RESEARCH ARTICLE

Editorial Process: Submission:06/14/2025 Acceptance:02/27/2026 Published:03/06/2026

Cytogenetic Profile of Newly Diagnosed Acute Myeloid Leukemia Patients: Insights from a Study at a Tertiary Care Centre in South India

Devipriya Padmakumar[1], Vineetha Radhakrishnan Chandraprabha[1], Jagathnath Krishna Kumarapillai Mohanan Nair[2], Akhila Raj Thampirajan Vimala Devi[1], Geetha Raj John Anitha[1], Mahitha Mohanan Sreelatha[1], Amritha Padmakumar[1], Suraj Lathika Surendran[1], Geetha Narayanan[3], Hariharan Sreedharan[2]*

Abstract

Purpose: Acute Myeloid Leukemia (AML) is a heterogeneous hematologic malignancy characterized by a wide range of cytogenetic abnormalities that have critical diagnostic and prognostic implications. South Indian populations are underrepresented in global AML research, warranting region-specific cytogenetic profiling. **Methods:** We performed a cytogenetic analysis of 400 newly diagnosed adult AML patients at a tertiary care center in South India. Conventional karyotyping and fluorescence in situ hybridization (FISH) were performed, and findings were correlated with clinical parameters according to the 2016 WHO and FAB classifications. **Results:** Abnormal karyotypes were observed in 49.5% of cases, while 50.5% showed normal karyotypes. The most frequent abnormalities were t(15;17) (16.2%), t(8;21) (6.7%), and inv(16) (3.7%). Other notable findings included trisomy 8 (1.7%), trisomy 21 (1%), and complex karyotypes (6.5%). AML-M4 (33.5%) was the most common FAB subtype. Significant associations were noted between cytogenetic risk groups and variables such as age, gender, and white blood cell count. The distribution of cytogenetic aberrations revealed both similarities and distinct differences when compared with global data, reflecting ethnic and geographical influences. **Conclusion:** This study highlights the cytogenetic diversity of AML in a South Indian cohort and confirms the importance of cytogenetic analysis in disease classification, risk stratification, and therapeutic decision-making. The findings underscore the need for regional data to refine AML diagnosis and optimize management strategies across different populations.

Keywords: Acute myeloid leukemia- cytogenetics- chromosomal abnormalities- karyotyping- South India

Asian Pac J Cancer Prev, **27 (3)**, 921-929

Introduction

Acute myeloid leukemia (AML) occurs when transformed hematopoietic stem cells (HSCs) undergo clonal expansion due to the acquisition of genetic abnormalities, including chromosomal rearrangements and mutations in multiple genes [1]. It is the second most frequently diagnosed leukemia in both adults and children, although the majority of patients manifest in adults. Despite an overall 5-year survival estimate of 28.3% for all AML cases, individuals aged 60 years or older face a significantly lower survival rate, ranging from 3% to 8% [2].

Cytogenetic analysis reveals clonal chromosome aberrations in around 50% of individuals diagnosed with de novo AML. These chromosomal abnormalities offer valuable insights into the pathogenesis of AML [3]. Karyotype analysis must be carried out as part of the standard diagnostic procedure of AML. Analysis of cytogenetic abnormalities is crucial in AML, serving as the foremost prognostic factor for cases. Indeed, cytogenetic studies aid in classifying prognosis groups, guide in making better treatment strategies, and enhance patients' overall outcomes, thereby improving their chances of recovery [4]. The identification of specific chromosomal abnormalities and their correlation with cytomorphologic features, immunophenotype, and clinical outcome aids in the understanding of the heterogeneity of AML. The classification of AML is determined by the World Health Organization (WHO). As per the WHO

*[1]Laboratory of Cytogenetics and Molecular Diagnostics, Division of Cancer Research, Regional Cancer Centre, Thiruvananthapuram, University of Kerala, India. [2]Division of Cancer Epidemiology and Statistics, Regional Cancer Centre, Thiruvananthapuram, India. [3]Medical Oncology, Regional Cancer Centre, Thiruvananthapuram, India. *For Correspondence: drshariharan@gmail.com*

guidelines, diagnosis of AML is confirmed when there is an observation of 20% or more leukemic myeloblasts in either the peripheral blood (PB) or bone marrow (BM) [5]. Among the numerous cytogenetic abnormalities observed in AML, patients with acute promyelocytic leukemia (APL) consistently demonstrate favorable outcomes when presenting with t (15;17) (q22;q12). Additionally, the presence of t (8;21) (q22;q22) and inv (16) (p13q22)/t (16;16) (p13;q22) has been consistently linked to improved prognosis. Conversely, adverse prognostic outcomes are frequently associated with abnormalities such as 3q (abn(3q)) deletions of 5q (del(5q)), monosomy of chromosomes 5 and/or 7 (-5/-7), t(9;22), or complex chromosomal aberrations [6]. Nevertheless, nearly 50% of adult AML patients receive a diagnosis of a normal karyotype (NK), indicating the absence of identified structural aberrations during cytogenetic analysis.

The diagnostic karyotype is a highly influential and autonomous prognostic factor in acute myeloid leukemia (AML). It plays a crucial role in delineating biologically distinct disease categories and has gained widespread acceptance as the basis for tailoring treatment strategies according to risk profiles. In the present study, we aimed to analyze the association between cytogenetic and clinical parameters and their frequencies in different AML subtypes in a large cohort of 400 newly diagnosed adult AML cases.

