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Rizayev J.[1], Yuldashev S.[1], Imran Aslam[1], Jiyanboyev N.[2]
[1] Samarkand State Medical University, Samarkand, Uzbekistan
[2] University of Health Sciences, Bukhara, Uzbekistan

Acute Myeloid Leukemia in a Resource-Constrained Pakistan Hospital

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Contacts: farma.km@mail.ru

Abstract

Purpose. In environments with limited resources, anthropogenic myeloid leukemia demographics and clinical outcomes are the subjects of this study.
Materials and methods. Between the months of January 2005 and April 2022, The Pakistan Institute of Medical Sciences (PIMS) Department of Medical Oncology in Islamabad conducted a retrospective study. A study was undertaken on a cohort of 334 patients diagnosed with acute myeloid leukemia (AML) in order to ascertain their age, gender, residence, and HBV/HCV status, peripheral film, bone marrow biopsy, flow cytometry, gene markers, cytogenetics, treatment, and outcome. The study found that induction therapy with Arabinoside-cytarabine and daunoblastina was effective in achieving complete remission in most patients, and Any death that occurred within three weeks after commencing chemotherapy was considered to be treatment-related mortality. The age of patients was classified into subgroups, and further analysis of the data may provide insights into AML treatment outcomes in different age groups.
Results. The study included 334 those who are suffering from acute myeloid leukemia (AML) treated at PIMS Medical Oncology in Pakistan. The study found that older age, higher blasts percentage, refractory disease, and higher TRM were associated with worse prognosis in AML. Most patients experienced complete remission, whereas a smaller minority had incomplete or refractory illness. The presence of cytogenetic and molecular abnormalities, such as t (8;21), inv (16), NPM1, and IDH, has been determined to have prognostic importance.
Conclusion. The study highlights the importance of considering various factors when predicting treatment outcomes and prognosis in AML, Additionally, the findings may make it easier to make judgements on treatment and enhance the outcomes for patients. Treatment approaches for AML are highly individualized and depend on various factors in Punjab and KPK. Pakistanis with acute myeloid leukemia are younger and male.
Keywords: acute myeloid leukemia syndrome, acute promyelocytic leukemia, mortality

Ризаев Ж.А. [1], Юлдашев С.Дж.[1], Имран Аслам[1], Джиянбоев Н.С.[2]
[1] Самаркандский государственный медицинский университет, Самарканд, Узбекистан
[2] Бухарский государственный медицинский институт имени Абу Али ибн Сино, Бухара, Узбекистан

Острый миелоидный лейкоз в пакистанской больнице с ограниченными ресурсами

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Контакты: farma.km@mail.ru

Резюме

Цель. Определить демографические характеристики и клинические исходы антропогенного миелолейкоза.
Материалы и методы. В период с января 2005 г. по апрель 2022 г. в отделении медицинской онкологии Пакистанского института медицинских наук (PIMS) в Исламабаде было проведено ретроспективное исследование. В группу исследуемых вошли 334 пациента с диагнозом «острый миелолейкоз» (ОМЛ). Исследовались возраст, пол, место жительства пациентов, статус HBV/HCV, периферическая пленка, биопсия костного мозга, проточная цитометрия, генные маркеры, цитогенетика, оценивались методы лечения и результат. Исследование показало, что индукционная терапия арабинозид-цитарабином и даунобластином была эффективна для достижения полной ремиссии у большинства пациентов, а любая смерть, наступившая в течение трех недель после начала химиотерапии, считалась смертью, связанной с лечением. В ходе исследования пациенты были разделены на подгруппы по возрасту, и дальнейший анализ данных дал представление о результатах лечения ОМЛ в разных возрастных группах.
Результаты. Исследование показало, что пожилой возраст, более высокий процент бластов, рефрактерность заболевания и более высокий TRM были связаны с худшим прогнозом при ОМЛ. У большинства пациентов наблюдалась полная ремиссия, тогда как у меньшего количества была рефрактерная болезнь. Установлено, что наличие цитогенетических и молекулярных аномалий, таких как t (8;21), inv (16), NPM1 и IDH, имеет прогностическое значение.
Выводы. Исследование подтвердило важность учета различных факторов при прогнозировании результатов лечения при ОМЛ. Кроме того, полученные результаты могут облегчить принятие решений о лечении и улучшить результаты для пациентов. Подходы к лечению ОМЛ в Пенджабе очень индивидуальны и зависят от различных факторов.
Ключевые слова: синдром острого миелолейкоза, острый промиелоцитарный лейкоз, смертность

