*Original Article*

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# Clinical Profile and Outcomes of Acute Myeloid Leukemia: An Institutional Experience from South India

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**Abstract**

*Background:* Acute myeloid leukemia is a heterogenous clonal disorder of hematopoietic progenitor cells with different molecular genetic abnormalities, clinical characteristics and variable outcomes with currently available treatment. Aim of the study is to analyse the clinical profile & outcomes of AML, an institutional experience where BMT facility is not available. *Aims:* Clinical profile and outcomes of Acute myeloid leukemia is evaluated. *Material and Methods:* Retrospective chart review of 51 patients diagnosed of AML with clinical and therapeutic data analysed. *Results:* 51 patients were analysed (males 30, females 21) with a male predominance. 90% (46/51) of patients were in the age group of <60 yrs & nearly 40% (20/51) were 15–30 yrs which is significant. M2 was the most common FAB subtype with 23/51 (45%) cases and most common presentation is fever. The observed average baseline parameters were: Hb of 6–8 gr% with 30% showed <6 gr%,TLC >15,000 in 90% of cases which confer poor outcomes (60% cases – >50,000 and 30% – >1 lakh). The average platelet count was 20,000–40,000 (25% cases – <20,000). Most patients had a baseline blasts% of >70. The average number of transfusions required during induction were in the range of (PRBCs-4–6, RDPs-20–30, SDPs-2–4 & overall 25–35). Among 51 patients, approxly 75% (38/51) were treated with intensive chemotherapy and 13 were on BSC. Remission rate was found to be 42% (16/38) in patients who received induction chemotherapy while >95% of them relapsed. As most of the patients were not on follow up or died, no follow up data was found to calculate the survivals. *Conclusions:* AML is an aggressive malignancy with poor outcomes and high relapse rates, especially without BMT. Supportive care constitutes a major component of management. As most of the patients were presenting very late and in poor PS (bad parameters at baseline) early aggressive treatment with strong supportive care improve the cure rates and survival.

**Keywords:** AML (Acute myeloid leukemia); Clinical profile; BMT (Bone marrow transplant).

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## Introduction

Leukaemias are a heterogeneous group of hematopoietic malignancies that include many diverse and biologically distinct subgroups. The four major subtypes of leukemia described by most cancer registries include acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphoblastic leukemia (CLL), and chronic myeloid leukemia (CML). Several reports have studied the trends in leukemia incidence and survival. Many of these studies have either addressed leukemia overall or have focused on young patients. Ecologic data that explore trends in cancer incidence can provide important information regarding potential changes in risk factors and can reflect underlying changes in diagnostic classification AML, the second largest subgroup in children but the most common leukemia type

among adults,[1] represents 15–20% of leukemia cases in children, and is responsible for up to 30% of pediatric leukemia related deaths.[2,3]

The purpose of this review is to summarize the published literature on reported current clinical profile and outcomes of AML in south India. Present study aims to evaluate Clinical profile and outcomes in acute myeloid leukemia.

## Materials and Methods

Data were obtained from the tertiary care center for cancer in south India. Study done to evaluate Clinical profile and outcomes in Acute myeloid leukemia. Data was reviewed The oncology center has all oncology services including hematology and hematopoietic stem cells (HPSC) in the bone marrow transplant service. This is a case series retrospective study that included all patients diagnosed with any AML subtypes from 2006 to 2013. Patients with mixed phenotypes leukemia were excluded. The data was retrieved manually from medical records, and electronically from the hospital electronic medical record system for clinical data and the laboratory information system for flow cytometry and immunopheno type results. The data collected included patients' demographics data and FAB pathologic subtypes of the disease, treatment protocol and response to treatment. The molecular genetic tests were either not done or not available for the majority of patients.

About 51 patients are diagnosed with AML all children and adult patients with AML included in study. The whole population was studied, so no sampling was required. Data were entered into excel spreadsheets and then managed with SPSS (IBM SPSS version 16.0) using descriptive methods: Mean, standard deviation for numerical variables, percentages, frequencies for all categorical variables.

## Results

Fifty-one patients were analysed (males 30, females 21) with a male predominance. 90% (46/51) of patients were in the age group of <60 yrs & nearly 40% (20/51) were 15-30 yrs which is significant. M2 was the most common FAB subtype with 23/51 (45%) cases (Table 1).

M2 subtype is the most common FAB subtype with 23/51 (45%) cases (Fig. 1).

