International Journal of Medical Science and Education
pISSN- 2348 4438 | eISSN-2349- 3208
Published by Association for Scientific and Medical Education (ASME)
Int.J.Med.Sci.Educ. Jan.-Feb. 2021; 8(1) : 61-64
Available Online at www.ijmse.com
Original Research Article

OUTCOMES OF ACUTE MYELOID LEUKEMIA FROM A TERTIARY CENTRE IN NORTH INDIA

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***Received:* 11/01/2021** ***Revised:*20/03/2021** ***Accepted:* 25/03/2021**

ABSTRACT

Background: The outcomes of Acute Myeloid Leukemia (AML) remain inferior in developing countries owing to poor accessibility of treatment and supportive care. **Methodology:** This study is a single-center retrospective observational study of patients diagnosed with AML in the preceding 2 years. **Results:** Forty-two patients were diagnosed with AML during the study duration. The median age was 38 years with a male preponderance. The majority of patients had an intermediate-risk genetic profile. 23.8% of patients presented with infection at the time of presentation. Patients received the following treatment regimens- 3+7 induction (36%), ATRA-based induction for APML (12%), metronomic therapy (19%), Hypomethylating agents (HMA) (7%), HMA+venetoclax (5%), and best supportive care only in 21%. Amongst patients receiving 3+7 induction- all developed febrile neutropenia, 80% developed CR, 33.3% had relapsed after CR. 45.2% of the total patients are currently alive. **Conclusions:** Treatment with curative intent was given to less than half of AML patients. There was a high prevalence of infections both at presentation and during chemotherapy. Induction mortality was 13.3%.

Keywords: Acute myeloid leukemia, 3+7 induction, metronomic chemotherapy, Azacitidine.

INTRODUCTION

The treatment of Acute Myeloid leukemia (AML) has undergone a paradigm shift in the last 5 years with many novel targeted agents gaining approval for use in the first line as well as relapse. (1)(2) However, the non-availability and poor affordability of these agents has ensured that in low and middle-income countries (LMICs), the older regimens of intensive chemotherapy remain the preferred modality of treatment.

The treatment of AML in resource-poor settings is hampered by high rates of infections, inadequate transfusion support, and high cost of treatment. The management of complications of intensive induction therapy remains an unmet need in our country. The use of antibiotics, antifungals, and transfusions increases treatment-related costs. The availability of donors for multiple transfusions also proves to be a hindrance. The result of this being that a large number of patients who would otherwise be eligible for chemotherapy with curative intent are ultimately unable to receive the same. While selecting the optimal management for patients of AML, the treating clinician has to take into consideration the social, financial issues, along with patient fitness and willingness.

Owing to these issues there is a vast divergence in the outcomes of patients with AML in trial settings versus those in the real-world setting. Also, there is a lot of heterogeneity in the choice of an initial treatment regimen. Since these issues are not routinely highlighted in trial data, we undertook this retrospective study to present the real-world experience of treating AML in a resource-limited setting.

METHODOLOGY

This was a single-center retrospective observational study done at a tertiary teaching hospital in North India. Patients who had been diagnosed with Acute myeloid leukemia at our center from 1st March 2019 to 31st December 2020 were included. The diagnosis was considered only if confirmed by flow cytometry analysis on either blood or bone marrow aspiration. This also included cases with acute promyelocytic leukemia (AML-M3).

Patients with other types of leukemia (chronic leukemias, lymphoblastic leukemia) or those who did not undergo flow cytometry evaluation for acute leukemia were excluded. Data were collected by retrospective review of hospital records. All data available till the last hospital visit was compiled. Demographic data, disease subtyping, risk stratification, treatment, and outcomes data were collected. Tabulation of data and statistical analysis was done in MS Excel.

RESULTS

A total of 42 patients were diagnosed with AML at our center during the study duration. The median age was 38 years with a male preponderance. (Table-1) Risk stratification was done by karyotyping and molecular assessment. Due to poor affordability, nearly a third of the patients did not get a risk stratification assessment done. Out of the remainder, the majority were an intermediate risk. 23.8% of patients presented with infection at the time of presentation. Treatment with curative intent was given in 48% of patients out of which 36% received 3+7 induction (Daunorubicin + cytarabine) 12% received all-trans retinoic acid (ATRA) based treatment for Acute promyelocytic leukemia (APML). 19% of patients were treated with oral metronomic treatment with oral prednisolone, 6-mercaptopurine, and etoposide. 21% of patients did not receive any disease-directed treatment and were managed with the best supportive care. (Figure-1)

There were 8 patients above the age of 60; 2 were treated with Venetoclax with Azacitidine and attained CR, 2 were treated with azacytidine alone and 1 achieved CR, and the rest by metronomic therapy and supportive care. All patients who received 3+7 induction developed febrile neutropenia. In this group, there were 2 deaths due to sepsis and 1 patient was refractory. (Table-2)

In all, 20 patients attained CR out of which 6 experienced relapse (12 and 4 respectively in the 3+7 group). 45.2% of the total patients are currently alive.