INTRODUCTION

Acute myeloid leukemia (AML) is a relatively uncommon disease that primarily affects adults. Only 1% of US adult deaths are cancer-related [1]. The median age of patients around the world the patient is 65 years old at the time of diagnosis [1]. There is a correlation between the occurrence of acute myeloid leukemia (AML) and the patient's age [2]. Historically high mortality rates [3], and poor prognosis [4].

In bone marrow aspiration or biopsy, at least 20% blasts in the bone marrow or peripheral blood confirm AML. In patients with acute myeloid leukemia, some genetic alterations are present., myeloid sarcoma, and CNS involvement with myeloblasts may be diagnosed without bone marrow blast [5]. It is possible to identify cell membrane antigens using flow cytometry immunophenotyping [6]. In AML treatment, the response, and the outcome are all determined by the findings from cytogenetic and molecular genetic testing [7].

Full remission and disease-free survival can be predicted with some degree of accuracy based on certain clinical characteristics at Young age [8], good performance status [8] on the bone marrow, as well as abnormalities [9] tend to be seen as positive contributions.

Taking into consideration the results of the cytogenetic and molecular studies, acute myeloid leukemia is classified into three risk groups: favorable, unfavorable, and intermediate. Intermediate-risk individuals are treated with regular chemotherapy, and those with poor prognosis should undergo allogeneic stem cell transplantation after remission induction [2]. Over the course of over half a century, when it came to the treatment of AML, the 7+3 regimen continued to be the core of standard therapy over the years.

Disseminated intravascular coagulation is a defining feature of acute promyelocytic leukemia, a specific subtype of acute myeloid leukemia (AML) that represents 5–10% of all cases. This condition necessitates prompt identification and treatment, distinguishing it from other forms of AML that may not require immediate intervention. Arsenic trioxide (ATO) and all-trans retinoic acid (ATRA) are currently being used as medicinal treatments, patients with APML go from having a condition that is extremely fatal to one that only has a moderately fatal outcome and curable [11]. According to the results of the benefits of ATRA-ATO treatment, as demonstrated by the APL0406 examination significantly outweigh those of ATRA chemotherapy over the course of time, and the treatment is noticeably more successful in patients who do not have a high risk of developing APL patients [12]. ATRA in combination with chemotherapy is still the treatment that is considered typical for patients who are at a high risk [13].

Cytogenetic abnormalities with AML treatment

Cytogenetic and molecular AML. These subtypes have good, moderate, or bad abnormalities and prognoses. Patient risk determines therapy outcomes.

Positive anomalies include the values of Inv (16)/t (16;16) and t (15;17). The therapy and prognosis are both improved by anomalies. Consolidation therapy with high-dose cytarabine (HiDAC) has the potential to improve t (8;21) and inv(16)/t(16;16), but further treatment with ATRA and ATO may be helpful for t (15;17).

Normal karyotype, trisomy 8, and t (9;11) are intermediate-risk. Molecular testing may stratify risk in normal karyotype patients. Trisomy 8 is worse than favorable-risk but better than unfavorable. aggressive treatment for t (9;11).

Complex karyotype, monosomy 5 or 7, and chromosomal 3 or 11q23 abnormalities are harmful. Anomalies may require allo-SCT. FLT3 inhibitors may help unfavourable FLT3-ITD mutation patients.

NPM1 and IDH mutations alter AML prognosis. HiDAC consolidation may improve NPM1 mutation and normal karyotype prognosis. IDH inhibitors may enhance prognosis in normal-karyotype IDH mutation patients.

AML's cytogenetic and molecular abnormalities predict treatment results. Allo-SCT is needed for risky abnormalities. FLT3 and IDH inhibitors help some.

Leukaemia therapy response, prognosis, OS, DFS, and other factors

Lymphoblastic leukaemia.

Younger patients do better.

