancer Observatory (GLOBOCAN 2020), approximately 474,519 new cases of leukemia were diagnosed worldwide, accounting for about 2.5% of all new cancer cases, with an estimated 311,594 deaths attributed to the disease. Leukaemia constitutes roughly one-third of all blood cancers globally**.**

Among children with cancer, about one-third have leukaemia, most commonly acute lymphoblastic leukaemia (ALL). In infants under one year, leukaemia is the second most common cancer, and in older children, it is the most common type.[25]

5. Pathology of Acute Myeloid Leukemia

1. Nature of the Disease

Acute Myeloid Leukemia (ACUTE MYELOID LEUKEMIA) is a clonal hematopoietic disorder that originates from the uncontrolled proliferation of immature myeloid precursor cells (myeloblasts) in the bone marrow. These abnormal cells fail to mature properly and accumulate, eventually replacing normal hematopoietic cells. This leads to bone marrow failure, characterized by anemia, thrombocytopenia, and leukocytosis or leukopenia.

2. Cellular and Molecular Pathogenesis

The pathology of ACUTE MYELOID LEUKEMIA is driven by genetic mutations and chromosomal abnormalities that disrupt normal cell differentiation and apoptosis. Key molecular lesions include.

ACUTE MYELOID LEUKEMIA arises from hematopoietic stem cells that acquire these mutations over time, resulting in clonal expansion. Modern studies using deep sequencing have identified both founding clones and subclones, explaining relapse and treatment resistance.

3. Morphological Features

In bone marrow smears and peripheral blood.

The marrow is hypercellular, with suppression of normal erythroid and megakaryocytic elements.

Myeloblasts comprise ≥20% of nucleated marrow cells (as per WHO criteria).

Auer rods—needle-like cytoplasmic inclusions—are pathognomonic for myeloid lineage. The blasts are large, with fine chromatin, prominent nucleoli, and moderate cytoplasm.

Infiltration of blasts may occur in the liver, spleen, lymph nodes, gums, and skin.[26-29]

6. Leukemia Symptoms Signs and Causes

Leukemia affects the bone marrow and blood, disrupting the production of normal blood cells. As a result, patients experience a range of systemic symptoms. Common signs and symptoms include.

i. Anemia-related: fatigue, weakness, and pale skin due to decreased red blood cells.
ii. Bleeding tendencies: easy bruising, frequent nosebleeds, bleeding gums, and prolonged bleeding from minor cuts due to low platelet count (thrombocytopenia).
iii. Infection-related: recurrent infections, sore throat, mouth ulcers, fever, and pneumonia due to reduced healthy white blood cells.
iv. Constitutional symptoms: fever, chills, night sweats, unexplained weight loss, and flu-like symptoms.
v. Bone and joint pain: due to bone marrow expansion from excess blast cells.
vi. Swelling: enlarged lymph nodes, spleen, or liver.
vii. Skin manifestations: petechiae (small red spots), gum hypertrophy, and pallor. In advanced stages, leukemia can affect other organs like the brain, heart, and kidneys, leading to

headaches, confusion, or visual disturbances.[30-33]

6.1 Symptoms of Leukaemia

1. General Symptoms

- Fatigue and Weakness: Common in both acute and chronic forms of leukemia, often due to anemia or bone marrow suppression.
- Fever or Chills: May occur without an obvious infection, indicating systemic involvement.
- Unexplained Weight Loss: Often accompanied by loss of appetite and night sweats.
- Frequent or Severe Infections: Result from a weakened immune system due to ineffective white blood cells.

2. Hematologic Symptoms

- Easy Bruising or Bleeding: Due to low platelet counts, leading to spontaneous bleeding or prolonged bleeding from cuts.
- Recurrent Nosebleeds or Bleeding Gums: Indicative of thrombocytopenia or platelet dysfunction.
- Petechiae: Tiny red spots under the skin caused by small blood vessel rupture.

3. Lymphatic and Organ Involvement

- Swollen Lymph Nodes: Painless lumps, often in the neck, armpits, or groin.
- Enlarged Liver or Spleen (Hepatosplenomegaly): May cause a feeling of fullness or discomfort in the abdomen.