Materials and Methods

Patient Cohort

The study subjects comprised 400 de novo AML patients who attended the outpatient clinics of the Regional Cancer Centre, Thiruvananthapuram, from January 2020 to June 2022. Patients between the ages of 18 and 74 were included in the study. The diagnosis of AML was established according to the 2016 World Health Organization (WHO) classification and subtyped by following the French–American–British (FAB) classification, which includes eight subtypes ranging from M0 to M7 by the morphological analysis of bone marrow aspiration [7]. 2 ml of Bone Marrow samples were collected from all the patients after getting written informed consent from all the patients selected for the study. All procedures were performed in accordance with the ethical standards of the institution and the 1975 Helsinki Declaration and its later amendments. The study was approved by the Institutional Review Board (IRB) and Human Ethics Committee of the Regional Cancer Centre (HEC No: 23/2020).

Cytogenetic analysis

Cytogenetic analysis was performed on pretreatment bone marrow samples. The samples were cultured in the RPMI 1640 medium (Sigma), supplemented with fetal bovine serum. The harvesting procedure was followed by incubation, centrifugation, and the addition of a hypotonic solution(0.56% KCl). Following the addition of the fixative, consisting of a 3:1 ratio of methanol and glacial acetic acid, trypsin treatment and Giemsa staining were carried out. A total of 20 well-spread metaphase cells were analyzed, and G-banded karyotypes at the 550 band levels were constructed in each patient. Twenty metaphases were karyotyped using cytogenetic software (Genasis, Applied Spectral Imaging, Migdal Ha'Emek, Israel, and Cytovision, USA) and Ikaros karyotyping software (MetaSystems GmbH, Altlussheim, Germany). Karyotypes were described based on the International System for Human Cytogenetic Nomenclature (ISCN, 2020).

Fluorescence in situ hybridization (FISH)

FISH analysis for the confirmation of chromosomal abnormalities such as t(8;21)(q21.3;q22), t(15;17)(q24;q21), inv(16) (p13q22)/t(16;16)(p13;q22) and t(9;22)(q34;q11) were performed by using corresponding Vysis probe (Abbott, USA). Bone marrow samples collected in heparin were harvested directly or after chromosome culture. After denaturation at 75°C for 10 min, the cells on slides were hybridized at 37°C overnight. On the 2nd day, the slides were washed to remove nonspecifically coupled probes and then counter-stained with DAPI. Approximately 200 cells were analyzed under a BX51 fluorescence microscope (Olympus, Japan) equipped with appropriate filter sets to discriminate between a maximum of 5 fluorochromes and the counterstain DAPI (4′,6-diamidino-2-phenylindole). The hybridization signals were captured using a Spectra Cube SD200 spectral imaging system (Genasis, Applied Spectral Imaging, Migdal Ha'Emek, Israel, and Cytovision, USA)

Statistical Analysis

Age, gender, and types of cytogenetic abnormalities were included for analysis, and results were expressed as frequencies and percentages. For categorical variables such as sex, the chi-square test or Fisher's exact test was used. The significance between karyotype status and clinical parameters was calculated by the Mann-Whitney U Test. Kruskal-Wallis Test was used for comparison between the risk groups. A p-value of <0.05 was taken as significant.

Results

Patient characteristics and morphological subtypes

The study cohort comprised a total of 400 de novo AML cases. There were slightly more females than males, with a ratio of 1:1.05(M/F-195/205) (Table 1). The median age of the patients was 47.5. According to the FAB classification system, AML M4(134, 33.5%) accounts for the most frequent subtype in our study group, which is followed by AML M5(72, 18%), then AML M1(67, 16.7%), AML M2(47, 11.7%), and AML M3(65, 16.2%). There were 13(3.2%) patients belonging to the AML M0 subtype, while only one patient each belonged to the AML M6 and M7 subtypes (Table 1).

Cytogenetic Characteristics

Out of 400 patients with successful cytogenetic results, normal karyotypes were observed in 202(50.5%) cases. Abnormal karyotypes were found in 198(49.5%) cases. The most common abnormalities identified were t(8;21)

Table 1. Patient Characteristics, Morphology, and Cytogenetic Risk Stratification of AML Cases

Characteristics	Total
Total No of Cases	400
Median age(range), (years)	47.5 (17-75)
Sex ,n(%)	
Male	195 (48.8)
Female	205 (51.2)
FAB Classification, n (%)	
M0	13 (3.2)
M1	67 (9.2)
M2	47 (11.7)
M3	65 (16.2)
M4	134 (33.5)
M5	72 (18)
M6	1 (0.2)
M7	1 (0.2)
Risk Stratification n (%)	
Favourable	107 (26.7)
t(8;21)	27 (6.7)
inv(16)	15 (3.7)
t(15;17)	65 (16.2)
Intermediate	241 (60.2)
Normal	202 (50.5)
Trisomy 8	7 (1.7)
Trisomy 21	4 (1)
Other abnormalities	28 (7)
Adverse	52 (13)
-7/del7q	9 (2.2)
-5/del5q	5 (1.2)
t(6;9)	5 (1.2)
Inv(3)	5 (1.2)
t(9;22)	2 (0.5)
Complex abnormalities	26 (6.5)

(q22;q22), inv(16)(p13;q22) and t(15;17)(q22;q21), which were found in 27(7%), 15(3.7%) and 65(16.2%) respectively belongs to the favourable prognostic group. In the adverse prognostic group, there were 2(0.5%) patients with t(9;22) (q34;q11)(0.5%), 9(2.2%) patients with -7/del7q, 5(1.2%) patients with -5/del5q, 5(1.2%) patients with inv(3), another 5(1.2%) patients with t(6;9) and complex abnormalities with ≥3 chromosomal abnormalities were found in 26 (6.5%) cases (Figure 1). Among patients with t(8;21), there were 2(0.8%) patients with loss of Y chromosome (-Y) also found. Among patients with complex abnormalities, two exhibited an 11q23 abnormality in combination with additional chromosomal abnormalities. The abnormalities found in the intermediate risk group, including trisomy 8 and trisomy 21, were found in 7(1.7%) and 4(1%) cases, respectively. (Table 1) Other abnormalities were observed in 28(7.7%) patients, including some clonal abnormalities such as trisomy, loss or gain of chromosomal arms, polyploids (3n and 4n), hyperdiploids, and hypodiploids without any clonal loss and gains, etc.

