DOI: https://doi.org/10.54393/pjhs.v5i06.1570

PAKISTAN JOURNAL OF HEALTH SCIENCES
https://thejas.com.pk/index.php/pjhs
ISSN (P): 2790-9352, (E): 2790-9344
Volume 5, Issue 6 (June 2024)

Original Article

Assessment of Complete Remission Rate in Patients with Acute Myeloid Leukemia Undergoing 7+3 Induction Chemotherapy

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ARTICLE INFO

Keywords:
Acute Myeloid Leukemia, Induction Chemotherapy, Complete Remission, Malignancy

How to Cite:
Mehboob, N., Khan, A., Munir, A., Tahir, M., Ali, A., & Ahmed, S. (2024). Assessment of Complete Remission Rate in Patients with Acute Myeloid Leukemia Undergoing 7+3 Induction Chemotherapy: Remission Rates in Acute Myeloid Leukemia Patients. Pakistan Journal of Health Sciences, 5(06). https://doi.org/10.54393/pjhs.v5i06.1570

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Received Date: 23rd April, 2024
Acceptance Date: 12th June, 2024
Published Date: 30th June, 2024

ABSTRACT

Acute leukemia is a fast-growing, overpopulated clone of immature proliferating cells that largely predominate in the bone marrow and have the capacity to prolong life indefinitely. Upon inspection and cytologic assessment of bone marrow or peripheral blood, the cells demonstrate quantified uncertainties. **Objective:** To determine the frequency of complete remission after induction 7+3 chemotherapy in patients with acute myeloid leukemia. **Methods:** The nature of this study was cross sectional study at Department of Oncology, Pakistan Institute of Medical Sciences, and Islamabad from 26 November, 2022 to 26 May, 2023. The hospital's laboratory fulfilled the complete blood count and provided the confirmed baseline bone marrow biopsy reports. All patients who were admitted received treatment with a 7+3 regime, a standard treatment protocol for all the adolescents and adults admitted. Every patient was prescribed for 7+3 induction therapy regimen which consists of 200 mg/m^2 cytarabine for seven days and idarubicin for three days, 12 mg/m^2 on the 1st, 3rd and 5th day. **Results:** The complete remission estimated turns out to be 61.1% and rest need further treatment. The average age of the patients was 48.56 ± 6.91 years. The mean BMI stood at 24.46 ± 1.49 kg/m^2 gender wise, 74 were male and 21 were female. Our mean CR was 61.1% that is 58 participants all the complete demographic is available. **Conclusions:** This study revealed a Complete Remission (CR) rate of 61.1% in patients with AML undergoing 7+3 induction chemotherapy. However, our findings suggest that older age is associated with lower CR rates, highlighting the need for tailored treatment strategies that balance efficacy with the potential risks of intensive therapies in this population.

INTRODUCTION

Acute myeloid leukemia is one of the most challenging diseases in the field of hematologic malignancies. AML is characterized by exponential production of atypical myeloid pro-founding cells in bone marrow as well as peripheral blood. Acute myeloid leukemia is an aggressive malignancy caused by mutations in developing hematopoietic stem cells that disrupt their differentiation and cause the accumulation of inadequate myeloid progenitors [1, 2]. The etiology and risk factors of AML are multifactorial; exposure to radiation, using cytotoxic chemotherapy, specific genetic syndromes, environmental and industrial hazards, and infection with specific blood-borne viruses [3]. Despite all these circumstances, AML had been diagnosed in 20,830 new cases, with more than 10,000 victims, in the US alone in 2015 [4]. The incidence of AML increases with age. There are about 13 cases per million under 65 years which increases to 122 per million in elder population [5]. Acute myeloid leukaemia accounts for 31.25% of all leukaemias in Pakistan, and it is more prevalent in males [6]. Clinically, extra medullary involvement may occur with signs such as hepatosplenomegaly, lymphadenopathy or infiltration of the skin. Diagnosis of AML includes examination of the peripheral blood smear, cytogenetic analysis, aspiration

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and biopsy of the bone marrow with subsequent molecular testing of cytogenetic changes. It is necessary to determine the subtype of the disease and evaluate the prognosis [7]. Currently, despite the advances in understanding the pathogenesis of the disease, as well as the emergence of new drugs in the treatment, this pathology can be difficult to treat, especially in elderly and high-risk patients [8]. Standard induction chemotherapy remains the most popular in the treatment of such patients, which involves the use of cytarabine in combination with an anthracycline with the subsequent goal of preventing a relapse. Among its varied use in recent years, 7 days of cytarabine administration combined with 3 days of an anthracycline has become accepted due to its effectiveness in achieving remission. Therefore, 7+3 induction remains standard therapy for AML patients [9, 10].