4. Bone and Joint Symptoms

- Bone Pain or Tenderness: Often in the chest, arms, or legs, due to infiltration of leukaemia cells in the bone marrow.
- Joint Pain: Less common but may occur in certain leukaemia subtypes.

5. Advanced Symptoms

- Shortness of Breath: Can result from anaemia or leukostasis (high white blood cell count).
- Confusion or Neurological Symptoms: May indicate central nervous system involvement.[34-37]

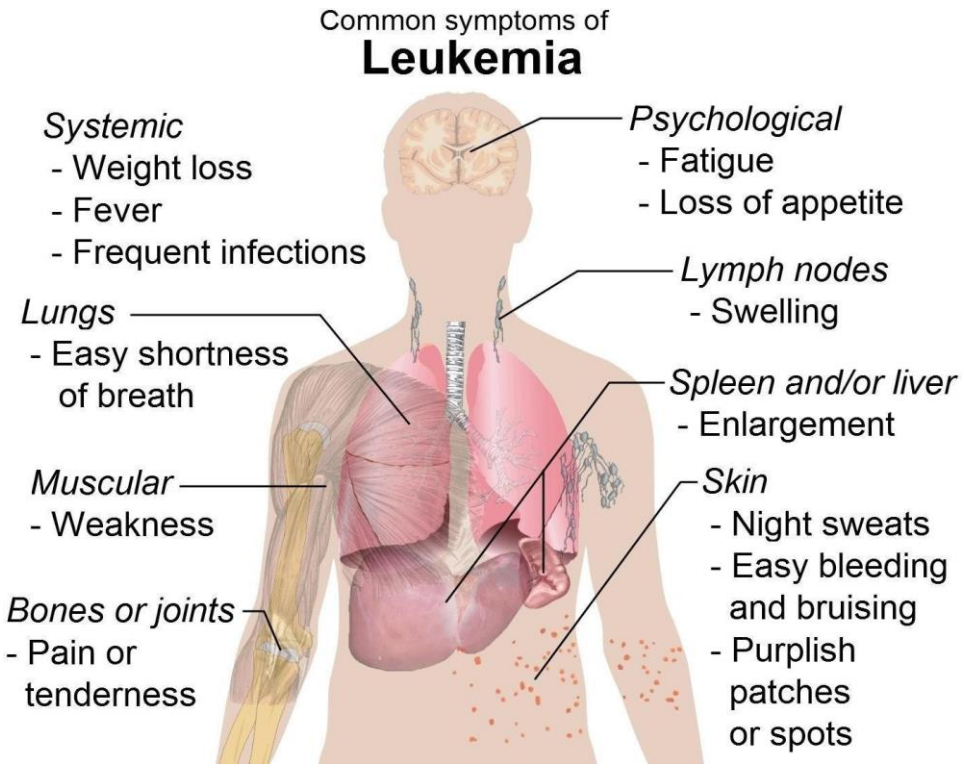


Fig 1: common symptoms of leukemia.[10]

6.2 Causes and Risk Factors

While leukemia has no single known cause, several genetic, environmental, and lifestyle factors increase risk.

Etiological Factors and Risk Contributors of Acute Myeloid Leukemia.

1. Genetic Mutations

Changes in specific genes can either activate *oncogenes* (genes that promote cell growth) or deactivate *tumor-suppressor genes* (genes that control cell division). Common mutations seen in ACUTE MYELOID LEUKEMIA include Tyrosine Kinase 3, NUCLEOPHOSMIN 1, and, which lead to uncontrolled proliferation of abnormal myeloid cells. These mutations also help classify ACUTE MYELOID LEUKEMIA into prognostic subtypes and guide targeted therapy.

2. Radiation Exposure

Exposure to high doses of ionizing radiation, such as during cancer radiotherapy or accidental environmental exposure (e.g., nuclear accidents), can damage the DNA of bone marrow cells. Over time, this damage may cause malignant transformation of hematopoietic stem cells, leading to ACUTE MYELOID LEUKEMIA.

3. Chemical Exposure

Long-term or repeated exposure to certain industrial chemicals such as benzene, petrochemical solvents, and some hair dyes is strongly associated with an increased risk of developing ACUTE MYELOID LEUKEMIA. Benzene, in particular, is known to suppress normal bone marrow function and induce chromosomal abnormalities.