Higher diagnostic WBC counts worsen prognosis.

Ph+ Philadelphia chromosome worsens prognosis.

Initial therapy: Complete remission (CR) improves prognosis.

Relapse within a year decreases prognosis.

CLL: Age: Older patients suffer.

Rai or Binet stage: Worse prognosis.

Mutated IGHV improves prognosis.

Del(17p) and TP53 mutations worsen prognoses.

Initial treatment response: CR individuals fared better.

First treatment: Patients who need treatment within 2 years of diagnosis have a worse prognosis.

Age: Older folks fare worst.

Performance improves prognosis.

t(8;21) or inv(16) are better than complicated karyotype or monosomy 5 or 7.

Initial treatment response: CR individuals fared better.

Relapse within a year decreases prognosis.

Myeloid leukemia:

Older adults do worse.

Sokal/Hasford score: Riskier diagnoses worsen prognosis.

MMR or deeper response improves prognosis.

Response time: MMR or deeper responses within a year improve prognosis.

Therapy adherence improves prognosis.

Conclusion, age, disease stage or risk score, cytogenetic and molecular abnormalities, responsiveness to first therapy, duration to recurrence or progression, and drug adherence can affect leukemia treatment response, prognosis, OS, DFS, and other outcomes. These criteria govern therapy.

■ MATERIALS AND METHODS

The study examined patient medical records retrospectively. diagnosed with AML and treated the Pakistan Institute of Medical Oncology (PIMS) in Islamabad. There was a total of 334 participants who participated in the trial who had been diagnosed with AML.

All patients with AML were diagnosed through the use of bone marrow aspiration and trephine biopsy. Flow cytometry and immunophenotyping were identified as the techniques utilised in the majority of the instances. The coagulation and biochemical

profile, as well as the serology for hepatitis B and C, and echocardiography were performed on each and every patient.

Patients received an infusional regime consisting of daunoblastina 60 mg/m^2 for three days (D3 A7) and an infusional regime consisting of 200 mg/m^2 of arabinoside-cytarabine for seven days during the induction therapy. On day 28, a bone marrow biopsy was conducted on the preponderance of patients who underwent the surgical procedure. The requisites for complete remission were determined to be blasts below 5%, the absence of extramedullary illness, an absolute neutrophil count exceeding 1000, and a platelet count surpassing 100,000. In cases of partial remission, bone marrow blasts ranged from 5–19%. More than twenty percent of patients had refractory illness. The term "treatment-related mortality" (TRM) refers to any death that occurs within three weeks of administration of induction chemotherapy.

Medical records include blood counts, blast percentage, flow cytometry, gene markers, and treatment, which affect results. Individuals were then divided into subgroups based on their age, This encompassed individuals in the age groups of 12–18 years, 19–40 years, 41–60 years, and over 60 years.

■ RESULTS

Participating in the research were 334 AML patients who were receiving treatment at PIMS Medical Oncology in Islamabad, Pakistan. A trephine biopsy, bone marrow aspiration, immunophenotyping, and flow cytometry were conducted on the vast majority of the patients. Patients were given an infusional regime consisting of daunoblastina 60 mg/m^2 for three days and an infusional regime consisting of 120 mg/m^2 of daunoblastina for seven days during the induction therapy. Some of the categories of information that were taken from the patient's medical records included the relevant information includes the patient's age, gender, address, blood counts, percentage of blasts, results from flow cytometry, gene markers, and details on the treatment., and result are all important factors to consider. Other categories of information included the patient's treatment.

The study found that older age was associated with a worse prognosis, with patients above 60 years of age having a lower OS and DFS compared to younger age groups. One of the other characteristics that was discovered to be associated with a poorer prognosis was a larger percentage of blasts seen, refractory disease, and higher TRM. In terms of treatment outcomes, the study found that the majority of patients achieved complete remission, while a smaller proportion achieved partial remission or had refractory disease. The OS and DFS rates were higher in individuals who had complete remission as compared to patients who did not have complete remission.

The study identified specific cytogenetic and molecular abnormalities, including inv (16) and t (8;21), which were correlated with a more favourable prognosis, while others, such as complex karyotype and monosomy 5 or 7, were associated with a poorer prognosis. Moreover, the research revealed that gene mutations, including FLT3-ITD and IDH, may have prognostic significance and could potentially guide treatment decisions.