Association of cytogenetic risk groups with clinical parameters

The median age of disease diagnosis was found to be 47.5 years. By comparing the clinical parameters of patients with normal karyotypes and abnormal karyotypes, a significant association was found in the sex distribution with a slightly higher male-to-female ratio (p=0.032). A significant association was also found with age (p=0.026), WBC count (p=0.018), and LDH level (p=0.040) among the two groups. At the same time, no significant relation was found in terms of platelets (p=0.998), Hemoglobin (HB)(p=0.090), Peripheral Blood Blast (p=0.600), and Bone Marrow Blast (0.190). Among different cytogenetic risk groups, there was a significant association with male-to-female ratio (p=0.014), median age (p=0.003), and WBC count (p=0.023) (Table 2).

Table 2. Association of Clinical Parameters with Karyotype Status and Risk Groups

Clinical parameters	Karyotype Status			Risk Groups			
	Normal	Abnormal	P-value	Favourable	Intermediate	Adverse	P-value
Sex Ratio(M:F)	01:01.2	01:01.1	0.032	1.5:1	01:01.3	01:01.3	0.014
Age, Median	45.6	45.45	0.026	41.6	45.7	49.8	0.003
(Range)	(17-74)	(17-60)		(17-74)	(17-74)	(18-60)	
LDH (IU/L),	597.2	757.7	0.04	660.3	730.5	509.3	0.089
Median,(Range)	(99-3228)	(130-6029)		(135-3228)	(99-6027)	(164-3428)	
Hb (g%)	8.3	8.09	0.09	8.4	8.1	8.1	0.374
Median,(Range)	(1.3-14)	(1.06-15.2)		(3.5-15.2)	(1.3-14.8)	(1.06-13.6)	
Platelet (X 10^9/L)	65.3	68.7	0.998	52.4	68.5	80.9	0.264
Median,(Range)	(2-1080)	(5-1298)		(5-272)	(2-1080)	(5.8-1298)	
WBC (X 10^9/L)	40.6	48.1	0.018	44.6	45.4	45.1	0.023
Median, (Range)	(0.4-909)	(5-1298)		(0.4-1213)	(0.06-909)	(1.2-4017)	
BM Blast(%)	61.6	64.9	0.19	61.4	64.1	61.5	0.509
Median,(Range)	(0-96)	(1-99)		(1-98)	(0-97)	(10-99)	
Pb Blast (%)	54.3	55.8	0.6	54.9	55.4	54.1	0.964
Median, (Range)	(5-95)	(2-97)		(3-97)	(5-95)	(2-93)	

Table 3. Distribution of Cytogenetic Findings among Different FAB Subtypes

Cytogenetic Findings	FAB Subtypes							
	AML-M0 n=13	AML-M1 n=67	AML-M2 n=47	AML-M3 n=65	AML-M4 n=134	AML-M5 n=72	AML-M6 n=1	AML-M7 n=1
Normal karyotype	11 (84.6)	45 (67.1)	9 (19.1)	_		45 (62.5)	1	1
Abnormal karyotype	2 (15.3)	22 (32.8)	38 (80.8)	65 (100)		27 (37.5)	_	_
t(8;21)	_	3 (4)	21 (44.6)	_			_	_
inv(16)	_	2 (2.9)	1 (2.1)	_		1 (1.3)	_	_
t(15;17)	_	_	_	65 (100)		_	_	_
t(9;22)	_	1 (1.4)	1 (2.1)	_		_	_	_
Trisomy 8	_	1 (1.4)	1 (2.1)	_		1 (1.3)	_	_
Trisomy 21	_	_	2 (4.2)	_		_	_	_
t(6;9)	_	_	1 (2.1)	_		2 (2.7)	_	_
Inv(3)	_	2 (2.9)	1 (2.1)	_		2 (2.7)	_	_
-7/del7q	_	2 (2.9)	_	_		3 (4.1)	_	_
-5/del5q	1 (7.6)	1 (1.4)	_	_		2 (2.7)	_	_
Complex abnormalities	_	5 (7.4)	4 (8.5)	_		7 (9.7)	_	_
Other abnormalities	1 (7.6)	5 (7.4)	6 (12.7)	_		9 (12.5)	_	_

Frequency of cytogenetic aberrations within FAB Subtypes

The frequency of cytogenetic aberrations among different FAB subtypes is shown in Table 3. Among patients with successful karyotyping, normal karyotypes were most frequently observed in the M4 subtype, accounting for 73 patients (62.3%), followed by the M5 subtype, with 40 patients (59.7%). Chromosomal abnormalities were also most frequently observed in the M3 subtype, with 65 (100%) patients by combined conventional and molecular cytogenetic analysis. This is followed M2 subtype, in which most of the aberrations observed were t(8;21)(44.6%). The other abnormalities were trisomy 8(2.1%), trisomy 21(4.2%), t(6;9)(2.1%), inv(3)(2.1%), complex abnormalities(8.5%) etc. Other cytogenetic abnormalities(12.7%) are also more prevalent in the M2 subtype. Inv(16)(8.2%) mostly found an association with the M4 subtype. Trisomy 8(2.9%), -7/del7q(2.9%), -5/del5q(0.7%), complex abnormalities(7.4%) were the other abnormalities found in the M4 subtype (Table 3).

Discussion

Most AML patients exhibit acquired clonal chromosome aberrations. Understanding the relationship between specific chromosomal abnormalities, cytomorphologic features, immunophenotype, and clinical outcome has reshaped our perception of AML, recognizing it as a heterogeneous collection of biological entities. The increasing importance of cytogenetic findings in AML classification and elucidation of pathogenetic mechanisms is evident in the WHO classification of AML [8]. Even though the morphological analysis of bone marrow aspiration and biopsy remains crucial for diagnosing AML, it's evident that the identification of specific cytogenetic abnormalities and acquired genetic mutations serves as a cornerstone in predicting prognosis and guiding treatment decisions.