4. Chemotherapy History

Individuals who have previously undergone chemotherapy for other cancers, especially using alkylating agents (like cyclophosphamide) or topoisomerase II inhibitors (like etoposide), have a higher likelihood of developing therapy-related ACUTE MYELOID LEUKEMIA (t-ACUTE MYELOID LEUKEMIA). This type of ACUTE MYELOID LEUKEMIA oftenappears several years after initial cancer treatment and may carry unfavorable cytogenetic abnormalities.

5. Smoking

Cigarette smoking introduces numerous carcinogens, including benzene and polycyclic aromatic hydrocarbons, which can damage DNA in blood-forming cells. Long-term smokers, therefore, have a higher risk of developing ACUTE MYELOID LEUKEMIA compared to non- smokers.[38–40]

7. Diagnosis

1. Clinical and Laboratory Features

The symptoms of acute myeloid leukemia (ACUTE MYELOID LEUKEMIA) mainly appear because the bone marrow stops making normal blood cells and is instead filled with immature cancerous cells called myeloblasts. This causes a shortage of healthy red cells, white cells, and platelets, leading to a range of clinical problems.

Patients often experience fatigue, weakness, and pale skin due to anemia (low red blood cell count). Fever and frequent infections occur because of neutropenia (low white blood cells), while easy bruising, bleeding gums, or small red spots on the skin (petechiae) result from thrombocytopenia (low platelet count). Many patients also have general symptoms such as fever, weight loss, loss of appetite, and night sweats.

In some cases, ACUTE MYELOID LEUKEMIA can cause enlargement of the liver, spleen, or lymph nodes, and patients may develop bone pain or gum swelling, especially in certain

subtypes of ACUTE MYELOID LEUKEMIA (like M4 and M5).

2. Bone Marrow Evaluation

Evaluation of the bone marrow is a key step in confirming the diagnosis of acute myeloid leukemia (ACUTE MYELOID LEUKEMIA). The test is performed by collecting samples through bone marrow aspiration and biopsy, which allow detailed examination of the cells under a microscope.

According to the World Health Organization (WHO) classification, the diagnosis of ACUTE MYELOID LEUKEMIA is established when 20% or more of the cells in the bone marrow or peripheral blood are myeloblasts—the immature precursor cells of the myeloid lineage. However, there are a few important exceptions to this rule. For instance, **in acute promyelocytic leukemia** (APL) or other ACUTE MYELOID LEUKEMIA subtypes with specific genetic abnormalities such as the diagnosis can be made even if the blast count is lower than 20%, because these genetic features are considered diagnostic.

Morphological examination of the bone marrow smears helps identify the size, shape, and maturity of the abnormal cells. The presence of Auer rods (needle-like inclusions within blasts) is a characteristic finding that supports a myeloid origin.

Cytochemical staining techniques, such as **myeloperoxidase** (MPO) and Sudan Black B, are sometimes used to confirm the presence of myeloid enzymes within the blasts. These tests help differentiate ACUTE MYELOID LEUKEMIA from **acute lymphoblastic leukemia** (ALL), which lacks these enzymes.

Immunophenotyping by flow cytometry is now an essential diagnostic tool. It uses antibodies tagged with fluorescent markers to detect specific surface and intracellular antigens **(CD markers)** on the leukemia cells. This technique accurately determines the cell lineage (myeloid vs. lymphoid) and further classifies ACUTE MYELOID LEUKEMIA into subtypes based on the pattern of antigen expression.[41]

Finally, cytogenetic and molecular testing of the bone marrow sample helps detect chromosomal translocations and gene mutations that influence both prognosis and treatment planning. Together, these studies provide a complete diagnostic and biological profile of ACUTE MYELOID LEUKEMIA.

3. Cytogenetics and Molecular Testing

Cytogenetic and molecular studies are now an essential part of the diagnostic workup for acute myeloid leukemia (ACUTE MYELOID LEUKEMIA). These tests help identify chromosomal abnormalities and gene mutations that not only confirm the diagnosis but also play a major role in determining the prognosis, treatment plan, and eligibility for stem cell transplantation.

Cytogenetic analysis involves examining the chromosomes of leukemia cells under a microscope using techniques such as karyotyping and fluorescence in situ hybridization (FISH). These tests detect structural changes in chromosomes, such as translocations, inversions, deletions, or duplications. Some of the most common chromosomal abnormalities include.