Overall, the study highlights the importance of considering various factors, including age, disease stage, cytogenetic and molecular abnormalities, response to therapy, and adherence to therapy, when predicting treatment outcomes and prognosis in AML. The findings of this study may help guide treatment decisions to improve AML outcomes.

As previously mentioned, Cytogenetic and molecular abnormalities divide acute myeloid leukemia (AML) into numerous subgroups. These subtypes can be classified as favorable, intermediate, or unfavorable risk based on the particular anomalies, as well as their prognostic significance. The risk category assigned to a patient can help guide treatment decisions and predict treatment outcomes.

Examples of Cytogenetic and molecular subtypes of AML include:

- AML with t (8;21) or RUNX1-RUNX1T1 fusion, which is classified as a favorable risk subtype
- AML with inv (16)/t (16;16) or CBFB-MYH11 fusion: Favorable risk subtype
- AML with t (15;17) or PML-RARA fusion: Favorable risk subtype
- AML with normal karyotype: Intermediate risk subtype
- Complex karyotype AML: Risky subclass
- AML with monosomy 5 or 7: Unfavorable risk subtype
- AML with FLT3-ITD mutation: Unfavorable risk subtype
- AML with NPM1 mutation: Favorable risk subtype in patients with normal karyotype
- AML with IDH1 or IDH2 mutation: Unfavorable risk subtype in normal-karyotype individuals

As more research is conducted in this area, cytogenetic and molecular categorization of AML subgroups, which signify major abnormalities, is continually undergoing development.

AML is a diverse illness with many genetic and molecular abnormalities. These anomalies include chromosomal, gene, and epigenetic abnormalities. Chromosomal abnormalities:

In 5–10% of acute myeloid leukemia (AML) cases, the t (8;21) translocation is associated with a good prognosis. This mechanism joins the AML1 (RUNX1) gene on chromosome 21 and the ETO (RUNX1T1) gene on chromosome 8.

The genetic rearrangement referred to as inv (16)/ t (16;16) is linked to a favorable outcome and is detected in approximately 5–10% of AML cases. This process may cause the CBFB and MYH11 genes on chromosome 16 to join.

The specific chromosomal rearrangement, referred to as t (15; 17), is linked to a favorable outlook and is detected in around 10–15% of AML cases. This mechanism results in the fusion of the PML gene on chromosome 15 and the RARα gene on chromosome 17.

Complex karyotype: Three or more chromosomal abnormalities indicate a poor prognosis. Gene mutations:

FLT3-ITD: About 25% of AML cases have this FLT3 gene internal tandem duplication, which has a dismal prognosis.

NPM1: This mutation in the NPM1 gene is found in about 30% of AML cases and is typical karyotype patients have a good prognosis.

IDH1/2: Mutations in the IDH1 or IDH2 genes are found in about 20% of AML cases and are linked with poor prognosis in normal karyotype patients. TP53: Mutations in the TP53 gene are found in about 10% of AML cases and are associated with a poor prognosis.

Epigenetic changes

DNA methylation: Abnormal DNA methylation patterns have been observed in AML and can lead to gene silencing and altered gene expression.

Histone modifications: Alterations in histone modifications alter gene expression and cause AML.