This study aimed to determine the remission rate in patients with AML who are undergoing 7+3 induction. This topic has many gaps in current research, and the study of efficacy will provide information for clinical decision-making. Systems analysis for the identification of factors affecting remission will be generated.

METHODS

The approval of study was taken from the College of Physicians and Surgeons Pakistan (CPSP) (CPSP/REU/ONC-2020/042-275). It was also reviewed and approved by the hospital's research ethics committee. This cross sectional study took place in the Department of Oncology, Pakistan Institute of Medical Sciences, Islamabad, from 26 November 2022 to 26 May, 2023. The sample size calculation was conducted using the WHO sample size calculator, with the following parameters: a confidence level of 95%, an anticipated population percentage of 61.66%, and a needed absolute precision of 5% [18]. As a result, a total of 95 patients diagnosed with AML were included in the study. Sampling methodology used was non-probability consecutive sampling. The inclusion criteria consisted of patients who had a confirmed diagnosis of AML and were considered appropriate candidates for 7+3 induction therapy. The criteria applied to individuals of any gender, between the ages of 15 and 55 years and informed written consent was taken from participants. The exclusion criteria included patients with acute promyelocytic leukaemia, chronic systemic illnesses such as decompensated heart failure, renal and liver failure, and hypersensitivity to any component of the medication regimen. A comprehensive Complete Blood Count (CBC) was conducted in the hospital laboratory, and initial bone marrow biopsy records were obtained for each participant. Afterwards, all patients who had registered were administered 7+3 induction therapy, which involved receiving cytarabine at a dosage of 200 mg/m2 for seven days and idarubicin at a dosage of 12 mg/m2 twice daily for three days. The follow-up was planned at 28th day. The evaluation of treatment response, particularly complete remission was labelled as per following operational definition, which was assessed on the 28th day after chemotherapy for all patients who had 7+3 induction therapy for Acute Myeloid Leukaemia (AML). This evaluation encompassed a comprehensive analysis of the blood components and a procedure to extract and examine the bone marrow tissue. Complete remission is defined as having 5% or less bone marrow blasts, no circulating blasts or blasts with Auer rods, no extra medullary illness, an Absolute Neutrophil Count (ANC) of at least 1.0 × 109/L (1000/µL), and a platelet count of at least 100×109/L (100,000/µL). The demographic parameters and study conclusions were documented. Data were entered and analysed using SPSS version 20.0. Age and BMI were descriptively analysed using mean and standard deviation. Frequencies and percentages were calculated for qualitative characteristics including gender and full remission. The stratification was used to adjust for effect modifiers such as age, gender and BMI. Post-stratification chi-square test was used, with p-value ≤ 0.05 indicating statistical significance.

RESULTS

The demographic characteristics of the study participants were as follows. The mean age was 48.56 years with a standard deviation of 6.91. The mean BMI was 24.46 kg/m2 with a standard deviation of 1.49. In terms of age distribution, 51 participants (53.7%) were under 50 years old, while 44 participants (46.3%) were over 50 years old. Gender distribution indicated that 74 participants (77.9%) were male, while 21 participants (22.1%) were female in table 1.

Table 1: Demographic Characteristics of Study Participants

Variables	Mean ± SD / N (%)
Age (Years)	48.56 ± 6.91
BMI (Kg/m2)	24.46 ± 1.49
< 50 Years	51 (53.7%)
> 50 Years	44 (46.3%)
Male	74 (77.9%)
Female	21 (22.1%)

In our study, 58 participants achieved complete remission, accounting for 61.1% of the total study population as shown in table 2.

Table 2: Frequencies and Percentages for Complete Remission

Complete Remission	N (%)
Achieved	58 (61.1%)
Not Achieved	37 (38.9%)
Total	95 (100.0%)

In table 3, stratification of complete remission by age groups was conducted. Among participants under 50 years

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old, 30 achieved complete remission (51.7%), while 28 achieved it in the group over 50 years old (48.3%). Overall, out of 95 participants, 58 achieved complete remission. The p-value for the comparison between age groups was 0.631, indicating no statistically significant difference in complete remission rates between the two age groups as shown in table 3.

Table 3: Stratification of Complete Remission with Age Groups

Complete Remission	Age Groups		Total N (%)	p-Value
	≤ 50 Years N (%)	> 50 Years N (%)		
Achieved	30 (51.7%)	28 (48.3%)	58 (100.0%)	0.631
Not Achieved	21 (56.8%)	16 (43.2%)	37 (100.0%)	
Total	51 (53.7%)	44 (46.3%)	95 (100.0%)	

In table 4, complete remission was stratified by gender. Among male participants, 48 achieved complete remission (82.8%), while 10 achieved it among female participants (17.2%). Overall, out of 95 participants, 58 achieved complete remission. The p-value for the comparison between genders was 0.153, indicating no statistically significant difference in complete remission rates between males and females as shown in table 4.