In addition to cytogenetic studies, molecular testing is performed to detect specific gene mutations that influence disease behavior and treatment response. Commonly tested genes include Tyrosine Kinase 3, NUCLEOPHOSMIN 1, SOCITRATE DEHYDROGENASE 1, ISOCITRATE DEHYDROGENASE 2, TUMOR PROTEIN 53, and KIT PROTO-ONCOGENE.

Tyrosine Kinase 3 mutations (especially *Tyrosine Kinase 3)* are linked to a higher relapse risk and guide the use of Tyrosine Kinase 3 inhibitors such as midostaurin.

- NUCLEOPHOSMIN 1 and mutations are often associated with better prognosis, particularly in the absence of TYROSINE KINASE 3 mutations.
- SOCITRATE DEHYDROGENASE 1/2 mutations can be targeted by ISOCITRATE DEHYDROGENASE inhibitors like ivosidenib and enasidenib.
- TUMOR PROTEIN 53 mutations usually indicate poor-risk disease and resistance to standard chemotherapy.

Modern laboratories now use next-generation sequencing (NEXT-GENERATION SEQUENCING) panels that can test for multiple genetic mutations simultaneously. NEXT-GENERATION SEQUENCING provides a comprehensive genetic profile of ACUTE MYELOID LEUKEMIA, which helps clinicians personalize therapy, determine risk categories (favorable, intermediate, or adverse), and decide whether a stem cell transplant may be beneficial.

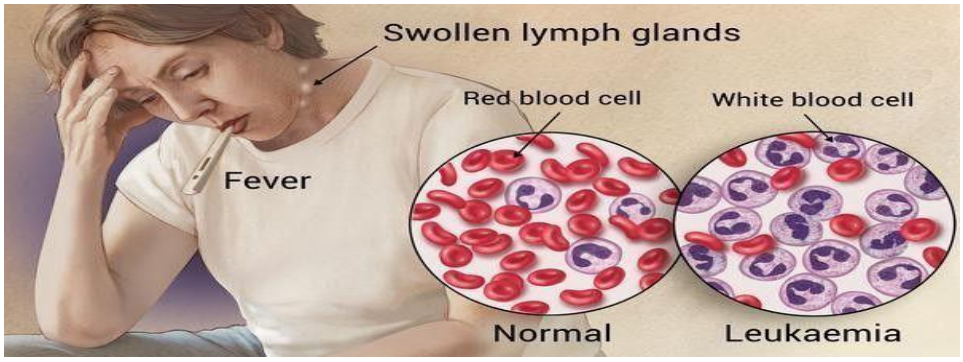
4. Additional Diagnostics and Baseline Assessments

Before starting treatment for **acute myeloid leukemia** (AML), several baseline investigations are essential to evaluate the patient's overall health, detect potential complications, and identify factors that may influence therapy choice.

Comprehensive infectious disease screening is crucial because ACUTE MYELOID LEUKEMIA patients are often immunocompromised at presentation. Tests commonly include hepatitis B and C, HIV, and **cytomegalovirus** (CMV) screening, since these infections can reactivate during chemotherapy or immunosuppression. Early identification allows for appropriate prophylaxis or modification of treatment regimens cardiac evaluation, such as echocardiography or **electrocardiogram** (ECG), is recommended—especially if an anthracycline-based regimen (e.g., daunorubicin or idarubicin) is planned. These drugs can cause cardiotoxicity, and assessing baseline heart function helps clinicians decide whether dose adjustments or alternative agents are needed.

In addition, a performance status and comorbidity assessment (using scales like ECG or Charlson Comorbidity Index) is performed to evaluate the patient's ability to tolerate intensive induction therapy. This helps distinguish patients suitable for standard induction from those who may require less intensive regimens or supportive care.