In our study cohort, young adult individuals with a median age of 47.5 years were affected with the disease, which is much younger when compared with a study by Wakui et al. [9] and Enjeti et al. [10]. A study from Turkey also showed a similar median age of 49 years [11]. In an Indian study by Philip et al., the median age was 40 years [12]. According to Philip et al., and Shysh et al., the reduced median age may result from both referral bias towards tertiary centres and a distinct population range in India and other developing nations, and it is characterized by a notably smaller proportion of individuals aged over 60 years. In addition to this, potential contributions from supplementary genetic and environmental factors cannot be disregarded [12, 13]. Among 400 AML cases, 195 were males and 205 were females, with a ratio of 1:1.05, with a slight female predominance observed in our study. A similar result was found in a study by Shin et al., where there is a female predominance over male patients [14]. A study by Thao et al., also showed a comparable male-to-female ratio of 1:1.07 [15]. Similarly, two South Indian studies also reported a higher female prevalence in their de novo AML study cohort [16, 17]. However, in most of the literature, male dominance was observed [13, 18, 19]. According to Nakase et al., compared to the Japanese population M4 subtype is most common in the Australian population, and Kakepoto et al also reported that M4 is most common [20–22]. The frequency of AML M2 in our study cohort is 11.75%, which is lower when compared to other studies [23]. The least prevalent subtypes in our study were M6 and M7 (0.2%). Abuhelwa et al. in Palestine reported that M4 and M7 were the most and least prevalent subtypes in their study [24].

In our study, normal karyotypes were observed in 50.3% of the cases. This frequency is slightly higher than what has been reported in some previous studies, although it aligns with findings from a study conducted in the United States [25]. Srivastava et al. reported a

Table 4. Comparison of Cytogenetic Patterns in the Present Study with Previous Reports

Country	This study	US (2002) (25)	UK (2006) (33)	Spain (2006) (34)	Egypt (2022) (31)	Turkey (2022) (11)	Tunisia (2002) (35)	Korea (2016) (39)	Malaysia (2024) (5)	China (2009) (36)	Japan (2008) (9)	Singapore (2004) (10)
No of Cases	400	1131	1709	1129	120	157	631	2717	245	1432	438	454
Median age(range)	47.5(17-75)	52(15-86)	65(16-99)	61(1-94)	36.5(18-86)	49(18-89)	37(0.08-95)	51(14-89)	39(0-81)	42(4-84)	45(15-66)	49(15-100)
Cytogenetic pattern(%)												
Normal Karyotype	50.5	48	45	36.5	56.7	42.8	37.1	41.4	69.6	42	41.8	39
Structural Abnormalities %												
t(8;21)	6.7	7.5	4	2.7	7.5	8	12.2	8.8	7.5	8	17.7	7.5
inv(16)	3.7	7.5	2	2.7	9.2	0.7	3.8	3.6	NA	NA	4.1	1.1
t(15;17)	16.2	9.2	8	14.8	7.5	3.6	13.2	8.6	2.3	14	5	11
t(9;22)	0.5	0.8	1	NA	0.8	0.7	NA	NA	NA	2	1.1	NA
11q23 abn	0.5	NA	1	3.3	7.5	2.2	3.5	2.1	NA	1.2	5	0.9
Inv(3)	1.2	NA	NA	NA	1.6	0.7	NA	NA	NA	NA	0.8	0.7
Numerical Abnormalities(%)												
-7/del7q	2.2	7	7.2	8.6	0.8	7.9	3	4.6	1.2	1	0.3	7
-5/del5q	1.2	7	4.7	9.1	NA	7.2	2.2	3.4	0.8	1	0.3	6.6
Trisomy 8	1.7	9	6	11.4	3.3	NA	7	7.7	3	2	NA	NA
Trisomy 21	1	NA	NA	NA	NA	NA	NA	2.8	0.2	2	NA	NA
Complex Abnormalities	6.5	10	15	NA	0.8	14.5	10.8	NA	7.3	6	NA	NA
Other Abnormalities	7	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