**Table 1:** Demographic details in present study

| Age groups | Males Number of patients (%) | Females Number of patients (%) | Total Number of patients (%) |
|---|---|---|---|
| 10–20 Years | 8 | 2 | 10 (19.6%) |
| 21–40 years | 8 | 10 | 18 (35.2%) |
| 41–60 years | 12 | 6 | 18 (35.2%) |
| >60 years | 2 | 3 | 5 (9.8%) |
| **Total** | **30** | **21** | **51** |
| Range | | 13–71 years | |

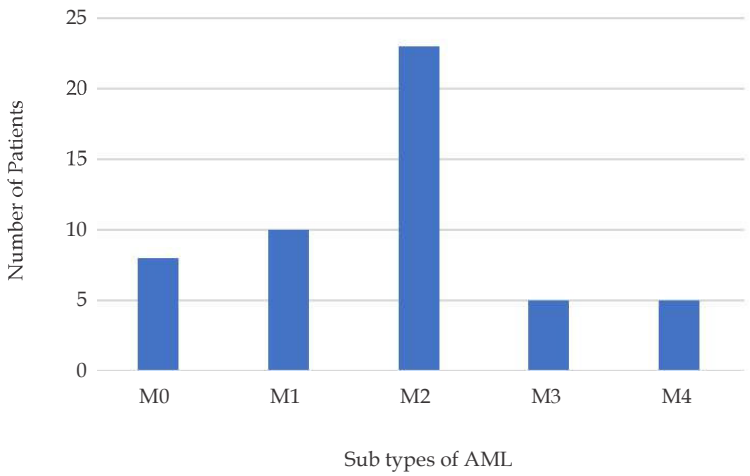


**Fig. 1:** Number of patients in subtypes in AML.

Most common presentation in present study is fever followed by fatigue, loss of appetite, weight. (Table 2).

The observed average baseline parameters were: Hb of 6–8gr% with 30% showed <6 gr%, TLC >15,000 in 90% of cases which confer poor outcomes (60% cases – >50,000 and 30% – >1lakh).The average platelet count was 20,000–40,000 (25% cases - <20,000). Most patients had a baseline blasts% of >70. 5 (9.8%) patients have <10% of blast cells. The average number of transfusions required during induction were in the range of (PRBCs-4–6,RDPs-20-30,SDPs-2–4 & overall 25–35) (Table 3).

**Table 2:** Common presentation in present study

| Symptom or complaint | Number of patients | Percentage |
|---|---|---|
| Fever | 51 | 100% |
| Loss of appetite | 7 | 13.7% |
| Loss of weight | 6 | 11.7% |
| Pain abdomen | 2 | 3.9% |
| Weakness | 4 | 7.8% |
| Cough or SOB | 5 | 9.8% |
| Fatigue | 16 | 31.3% |
| Bleeding gums | 7 | 13.7% |
| Misellenous | 6 | 11.7% |

**Table 3:** Baseline investigation details in present study

| Baseline investigation details | Number of patients (percentage) |
|---|---|
| **Diagnostic Part** | |
| Flow cytometry done | 38 (75%) |
| Cytogenetic analysis done | 13 (20%) |
| **Baseline Average Hb % in grams** | |
| 6–8 grms % | 15 (30%) |
| < 6 grms % | 36 (70%) |
| **Baseline average Total WBC count** | |
| >50,000 | 31 (61%) |
| > 1 Lakh | 20 (39%) |
| **Baseline Average Platelets** | |
| < 20,000 | 13 (25%) |
| 20,000–40,000 | 38 (75%) |
| **Baseline Average Blasts cells** | |
| >10% | 5 |
| 20–40% | 19 |
| 41–70% | 5 |
| >70% | 22 |
| Average Packed cell volumes (PRBCs) | 4–6 units |
| Average Random donor platelets (RDPs) | 20–30 units |
| Average Single donor platelets (SDPs) | 2–4 units |
| Average Overall transfusions | 25–35 units |

Among 51 patients, approxely 75% (38/51) were treated with intensive chemotherapy and 13 were on BSC. Remission rate was found to be 42% (16/38) in patients who received induction chemotherapy while >95% of them relapsed (Table 4).

As most of the patients were not on follow up/ died, no followup data was found to calculate the survivals.

**Table 4:** Treatment and response observed in present study.

| Conventional Treatment | % of Patients |
|---|---|
| Chemotherapy | 38/51 cases (75%) |
| Best supportive care (BSC) | 13/51 cases (25%) |
| **Response** | |
| Remission | 16/38 cases (42%) |
| Relapse | >95% of Patients |

## Discussion

In this retrospective study, we were able to show some of the clinical and pathological features of AML in South india patients treated at a single center. 51 patients were analysed (males 30, females 21) with a male predominance. AML studies showed gender differences in data taken from Yeh *et al*.,[4] the gender ratio (male/female) was 5/1, showing a clear male predominance. Contrastingly, data from Gilbert *et al*.[5] showed a clear female predominance with a gender ratio of 3/6. In both cases, study sizes were small (*n*=6 and *n*=9, respectively). The gender ratio was approximately 50:50 in larger studies, as reflected by studies by Guglielmi *et al*.[6] (*n*=63, gender ratio: 33/30) and Biondi *et al.* (*n*=54, gender ratio: 28/26).