In cases of suspected **acute promyelocytic leukemia** (APL), immediate molecular testing for the PROMYELOCYTIC LEUKEMIA – RETINOIC ACID RECEPTOR ALPHA. Fusion gene is essential. APL is a medical emergency due to its strong association with **disseminated intravascular coagulation** (DIC), a potentially fatal bleeding disorder. Therefore, **all-trans retinoic acid** (ATRA) therapy should be initiated as soon as APL is suspected, even before genetic confirmation, to reduce the risk of hemorrhagic complications and early death.[42- 45]



Fig, 2: Swollen Lymph Gland.[46]

8. TREATMENT

- **1. ALLOPATHY**

Table no, 2: medicine used for treating leukemia.[72-74]

Sr. No.	Drug Name	Usage / Indication	Typical Dosage / Regimen
1	Cytarabine (Ara-C)	Core component of induction and consolidation therapy; inhibits DNA synthesis in dividing cells	100–200 mg/m²/day by continuous IV infusion for 7 days (standard-dose); 1–3 g/m² every 12 h for 3 days (high- dose)
2	Daunorubicin	Anthracycline used in combination with cytarabine during induction ("7+3" regimen)	60–90 mg/m² IV daily for 3 days
3	Idarubicin	Anthracycline alternative to daunorubicin with similar efficacy	12 mg/m² IV daily for 3 days
4	Mitoxantrone	Used in reinduction or salvage regimens for relapsed/refractory ACUTE MYELOID LEUKEMIA	12 mg/m² IV daily for 3 days
5	Gemtuzumab ozogamicin	Anti-CD33 monoclonal antibody-drug conjugate; used in CD33-positive ACUTE MYELOID LEUKEMIA	3 mg/m² IV on days 1, 4, and 7 (induction or consolidation)
6	Midostaurin	TYROSINE KINASE 3 inhibitor; used with induction/consolidation chemotherapy in TYROSINE KINASE 3-mutated ACUTE MYELOID LEUKEMIA	50 mg orally twice daily on days 8–21 of each chemotherapy cycle
7	Venetoclax	BCL-2 inhibitor; used with hypomethylating agents in older/unfit patients	100–400 mg orally once daily (dose ramp-up)
8	Azacitidine	Hypomethylating agent; used in elderly or unfit ACUTE MYELOID LEUKEMIA patients and for maintenance	75 mg/m² subcutaneously or IV daily for 7 days every 28 days
9	Decitabine	Hypomethylating agent; similar use as azacitidine	20 mg/m² IV daily for 5 consecutive days every 4 weeks
10	CPX-351 (Vyxeos®)	Liposomal formulation of cytarabine + daunorubicin; used in therapy-related or secondary ACUTE MYELOID LEUKEMIA	100 units/m² (cytarabine 44 mg/m² + daunorubicin 10 mg/m²) IV on days 1, 3, and 5

Leukemia therapy includes chemotherapy, radiation therapy, stem cell transplantation, and newer approaches like targeted therapy and immunotherapy. Chemotherapy is the main treatment for most people, using drugs to kill leukemia cells throughout the body. Other therapies are chosen based on the type of leukemia, its stage, and the patient's overall health.

Common therapies

i. Chemotherapy

Chemotherapy is the primary and most widely used treatment for leukemia. It involves the administration of anticancer drugs that target and destroy rapidly dividing leukemia cells in the bone

marrow and blood. These drugs can be given orally, intravenously, or through injections, depending on the treatment plan.

Often, a combination of drugs is used to improve effectiveness and reduce the risk of resistance. Treatment is typically divided into phases.

Induction therapy, aimed at achieving remission by killing most leukemia cells. Consolidation (or intensification) therapy, which eliminates any remaining disease. Maintenance therapy, designed to prevent relapse in certain leukemia types.

While chemotherapy is highly effective, it can also damage normal cells, leading to side effects such as fatigue, infection risk, hair loss, and nausea.

ii. Radiation therapy

Radiation therapy uses high-energy X-rays or other ionizing radiation to destroy leukemia cells or inhibit their growth. It is less commonly used as a primary treatment for leukemia since leukemia affects the blood and bone marrow rather than forming solid tumors.

However, it plays a crucial role in specific clinical situations, such as when leukemia has spread to the brain, spinal cord, or other organs (central nervous system involvement). Radiation may also be used as part of conditioning therapy before a stem cell or bone marrow transplant to destroy residual cancer cells and suppress the immune system, allowing successful engraftment of donor cells.

iii. Stem cell transplantation

Stem cell transplantation (also called a bone marrow transplant) is a treatment used to replace diseased or damaged bone marrow with healthy stem cells. These new stem cells can make normal blood cells and restore the body's immune system.