NA, Data not available

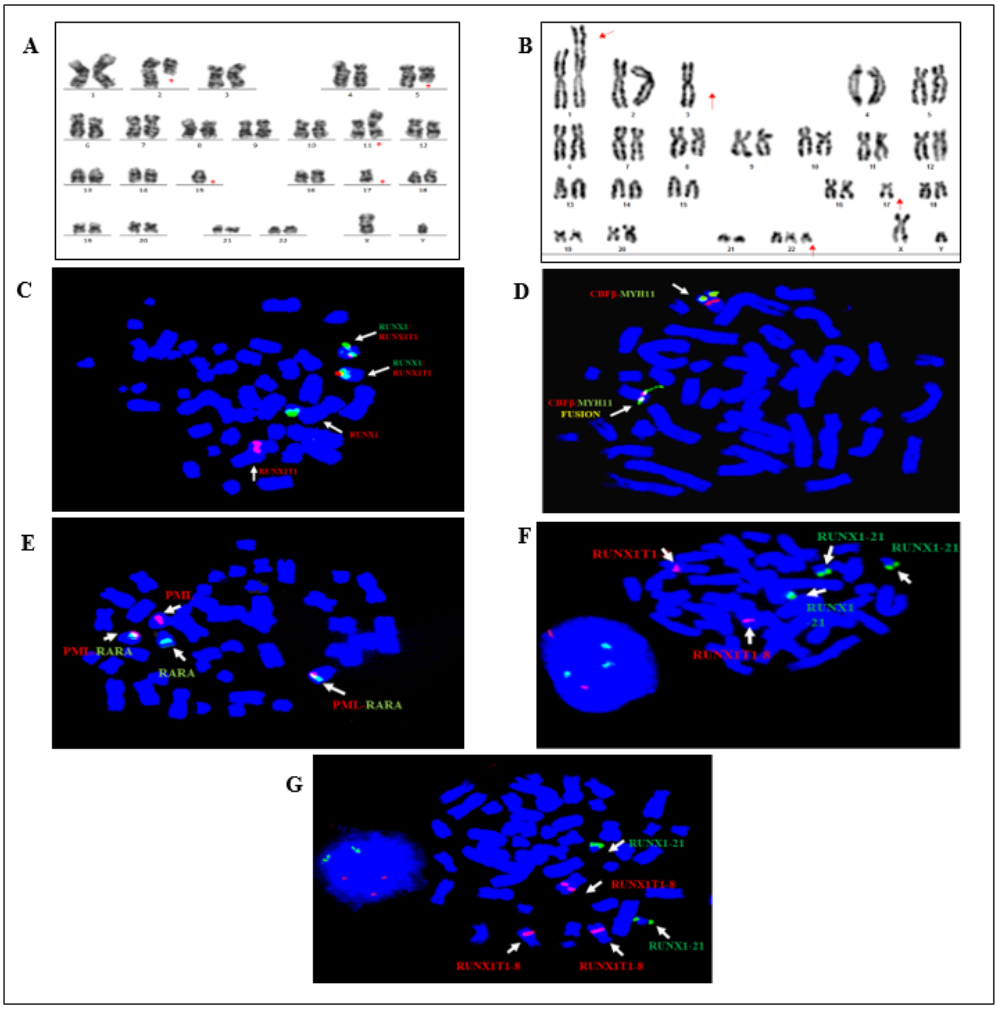

Figure 1. [A] GTG-Banded karyotype showing 46,XY,cpx(del(2)(q22q37),del(5)(q21q35),-15,17,i(11q). [B] GTG-Banded karyotype showing 46,XY,cpx(add(1)(p?)-3, -17, ,+21). [C] Metaphase FISH showing an abnormal 1R 1G 2F pattern, indicating the RUNX1::RUNX1T1 fusion (two fusion signals, one red, and one green). [D] Metaphase FISH showing an abnormal 1F 1R 1G pattern (one fusion, one separated red, and one separated green signal) indicating CBFB-MYH11 rearrangement. [E] Metaphase FISH with the dual-fusion probe showing a positive 1R 1G 2F pattern, indicating the PML::RARA fusion (two fusion signals, one red, and one green). [F] Interphase and metaphase FISH showing three green signals corresponding to the gain of chromosome 21. [G] Interphase and metaphase FISH showing three distinct red signals indicating gain of chromosome 8.

lower frequency of normal karyotypes at 36.1% [26]. Ambayya et al. highlighted the variability in reported rates of normal karyotypes across different countries, which ranged between 25% and 70% [27]. While cytogenetic abnormalities were identified in 49.5% of all AML patients analyzed. The result was almost consistent with a study from the US in which 52% of the patients were observed with abnormal cytogenetics [25]. Comparing the gender distribution among normal and abnormal karyotypes shows a significant association with a higher male-to-female ratio (p=0.032). A significant association was also found in the WBC count of patients with normal and abnormal karyotypes. An elevated white blood cell count at diagnosis is recognized as an independent prognostic indicator of poor outcomes in both adult and pediatric patients with AML [26]. It is also recognized as an additional risk factor in AML and is linked to poorer outcomes, even within patients classified under favorable and intermediate-risk groups. This adverse prognostic impact is particularly evident in patients with favorable cytogenetic abnormalities, such as t(8;21) and t(15;17), but it is also observed in patients with intermediate-risk cytogenetic profiles [26, 27]. In our study, the comparison of cytogenetic risk groups with mean WBC counts revealed a statistically significant difference between the favorable and adverse groups, with the poor risk group exhibiting higher mean WBC counts than the other risk categories(p=0.023).

In our study, AML patients were categorized into three prognostic groups: favorable (26.7%), intermediate (60.2%), and adverse (13%). A study on the Moroccan population by Oum Kaltoum Ait Boujmia et al., 17% of patients were favorable risk, 65.4% were in the intermediate-risk group, and 17.6% were adverse risk [28]. In another report by Khoubila et al. [29] patients were classified into the favorable group (19.5%), intermediate (68%), and adverse group (12.5%) [29]. However, the findings from Brazil differed, showing 21%

in the favorable group, 40% in the intermediate group, and 23% in the poor prognosis category [30]. Overall, the results were largely comparable across studies, with minor variations likely attributable to population-specific differences. Table 4 presents a comparison of the findings from this study with various population-based and regional studies.