In present study 90% (46/51) of patients were in the age group of <60 yrs & nearly 40% (20/51) were 15–30 yrs which is significant. In the Faleh AA[7] study, mean age at presentation was 36.9 years (range 2–74 years) which is much younger than described in the literature (58–63 years) which coincides with study done by Cheng Y *et al*.[8]

During the 1970's, a classification of AML was established by a group of experts called "The French-American-British (FAB) classification of AML." The classification divided AML into eight subtypes from M0 to M7 based on the morphology of blast cells and the degree of maturation of those cells. Recently, the WHO classification of AML was based mainly on the genetic changes, the etiologic factors of AML, and the morphologic classification of the disease. This new classification gives better insight for the causes of the disease, options of therapy and prognosis of AML.[9]

In present study M2 was the most common FAB subtype with 23/51 (45%) case. In study done by Faleh AA[7] showed predominance of M1 and M2, followed by M4 and M5 with cases of M0,M6 and M7 representing only around 5%. Another local study, on AML patients showed that M4 and M5 are the dominant subtypes.[10] Regarding the risk stratification for our patients', the majority was in the intermediate risk group with most of those patients having normal cytogenetic. However, as has been shown recently in many studies those patients with normal cytogenetic can be further stratified into favourable or high risk based on presence or absence of certain molecular genetic aberrations.

The observed average baseline parameters were Hb of 6–8 gr% with 30% showed <6 gr%, TLC >15,000 in 90% of cases which confer poor outcomes (60% cases – >50,000 and 30% – >1 lakh).The average platelet count was 20,000–40,000 (25% cases – <20,000). Most patients had a baseline blasts% of >70. 5 (9.8%) patients have <10% of blast cells. Intensive-chemotherapy based-treatment strategies are appropriate for patients regardless of the blasts percentage at AML diagnosis, suggesting this to be an appropriate strategy in all patients with blasts are ≥10%. However, among older patients, HMA therapy was associated with similar or improved outcomes compared with intensive chemotherapy approaches.

Among 51 patients, approxely 75% (38/51) were treated with intensive chemotherapy and 13 were on best supportive care. Remission rate was found to be 42% (16/38) in patients. The CR rate post induction chemotherapy in cohort was 73% after one induction cycle and 84% after one or more cycles which is more when compared but they r many studies in which relapse rate is less when compared with our study as in Table 5.

**Table 5:** Remission rate in comparision with other studies

| Study | Patients (n) | Remission rate (%) |
|---|---|---|
| Silverman[11] | 91 | 9 |
| Fenaux[12] | 103 | 33 |
| Seymour[13] | 107 | Nil |
| Thepot[14] | 138 | 14 |
| Maurillo[15] | 82 | 19 |
| Present study | 51 | 42 |

This high rate of CR in our patients population was seen in all risk groups. This response rate is higher than what has been reported from different clinical trials (60–70%) (Table 5). Another local study on AML patients showed that 65% of the study

population had first CR.[16] Possible explanations for the high response rate in our patients, we may have included some patients with favorable risk based on molecular genetic mutations, and usually those patients have high response rate. Another possible reason for this high complete response rate is inclusion of those who received multiple induction cycles, that is, more than one cycle and subsequently achieved a complete response.[17]

In present study patients who received induction chemotherapy relapse rate is 95%. Phase II combination-agent studies with CR2 rates ranging from 14 to 87%, and four phase III randomized studies with CR2 rates ranging from 40 to 89% which coincides with present study.[18–20]

The response to treatment is poor, and best treatment responses. It remains unclear whether these late relapses are a second AML, or relapse with the original clone. Reduction of relapse rates requires adoption of appropriate risk-stratified (including minimal residual disease if feasible) adapted treatment regimens based on the experience, infrastructure, and supportive care available at a center as proposed in recent guidelines. Most importantly, collaborative efforts, which promote treatment of patients on common protocols and encourage prospective multi-center clinical trials, are required. Collaboration among individuals and institutions regionally, nationally, and internationally has been fundamental to the remarkable progress made in India. Finally, it is important to point out the lack of data from India on late effects, in future, we improve survival while reducing late effects with acute leukemia in India.

## Conclusion

AML is a very aggressive malignancy with poor outcomes and high relapse rates, Supportive care constitutes a major component of management. Blood and blood products transfusions give symptomatic relief and improve quality of life of patients planned for BSC though this is temporary and short term. Early aggressive treatment with strong supportive care forms the cornerstone of management.

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