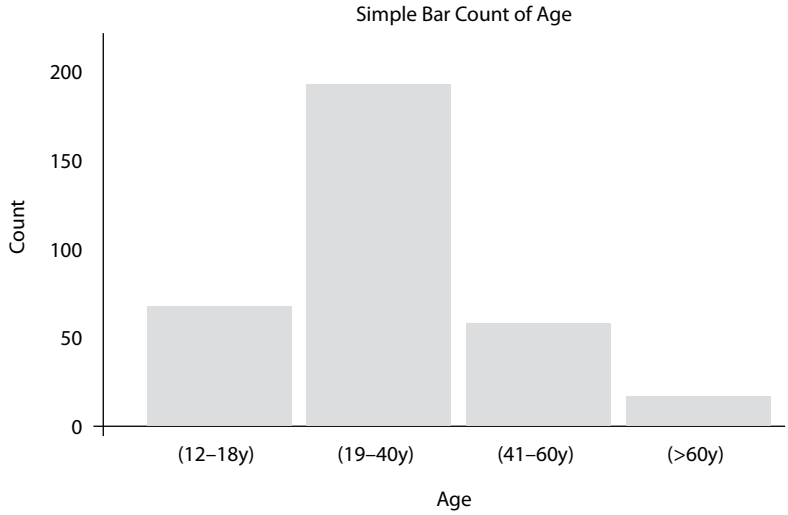

Fig. 1. Age distribution

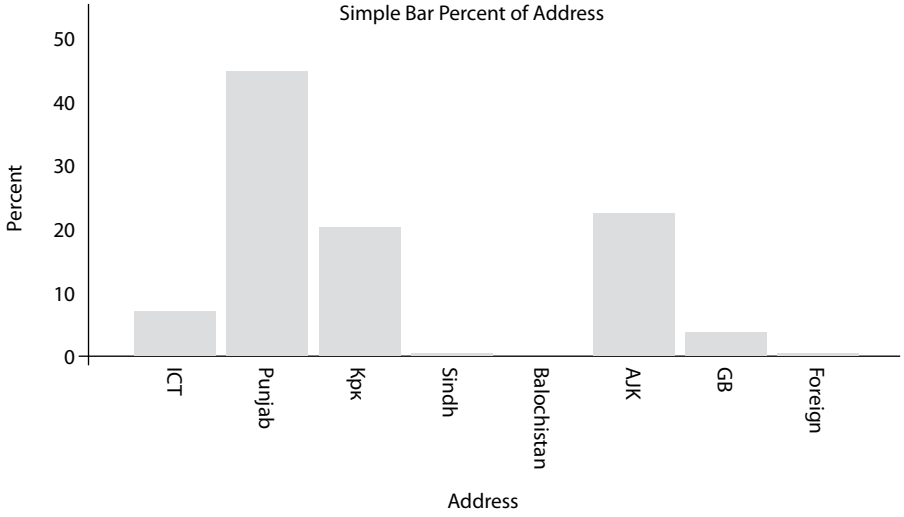

Fig. 2. Demographic distribution

Overall, the identification of these genetic and molecular abnormalities in AML can help guide treatment decisions and predict treatment outcomes.

■ DISCUSSION

The results of the study done at PIMS Medical Oncology in Islamabad, Pakistan, give important information about how people with acute myeloid leukemia (AML) are diagnosed, how they are treated, and how well they do afterward. The study looked

at 334 people who had been identified with AML. The aspiration of bone marrow was successful in confirming the diagnosis in the majority of the cases. techniques such as immunophenotyping, flow cytometry, and trephine biopsies.

According to the findings of the study, induction therapy with Arabinoside-cytarabine and daunoblastina did a good job of reaching the desired results. Patients have gone into complete remission in a significant number of cases. Complete remission entailed fewer than 5% blasts, no extramedullary illness, and 1,000 or more neutrophils and 100,000 platelets. Refractory illness was more than 20% bone marrow blasts, while partial remission was 5–19%. Any death within 3 weeks of induction chemotherapy was considered treatment-related mortality (TRM).

The study also identified several factors that can affect treatment response, prognosis, overall survival (OS), disease-free survival (DFS), and other outcomes in AML. These factors included age, performance status, cytogenetic and molecular abnormalities, response to initial therapy, and time to relapse. In particular, the presence or absence of specific cytogenetic and molecular abnormalities can help guide treatment decisions and predict treatment outcomes. For example, patients with AML and t (8;21), inv(16) / t (16;16), or t (15;17) abnormalities are associated with a better prognosis, while those with complex karyotype or FLT3-ITD mutations have a worse chance of getting better and may need more aggressive treatment, such includes the transplanting of stem cells from external sources.

Overall, the results of the study show how important it is for people with AML to get a correct diagnosis, a risk assessment, and individualized treatment. The identification of cytogenetic and molecular abnormalities can help guide treatment decisions and predict treatment outcomes, and this research may lead to novel targeted treatments that increase therapy efficacy and patient outcomes.

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