The most common cytogenetic abnormality found in our study cohort was t(15;17) (16.2%), which had a higher frequency (p<0.0001) than in Egypt(7.5%), Malaysia (2.3%), Japan(5%), the US(9.2%) and UK(8%) [5, 9, 25, 31, 32]. The frequency was consistent with those reported from Spain (14.8%, p=0.312), Tunisia (13.2%, p=0.276), and China (14%, p=0.298), with no significant differences observed [33–35] (Table 4) (Supplementary Table 1). This variation may be attributed to racial differences, environmental exposures, and the molecular genetic methods employed in different studies [35]. In our study, FISH analysis was performed in all the AML M3 patients to confirm t(15;17), often missed in poor-quality karyotypes, and to establish baseline values for post-treatment cytogenetic response.The second most prevalent abnormality is t(8;21)(6%) was found to be consistent with reports from the US(7.5%), Egypt(7.5%), Malaysia(7.5%) and China(8%) and was more common in UK(4%)(p=<0.0001) [5, 25, 31, 32, 35]. Approximately 44.6% of M2 subtype patients exhibited the t(8;21) translocation in the current study population. The t(8;21) translocation is associated with approximately 40% of myeloid leukemias of the FAB M2 subtype. According to FAB classification, patients with t(8;21) AML typically present with M2 morphology, with a minority of patients presenting M1 or M4 [36, 37]. The frequency of occurrence of inv [16](3.7%) was comparable to Spain(2%), UK(2%), Korea(3.6%), Tunisia(3.8%) and Japan(4.1%) but it was statistically different from studies reported from US(7.5%)(p=0.0091) and Egypt(9.2%)(p=0.028) [9, 25, 31, 32, 34, 38]. A study of the Moroccan population showed a similar occurrence of inv (16) in 3.3% of the patients [29]. The inv(16) abnormality may be undetected in patients with suboptimal morphology, particularly when cytogenetic findings are not correlated with bone marrow morphology. Therefore, FISH analysis was used for confirmation. Inv(3)(1.2%) was found to be more common than those reported from Turkey(0.7%), Japan(0.8%), and Singapore (0.7%)(p=1.000) [9–11]. However, a study from Southern Vietnam reported a similar frequency of occurrence of inv(3)(1.2%) [15] (Table 4).

Trisomy 8, trisomy 21, del7q, and del5q were the other chromosomal abnormalities found in the current study group. Trisomy 8, classified as an intermediate-risk cytogenetic abnormality with yet unclear pathogenic mechanisms, was identified in only 1.7% of patients in the present study. This frequency aligns with reports from the US (3.3%), Egypt (3.3%), Malaysia (3%), and China (2%), but remains lower(p=<0.0001) than rates observed in US(9%), Spain (11.4%), Tunisia (7%), and Korea (7.7%). Trisomy 8 is considered a secondary, disease-modifying event rather than a primary cytogenetic or molecular abnormality. Therefore, its presence should be assessed through gene expression analysis across all AML subtypes [39]. The frequency of trisomy 21(1%) was comparable to that from China and Korea(2-2.8%) and Malaysia(7.3%) [5, 35, 38]. -7/del7q and -5/del5q were observed in 2.2% and 1.2%, respectively, which is lower than the results from the US, UK, Spain, Turkey, and Singapore(p <0.0001) and found to be higher than the rates from Japan and China (9–11,25,33,34,36). Chromosomal abnormalities such as -7/del(7q) and -5/del(5q) are commonly seen in patients with prior exposure to alkylating agents or other carcinogens [5]. AML with 11q23 abnormalities represents a heterogeneous group involving various partner chromosomes, making risk stratification complex and often controversial. While generally associated with poorer outcomes compared to normal karyotype, some studies suggest that specific translocations, such as t(9;11), may confer a relatively favorable prognosis, particularly with intensive chemotherapy. In contrast, rearrangements like t(6;11) are linked to worse outcomes. In our study cohort, the frequency of 11q23 rearrangements was detected in 0.5% of the cases, and comparable with several studies where the frequencies were not more than 4% [11, 32–35, 38].

Complex karyotypes, defined by the presence of three or more chromosomal abnormalities, were observed in 6.5% of our patients. This is comparable to findings from China (6%) and Malaysia (7.5%), lower than those reported in the US (10%), UK (15%), Turkey (14.5%), and Tunisia (10.8%), but higher than Egypt (0.8%) [11, 25, 31, 32, 34]. These differences were statistically significant and appear to vary across studies. Most cytogenetic classification systems define a complex karyotype as having three or more abnormalities, with the exception of the Medical Research Council (MRC). The latest WHO classification specifies this as three or more unrelated abnormalities, excluding patients with t(15;17), t(9;11), or core-binding factor (CBF) leukemias. Complex karyotypes occur in about 10–12% of adult AML patients and are generally associated with poor prognosis, unless accompanied by favorable-risk translocations like t(8;21), t(15;17), or t(16;16)/inv(16), where increased complexity does not typically impact outcomes [5, 40].

This large-scale study from a South Indian tertiary centre highlights the distinct cytogenetic landscape of AML, revealing both common and region-specific chromosomal abnormalities. The variation in findings compared to global data suggests underlying ethnic and environmental influences. These results underscore the vital role of cytogenetic analysis in AML diagnosis, risk stratification, and treatment planning, while also emphasizing the need for region-specific research to enhance understanding of disease biology and improve patient outcomes.

Author Contribution Statement

All authors contributed equally in this study.

Acknowledgements

The author would like to acknowledge all the

co-authors for their valuable assistance support and instructions and also the first/lead author acknowledges financial support from the Council of Scientific and Industrial Research (CSIR), India, as fellowship.

Funding

This study got financial support from the Council of Scientific and Industrial Research (CSIR), India, under the scheme Junior Research Fellow and Senior Research Fellow (Grant No: No:1121831254) as fellowships.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1975 Helsinki declaration and its later amendments or comparable ethical standards.This study was approved by the Institutional Review Board (IRB) of Regional Cancer Centre (Approval No:23/2020).

Informed Consent

Informed consent was obtained from all individual participants included in the study. This study was approved by the Institutional Review Board (IRB) of Regional Cancer Centre (Approval No:23/2020).

Data availability

Data supporting the findings of this study can be obtained from the corresponding author upon reasonable request.

Registration

This study was not registered in any public registration database, as it is an observational laboratory-based research study.

Conflict of interest

The authors declare no conflict of interest in the study.