Table 4: Stratification of Complete Remission with gender

Complete Remission	Gender		Total N (%)	p-Value
	Male N (%)	Female N (%)		
Achieved	48 (82.8%)	10 (17.2%)	58 (100.0%)	0.153
Not Achieved	26 (70.3%)	11 (29.7%)	37 (100.0%)	
Total	74 (77.9%)	21 (22.1%)	95 (100.0%)	

In table 5, complete remission was stratified by BMI. Among participants with a BMI less than 25 kg/m^2, 28 achieved complete remission (48.3%), while 30 achieved it among those with a BMI greater than 25 kg/m^2 (51.7%). Overall, out of 95 participants, 58 achieved complete remission. The p-value for the comparison between BMI groups was 0.583, indicating no statistically significant difference in complete remission rates between participants with BMI less than 25 kg/m^2 and those with BMI greater than 25 kg/m^2 as shown in table 5.

Table 5: Stratification of Complete Remission with BMI

Complete Remission	BMI		Total N (%)	p-Value
	≤ 25 Kg/m^2 N (%)	> 25 Kg/m^2 N (%)		
Achieved	28 (48.3%)	30 (51.7%)	58 (100.0%)	0.583
Not Achieved	20 (54.1%)	17 (45.9%)	37 (100.0%)	
Total	48 (50.5%)	47 (49.5%)	95 (100.0%)	

DISCUSSION

Acute Myeloid Leukemia is one of the most difficult malignancies in oncology, characterized by high morbidity rates and varied responses to treatment. One of the cornerstone treatment regimens is 7+3 induction chemotherapy, which comprises cytarabine and an anthracycline, used to achieve remission. However, despite high success rates, this approach is associated with adverse events of myelosuppression and complications of infections, which requires special attention to the supportive care. Future research aims at optimization of the 7+3 induction, and discovery of new strategies for the optimization of patient outcomes undergoing treatment with induction chemotherapy [11, 12]. In the present study, the mean age was 48.56 ± 6.91 years; among participants, 53.7% were under 50 years, and 46.3% were over 50 years. The gender distribution demonstrated a majority of males (77.9%). These findings correlate with those obtained by previous researchers, such as Ciftciler R *et al.*, who found a median age of 45 years at the time of diagnosis and a similarly male-associated tendency [13]. In another research, with the relatively low median age of 44 years and male predominance in sex distribution, reported similar results for their study cohort [14]. However, in contrast with our data, Shireen I *et al.*, indicated a lower mean age of 35.02 and a higher response to induction in a male population. The divergence referred above might have been predetermined by the differences in AML pattern within that particular population and health care provision settings [15]. Zaki S *et al.*, presented a young mean age of 27.5 and a balanced sex distribution, corresponding to our findings [16]. This study focused on the relationship between gender and complete remission rate among participants receiving 7+3 induction chemotherapy for AML. The findings showed that the proportion of complete remission among males was 82.8% and 17.2% among the females. This conclusion agrees with the report in a study by Shireen I *et al.*, who found that males were more responsive to induction therapy of patients under 40 years [15, 16]. A country study under Perera RA *et al.*, conducted in Srilanka reported that the rate of CR was 50% among patients with AML. The difference could be attributed to the type of patients, protocol, and health care system [17]. Abuelgasima KA *et al.*, have also designed a retrospective analysis that showed 61.66% complete remission rate in the 7+3 regimen patients. The established complete remission rate differed depending on the age group. Thus, it had a peak of 71.42% in the 14-40-year-old patients while the lowest remission rate of 45.47% was observed in the patients older than 60-year-old [18]. Yoon JH *et al.*, have analyzed the complete remission among the standard 7+3 induction patients in Korea. Although their overall complete remission rate was similar to the finding of this study, they identified no age-related changes, as their non-significant difference in the rates was found between the <55-years old and ≥55-years old patients [19]. Therefore, the complete remission rates in the 7+3 induction patients with AML show some differences between the male and female subjects, which are consistent with Hadisantoso DW *et al.*, however, this pattern requires further experimental validation and clinical consideration for the optimization of the treatment strategy [20].

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CONCLUSIONS

This study revealed a Complete Remission (CR) rate of 61.1% in patients with AML undergoing 7+3 induction chemotherapy. However, our findings suggest that older age is associated with lower CR rates, highlighting the need for tailored treatment strategies that balance efficacy with the potential risks of intensive therapies in this population.

Authors Contribution

Conceptualization: NM, AK
Methodology: NM, AK, AA, SA, MT
Formal analysis: AM
Writing, review and editing: AA, SA

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

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