Before the transplant, the patient is given very strong chemotherapy and sometimes radiation therapy to destroy any remaining leukemia cells and to clear space in the bone marrow for the new cells to grow.

The healthy stem cells used for the transplant can come from two main sources.

Autologous transplant: the patient's own stem cells, collected earlier and stored for later use.

Allogeneic transplant: stem cells taken from a donor — usually a matched sibling or an

unrelated compatible person.

Stem cell transplantation is usually recommended for patients whose leukemia has come back (relapsed) or has not responded well to regular treatments.

Although this therapy offers a chance for a long-term cure, it also has serious risks, such as graft- versus-host disease (GVHD) (where donor cells attack the patient's body), infections, and damage to organs due to the high-dose treatments.

- **Side effects of the therapies mentioned above**

Chemotherapy, Radiation, Stem cell transplantation can result in infections, mucositis, and organ damage but remains potentially curative for high-risk cases. Where we can say that these therapies use to kill extreme growth of cells bus also affect the healthier side off the body thus newer therapies were introduced which were mentioned below.

9. ADVANCE THERAPHY

1. Targeted Therapy

Targeted therapy focuses on attacking **specific genetic or molecular abnormalities** that drive the growth of leukemia cells. Unlike traditional chemotherapy, which affects both healthy and cancerous cells, targeted drugs act only on cancer-specific pathways.

For example, **tyrosine kinase inhibitors (TKIs)** such as *midostaurin*, *gilteritinib*, and *quizartinib* are used to inhibit the **TYROSINE KINASE 3 mutation**, a common abnormality in acute myloid leukemia that promotes rapid cell division. Similarly.

SOCITRATE DEHYDROGENASE 1 and ISOCITRATE DEHYDROGENASE 2 inhibitors (*ivosidenib* and *enasidenib*) are used in patients whose leukemia cells carry those specific mutations. These therapies have improved outcomes by providing more personalized treatment options.

--Advantages

1. Precision Treatment

Targets specific genetic mutations (e.g., TYROSINE KINASE 3, SOCITRATE DEHYDROGENASE 1, ISOCITRATE DEHYDROGENASE 2) responsible for ACUTE MYELOID LEUKEMIA progression, leading to more effective results and fewer off-target effects.

2. Fewer Side Effects

Compared to conventional chemotherapy, targeted drugs spare most healthy cells, thereby reducing systemic toxicity.

3. Improved Survival and Remission Rates

When combined with standard chemotherapy, agents like *midostaurin* and *gilteritinib* have significantly improved remission and overall survival in mutation-positive ACUTE MYELOID LEUKEMIA patients.

4. Personalized Medicine Approach

Enables treatment customization based on individual molecular profiles, improving therapeutic precision.

2. Immunotherapy

Your immune system naturally protects you from infections and abnormal cells (like cancer).
However, sometimes cancer cells can "hide" from the immune system.
Immunotherapy helps by.

- **Boosting** the immune system to work harder or smarter.
- **Marking** cancer cells so the immune system can find and destroy them.

Immunotherapy is a form of medical treatment that **stimulates, enhances, or restores the natural defenses of the body's immune system** to recognize and destroy harmful cells, such as **cancer cells, viruses, or bacteria**. It works by either **activating the immune system** to attack specific disease-causing cells or by **supplying components** (like antibodies or immune cells) that help the immune system function more effectively. Immunotherapy plays a crucial role in modern medicine, particularly in the treatment of **cancer, autoimmune diseases, and certain infections**, by improving the body's ability to detect and eliminate abnormal or diseased cells while minimizing damage to normal, healthy tissues.

-- Advantages

1. Enhanced Immune System Activity

Boosts or redirects the body's own immune system to recognize and kill leukemia cells, offering a natural and sustained anti-tumor effect.

2. Specificity to Cancer Cells

Monoclonal antibodies like *gemtuzumab ozogamicin* selectively target leukemia-associated

antigens (e.g., CD33), minimizing damage to normal cells.

3. Reduced Relapse Risk

Immunotherapies can establish long-lasting immune memory, reducing the chances of leukemia recurrence.

4. Effective in Relapsed or Refractory ACUTE MYELOID LEUKEMIA

Especially beneficial in patients who do not respond to standard chemotherapy or have relapsed disease.