References

1. Pourrajab F, Zare-Khormizi MR, Hashemi AS, Hekmatimoghaddam S. Genetic characterization and risk stratification of acute myeloid leukemia. Cancer Manag Res. 2020;12:2231-53. https://doi.org/10.2147/cmar.S242479.
2. Abdallah M, Xie Z, Ready A, Manogna D, Mendler JH, Loh KP. Management of acute myeloid leukemia (aml) in older patients. Curr Oncol Rep. 2020;22(10):103. https://doi.org/10.1007/s11912-020-00964-1.
3. Atia TA. Cytogenetic studies of Acute Myeloid Leukemia. The Egyptian Journal of Hospital Medicine. 2010 Jan 1;38(1):131-9.
4. Bendari M, Khoubila N, Cherkaoui S, Hda N, Qachouh M, Lamchahab M, Quessar A. Current cytogenetic abnormalities in acute myeloid leukemia. InChromosomal Abnormalities 2020 Oct 20. IntechOpen.
5. Meng CY, Noor PJ, Ismail A, Ahid MF, Zakaria Z. Cytogenetic profile of de novo acute myeloid leukemia patients in malaysia. Int J Biomed Sci. 2013;9(1):26-32.
6. Shaikh MS, Ahmed ZA, Shaikh MU, Adil SN, Khurshid M, Moatter T, et al. Distribution of chromosomal abnormalities commonly observed in adult acute myeloid leukemia in pakistan as predictors of prognosis. Asian Pac J Cancer Prev. 2018;19(7):1903-6. https://doi.org/10.22034/apjcp.2018.19.7.1903.
7. Vakiti A, Reynolds SB, Mewawalla P. Acute myeloid leukemia. InStatPearls [internet] 2024 Apr 27. StatPearls Publishing; 1-11.
8. Jain h, shetty d. Role of cytogenetics and fluorescence in situ hybridization in the laboratory workup of acute myeloid leukemias. Indian j med paediatr oncol. 2023;44(06):543–53. https://doi.org/10.1055/s-0043-1768052.
9. Wakui M, Kuriyama K, Miyazaki Y, Hata T, Taniwaki M, Ohtake S, et al. Diagnosis of acute myeloid leukemia according to the who classification in the japan adult leukemia study group aml-97 protocol. Int J Hematol. 2008;87(2):144-51. https://doi.org/10.1007/s12185-008-0025-3.
10. Enjeti AK, Tien SL, Sivaswaren CR. Cytogenetic abnormalities in de novo acute myeloid leukemia in adults: Relation to morphology, age, sex and ethnicity - a single center study from singapore. Hematol J. 2004;5(5):419-25. https://doi.org/10.1038/sj.thj.6200544.
11. Cirakoglu A, Kuru RD, Yilmaz S, Deviren A, Ongoren S, Yalniz FF, et al. Cytogenetic profile of adult aml patients in turkey: A single center study with comprehensive comparison with literature. Afr Health Sci. 2022;22(3):183-91. https://doi.org/10.4314/ahs.v22i3.21.
12. Philip C, George B, Ganapule A, Korula A, Jain P, Alex AA, et al. Acute myeloid leukaemia: Challenges and real world data from india. Br J Haematol. 2015;170(1):110-7. https://doi.org/10.1111/bjh.13406.
13. Shysh AC, Nguyen LT, Guo M, Vaska M, Naugler C, Rashid-Kolvear F. The incidence of acute myeloid leukemia in calgary, alberta, canada: A retrospective cohort study. BMC Public Health. 2017;18(1):94. https://doi.org/10.1186/s12889-017-4644-6.
14. Sahin FI, Kizilkilic E, Bulakbasi T, Yilmaz Z, Boga C, Ozalp O, et al. Cytogenetic findings and clinical outcomes of adult acute myeloid leukaemia patients. Clin Exp Med. 2007;7(3):102-7. https://doi.org/10.1007/s10238-007-0130-2.
15. Thao LTT, Ha CT, Ha NTT, Beaupha SMC, Nghia H, Tung TT, et al. Cytogenetic characteristics of de novo acute myeloid leukemia in southern vietnam. Asian Pac J Cancer Prev. 2023;24(5):1789-95. https://doi.org/10.31557/apjcp.2023.24.5.1789.
16. Sarojam S, Raveendran S, Vijay S, Sreedharan J, Narayanan G, Sreedharan H. Characterization of cebpa mutations and polymorphisms and their prognostic relevance in de novo acute myeloid leukemia patients. Asian Pac J Cancer Prev. 2015;16(9):3785-92. https://doi.org/10.7314/apjcp.2015.16.9.3785.
17. Raveendran S, Sarojam S, Vijay S, Geetha AC, Sreedharan J, Narayanan G, et al. Mutation analysis of idh1/2 genes in unselected de novo acute myeloid leukaemia patients in india - identification of a novel idh2 mutation. Asian Pac J Cancer Prev. 2015;16(9):4095-101. https://doi.org/10.7314/apjcp.2015.16.9.4095.
18. Alshemmari SH, Almazyad M, Ram M, John LM, Alhuraiji A. Epidemiology of de novo acute myeloid leukemia in kuwait per the 2016 who classification. Med Princ Pract. 2022;31(3):284-92. https://doi.org/10.1159/000524641.
19. Dharmani C, Wang E, Tu N, Salas M, Kamel YM. Characteristics and outcomes of elderly patients with acute myeloid leukemia who receive no treatment in the surveillance, epidemiology and end results-medicare database. Future Oncol. 2023;19(2):159-71. https://doi.org/10.2217/fon-2022-0565.
20. Omer SH, Kordofani AA, Osman IM, Musa OH, Altayb HN,