Figure-1. Choice of initial treatment modality

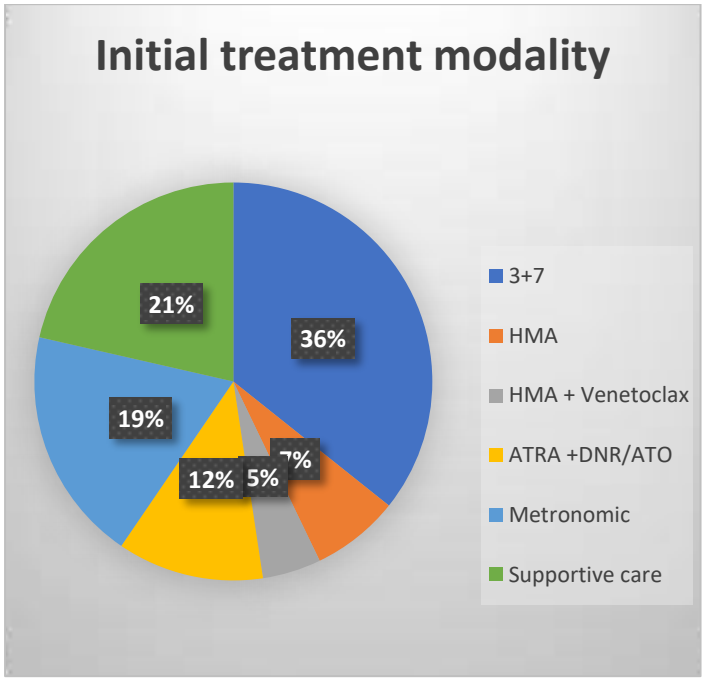

Table-1. Baseline characteristics of patients of AML (n=42)

Parameter	Result
Median age	38 years (3 – 72)
M:F	1.62:1
Risk stratification	N=27
Standard risk	9 (33.3%)
Intermediate risk	14 (51.85%)
Poor risk	4 (14.81%)
APML	5 (11.9%)
Baseline infection	10 (23.8%)

HMA- Hypomethylating agent (Azacitidine); ATRA- All-Trans Retinoic Acid; DNR- Daunorubicin; ATO- Arsenic trioxide

Table-2. Outcomes during 3+7 induction (n=15)

Parameter	Result
Infections during induction	15 (100%)
CR post-induction	12 (80%)
Death during induction	2 (13.33%)
Relapse after CR	4/12 (33.3%)

DISCUSSION

AML is a disease that may be seen in any age group and this was reflected in the wide age range of our patients. Current risk stratification guidelines advocate the use of conventional karyotyping along with molecular analysis with the help of PCR or next-generation sequencing. (3) However, these tests are quite costly and a large number of patients in LMICs are unable to get these done. A lot of patients with AML have delayed presentation to tertiary centers and hence they may have a serious infection at presentation as was the case in almost a quarter of our patients. 3+7 chemotherapy remains the standard treatment for patients fit for intensive treatment but not all patients can receive this. The reasons are lack of social, financial, and transfusion support. (4) Infections remain a significant concern with intensive chemotherapy, (5) and we observed all patients who received 3+7 developed febrile neutropenia. The mortality during induction used to be much more significant in the past but has improved in recent years due to ease of availability of apheresis platelets, broad-spectrum antibiotics, and antifungal agents along with increased sensitization towards hygienic practices. (6)

Older patients above the age of 60 are considered unfit for intensive induction and outcomes with low-dose cytarabine and hypomethylating agents (azacytidine and decitabine) used to be unsatisfactory. However, the introduction of BCL2 inhibitor Venetoclax has brought about a paradigm shift in the outcomes in this group. Venetoclax in combination with HMA is the current standard of care for patients unfit for intensive induction. (2) In this study it was observed that both patients who received this regimen attained a complete response. Venetoclax use in our country is limited due to difficulties in procurement and high cost.

Oral metronomic chemotherapy is inexpensive and less toxic although it carries a vastly inferior curative potential. It has been used in LMICs in patients who are not candidates for intensive chemotherapy. (7) It was used in 19% of patients in this study, none of these patients attained CR but many had stable disease for a few months.

There are several limitations of this study. It is a retrospective study and the sample size was small. Risk stratification and follow-up data were not available for all patients.

CONCLUSIONS

Owing to advanced age, poor performance status, and lack of social and financial support, treatment with curative intent was possible in less than half of AML patients. There was a high prevalence of infections both at presentation and during chemotherapy. Induction mortality was 13.3%.

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How to cite this article: Gupta N., Yadav A. Outcomes of acute myeloid leukemia from a tertiary center in north India. Int.J.Med.Sci. Educ 2021; 8(1):61-64