5. Combination Potential

Can be safely combined with chemotherapy or targeted therapy to enhance treatment effectiveness.

3. Oncolytic Virus Therapy

Oncolytic virus therapy is an innovative and experimental approach that uses **genetically modified viruses** to selectively infect and kill leukemia cells without harming normal cells. Once the virus infects the cancer cell, it replicates within it, causing the cell to burst (lysis). This process not only destroys the leukemia cells directly but also **stimulates the immune system** to recognize and attack remaining cancer cells. Although still under investigation, this therapy represents a potential future direction for ACUTE MYELOID LEUKEMIA treatment due to its dual action — **direct cytotoxicity and immune activation.**[47–53]

--Advantages

1. Dual Mechanism of Action

Destroys leukemia cells directly (through viral replication) and indirectly (by activating the immune system).

2. Selectivity for Cancer Cells

Genetically engineered viruses are designed to infect only malignant cells, sparing normal hematopoietic cells.

3. Immune System Stimulation

Viral infection triggers immune recognition of leukemia antigens, leading to a broader anti-leukemic immune response.

4. Low Systemic Toxicity

Since normal cells are largely unaffected, oncolytic virus therapy causes minimal systemic side effects.

5. Potential Synergy with Immunotherapy

Combining oncolytic viruses with checkpoint inhibitors or CAR T-cell therapy can enhance overall therapeutic efficacy.[68-71]

4. oxidative phosphorylation

oxidative phosphorylation is a process in the mitochondria that makes energy for the cell. Normally, healthy cells use this method to produce most of their energy, but cancer cells behave differently. Although many cancer cells use **glycolysis** (a faster but less efficient way of making energy), many cancer types still depend on **oxidative phosphorylation**, especially the stronger and more advanced cancers. These cancer cells change their mitochondria so they can make energy even when the tumor does not have enough oxygen or nutrients. They increase the number of mitochondria and use not only glucose but also fats and amino acids to continue producing energy.

This high activity of **oxidative phosphorylation** creates a lot of **reactive oxygen species (ROS)**—dangerous molecules that damage DNA. But instead of dying, cancer cells use this damage to grow faster, become more aggressive, and spread to other parts of the body. **oxidative phosphorylation** also helps cancer stem cells survive treatments like chemotherapy and radiation, which is why some cancers keep coming back. Because of this, scientists are developing drugs that block **oxidative phosphorylation** to cut off the cancer's energy supply and make treatments work better. In simple words, **oxidative phosphorylation** gives cancer cells the extra power they need to grow, survive, and resist treatment.

10. DKMS (Deutsche Knochenmarkspenderdatei) Organization

A city in Germany called Dresden saved the lives of 15 cancer patients through the help of citizens from all over the world. More than 30,000 people registered themselves on a website www.dkms-india.org, which helped in finding suitable donors and ultimately saving these patients.

This issue mainly concerns blood cancer, which causes more than 70,000 deaths annually. When treatments like chemotherapy and radiation therapy fail, the last option available is

Blood Stem Cell Transplantation (BSCT). In this procedure, a healthy person donates their stem cells to a cancer patient, which helps the patient's body fight cancerous cells. This process is similar to a blood transfusion.

However, there is a major difference between blood transfusion and blood stem cell transplantation. In blood transfusion, there are 8 common blood groups (A+, B+, AB+, O+, A–, B–, AB–, O–).

But in stem cell transplantation, the most important factor is matching the Human Leukocyte Antigen (HLA) type. For a successful transplant, the HLA type of the donor and the patient must match. Shockingly, there are more than 20,000 different HLA types, making it extremely difficult to find a match. The probability of finding a matching donor for stem cell transplantation is 1 in 100,000. Therefore, it is important for more people to register as donors.

This is where DKMS, a non-profit organization and the largest stem cell registry in the world, plays a major role. DKMS has more than 11 million registered stem cell donors globally.

The process of becoming eligible to save someone's life is very simple and completely free, as DKMS covers all the costs.

You just need to visit the website www.dkms-india.org and fill out an online form. It takes about 4 minutes to provide your basic details. A few days later, you will receive a cheek swab kit at your address with instructions. You simply need to take the swab, pack it along with the signed consent form, and return the kit. DKMS will arrange the pickup from your address.