Elamin BK. Prevalence of the different FAB sub type of acute myeloid leukemia related to hematological parameters in Sudanese. J Hematol Blood Disord. 2017;3(1):102.
21. Harani MS, Adil SN, Shaikh MU, Kakepoto GN, Khurshid M. Frequency of fab subtypes in acute myeloid leukemia patients at aga khan university hospital karachi. J Ayub Med Coll Abbottabad. 2005;17(1):26-9.
22. Nakase K, Bradstock K, Sartor M, Gottlieb D, Byth K, Kita K, et al. Geographic heterogeneity of cellular characteristics of acute myeloid leukemia: A comparative study of australian and japanese adult cases. Leukemia. 2000;14(1):163-8. https://doi.org/10.1038/sj.leu.2401638.
23. Basharat M, Khan SA, Din NU, Ahmed D. Immunophenotypic characterisation of morphologically diagnosed cases of acute myeloid leukaemia (aml). Pak J Med Sci. 2019;35(2):470-6. https://doi.org/10.12669/pjms.35.2.614.
24. Abuhelwa Z, Al Shaer Q, Taha S, Ayoub K, Amer R. Characteristics of de novo acute myeloid leukemia patients in palestine: Experience of an-najah national university hospital. Asian Pac J Cancer Prev. 2017;18(9):2459-64. https://doi.org/10.22034/apjcp.2017.18.9.2459.
25. Byrd JC, Mrózek K, Dodge RK, Carroll AJ, Edwards CG, Arthur DC, et al. Pretreatment cytogenetic abnormalities are predictive of induction success, cumulative incidence of relapse, and overall survival in adult patients with de novo acute myeloid leukemia: Results from cancer and leukemia group b (calgb 8461). Blood. 2002;100(13):4325-36. https://doi.org/10.1182/blood-2002-03-0772.
26. Su L, Gao S, Li W, Tan Y, Yang L, Liu Z, et al. Age-specific distributions of cytogenetic subgroups of acute myeloid leukemia: Data analysis in a chinese population. Acta Haematol. 2013;129(3):175-81. https://doi.org/10.1159/000345250.
27. de Jonge HJ, Valk PJ, de Bont ES, Schuringa JJ, Ossenkoppele G, Vellenga E, et al. Prognostic impact of white blood cell count in intermediate risk acute myeloid leukemia: Relevance of mutated npm1 and flt3-itd. Haematologica. 2011;96(9):1310-7. https://doi.org/10.3324/haematol.2011.040592.
28. Demontis S, Terao M, Brivio M, Zanotta S, Bruschi M, Garattini E. Isolation and characterization of the gene coding for human cytidine deaminase. Biochim Biophys Acta. 1998;1443(3):323-33. https://doi.org/10.1016/s0167-4781(98)00235-8.
29. Khoubila N, Bendari M, Hda N, Lamchahab M, Qachouh M, Rachid M, et al. Cytogenetic profile of a representative cohort of young adults with de novo acute myéloblastic leukaemia in morocco. Cancer Genet. 2019;238:1-9. https://doi.org/10.1016/j.cancergen.2019.06.010.
30. Padilha SL, Souza EJ, Matos MC, Domino NR. Acute myeloid leukemia: Survival analysis of patients at a university hospital of paraná. Rev Bras Hematol Hemoter. 2015;37(1):21-7. https://doi.org/10.1016/j.bjhh.2014.11.008.
31. Elnaggar MG, Mosad E, Makboul A, Shafik EA. Cytogenetic profile of adult acute myeloid leukemia in egypt: A single-center experience. Mol Cytogenet. 2022;15(1):43. https://doi.org/10.1186/s13039-022-00621-1.
32. Sanderson RN, Johnson PR, Moorman AV, Roman E, Willett E, Taylor PR, et al. Population-based demographic study of karyotypes in 1709 patients with adult acute myeloid leukemia. Leukemia. 2006;20(3):444-50. https://doi.org/10.1038/sj.leu.2404055.
33. Sierra M, Alonso A, Odero MD, Gonzalez MB, Lahortiga I, Pérez JJ, et al. Geographic differences in the incidence of cytogenetic abnormalities of acute myelogenous leukemia (aml) in spain. Leuk Res. 2006;30(8):943-8. https://doi.org/10.1016/j.leukres.2005.12.025.
34. Sennana h, elghezal h, temmi h, hichri h, gribaa m. Cytogenetic analysis in 139 tunisian patients with de novo acute myeloid leukemia. Ann genet. 2002;45:29–32. https://doi.org/10.1016/s0003-3995(02)01098-5.
35. Cheng Y, Wang Y, Wang H, Chen Z, Lou J, Xu H, et al. Cytogenetic profile of de novo acute myeloid leukemia: A study based on 1432 patients in a single institution of china. Leukemia. 2009;23(10):1801-6. https://doi.org/10.1038/leu.2009.107.
36. Mulloy JC, Cammenga J, MacKenzie KL, Berguido FJ, Moore MA, Nimer SD. The aml1-eto fusion protein promotes the expansion of human hematopoietic stem cells. Blood. 2002;99(1):15-23. https://doi.org/10.1182/blood.v99.1.15.
37. Vundinti BR, Kerketta L, Madkaikar M, Jijina F, Ghosh K. Three way translocation in a new variant of t(8;21) acute myeloid leukemia involving xp22. Indian J Cancer. 2008;45(1):30-2. https://doi.org/10.4103/0019-509x.40644.
38. Hematol a, byun jm, kim yj, yoon h, kim s, kim h, et al. Cytogenetic profiles of 2806 patients with acute myeloid leukemia — a retrospective multicenter nationwide study. Ann hematol. 2016 ;95(8):1223-32. https://doi.org/10.1007/s00277-016-2691-1.
39. Udayakumar AM, Pathare AV, Al-Kindi S, Khan H, Rehmen JU, Zia F, et al. Cytogenetic, morphological, and immunophenotypic patterns in Omani patients with de novo acute myeloid leukemia. Cancer genetics and cytogenetics. 2007 Sep 1;177(2):89-94.
40. Döhner H, Estey EH, Amadori S, Appelbaum FR, Büchner T, Burnett AK, et al. Diagnosis and management of acute myeloid leukemia in adults: Recommendations from an international expert panel, on behalf of the european leukemianet. Blood. 2010;115(3):453-74. https://doi.org/10.1182/blood-2009-07-235358.

This work is licensed under a Creative Commons Attribution-Non Commercial 4.0 International License.