This sample provides your HLA data, and you will be added to the global blood stem cell registry. Within a few days, you will receive an email confirming your registration. If your HLA type matches with a blood cancer patient, you will get a call from DKMS. You will then be offered the chance to donate your stem cells. These transplants and matching procedures are performed in high-tech labs located in Dresden, Germany. In India, DKMS centers are located in major metro cities (**Delhi**, **Mumbai**, **Kolkata Chennai**, **Bengaluru, Hyderabad**, **Pune**, **Ahmedabad).**

In this way, the DKMS organization helps save the lives of people fighting acute myeloid leukemia and other blood cancers.

DISCUSSION

The findiNext-Generation Sequencing from the reviewed data indicate that the incidence of blood cancers, particularly leukemia, is steadily increasing in Iran, consistent with global trends. The epidemiological reports from various Iranian provinces, such as Mazandaran and Western Azerbaijan, suggest a notable rise in Acute Lymphoblastic Leukemia (ALL) among children under 15 years of age, with non-Hodgkin lymphoma being the most prevalent type among adults. Studies by Tahmasebi et al. (2006) and Farahmand et al. (2011) confirm that between 2000 and 2008, both the incidence and mortality rates of hematologic malignancies showed an upward trend, highlighting the growing public health burden of these diseases.

In terms of clinical management, Acute Myeloid Leukemia (ACUTE MYELOID LEUKEMIA) remains a major therapeutic challenge due to its heterogeneous genetic mutations and high relapse rates. Although significant advances have been made in molecular diagnostics, cytogenetic profiling, and targeted therapy development, survival outcomes for ACUTE MYELOID LEUKEMIA patients have only improved modestly over the past decades. Traditional chemotherapy regimens such as the “7+3 protocol” (cytarabine and anthracycline) continue to serve as the mainstay of treatment; however, emerging therapies like TYROSINE KINASE 3, SOCITRATE DEHYDROGENASE 1/2, and BCL-2 (B-cell lymphoma 2) inhibitors (e.g., Midostaurin, Ivosidenib, Venetoclax) have demonstrated improved remission rates, particularly when combined with hypomethylating agents.

The introduction of CAR-T cell therapy and monoclonal antibodies has opened a new frontier in leukemia treatment, offering potential for durable remission in refractory and relapsed cases. Yet, these therapies carry substantial risks such as cytokine release syndrome (CRS) and neurological toxicity, emphasizing the need for careful patient selection and monitoring. Furthermore, minimal residual disease (MRD) detection through PCR and flow cytometry now plays a critical role in assessing treatment response and early relapse prediction.

Another critical observation is the growing application of Next-Generation Sequencing (NEXT- GENERATION SEQUENCING) and Artificial Intelligence (AI)-assisted diagnostics in ACUTE MYELOID LEUKEMIA classification and prognosis determination. These technologies allow for a personalized medicine approach, improving therapeutic decisions based on each patient’s unique genetic and molecular profile.

Overall, while the biological understanding and diagnostic precision in ACUTE MYELOID LEUKEMIA have advanced significantly, the clinical translation of these discoveries into long-term survival benefits remains limited. The persistence of therapy resistance and disease relapse underscores the need for multimodal therapeutic strategies, combining molecularly targeted agents, immunotherapies, and stem cell transplantation, integrated with precision diagnostics and supportive care.

CONCLUSIONS

Acute Myeloid Leukemia (AML) is a serious type of blood cancer that starts in the bone marrow and spreads quickly. It happens when genetic changes make immature blood cells grow out of control, stopping the production of normal blood cells. Over the years, scientists have learned a lot about how AML develops, but curing it completely is still very difficult because it often comes back after treatment.

The main treatments used are chemotherapy and stem cell transplantation. However, new and advanced methods like targeted therapy, immunotherapy, and oncolytic virus therapy are now giving better results with fewer side effects. These modern treatments work by attacking the cancer cells more precisely based on each patient's genetic makeup.

With the help of new technologies like Next-Generation Sequencing (NGS), doctors can now identify specific mutations in the cancer cells and choose the right treatment for each patient. Organizations like DKMS also play an important role by helping patients find stem cell donors when transplants are needed.

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