

Cytogenetic Characteristics of *de novo* Acute Myeloid Leukemia in Southern Vietnam

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Abstract

Background: The cytogenetic characteristics are important factors for risk stratification at diagnosis of acute myeloid leukemia (AML); however, cytogenetic profile of Vietnamese patients with AML remains undetermined. In this study, we present the chromosomal data of *de novo* AML patients in Southern Vietnam. **Methods:** We performed cytogenetic testing for 336 AML patients using G banding. If the patients had suspected abnormalities, fluorescence in situ hybridization with probes of $inv(3)(q21q26)/t(3;3)(q21;q26)$, $5q31$, $7q31$, $t(8;21)(q21.3;q22)$, $11q23$, $t(15;17)(q24;q21)$, $inv(16)(p13q22)/t(16;16)(p13;q22)$ were analyzed. Patients without above aberrations or with normal karyotype were tested by fluorescence in situ hybridization using probe $11q23$. **Results:** We found that the median age was 39 years. According to French – American – British classification, AML-M2 is the most frequent type with 35.1%. Chromosomal abnormalities were detected in 208 cases, accounting for 61.9%. Among structural abnormalities, $t(15;17)$ was the most common (19.6%), followed by $t(8;21)$ and $inv(16)/t(16;16)$ in 10.1% and 6.2%, respectively. In perspective of chromosomal numerical abnormalities, loss of sex chromosomes are the most common (7.7%), followed by +8 in 6.8%, $-7/del(7q)$ in 4.4%, +21 in 3.9% and $-5/del(5q)$ in 2.1%. The prevalence of additional cytogenetic aberrations accompanying with $t(8;21)$ and $inv(16)/t(16;16)$ were 82.4% and 52.4%, respectively. None of +8 cases was associated with $t(8;21)$. Regarding cytogenetic risk assessment according to European Leukemia Net 2017, there were 121 (36%) patients in favorable-risk, 180 (53.6%) in intermediate-risk and 35 (10.4%) in adverse-risk group. **Conclusion:** In conclusion, this is the first comprehensive cytogenetic profile of Vietnamese patients diagnosed with *de novo* AML, which helps clinical doctors in prognostic classification for AML patients in Southern Vietnam.

Keywords: Acute myeloid leukemia- karyotyping- cytogenetics- Vietnam

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Introduction

Acute myeloid leukemia (AML) is a clonal malignancy with abnormal differentiation and uncontrolled proliferation of myeloid progenitor cells, resulting in excessive blast presence in the bone marrow, peripheral blood and possibly in other organs. AML is more common in adults than in children, and the incidence increases with age. The disease is biologically heterogeneous, owing to the accumulation of genetic alterations in hematopoietic stem cells and/or progenitor cells. Based on chromosomal abnormalities, AML is divided into 3 groups of favorable, intermediate- and adverse-risk with different treatment regimens (Byrd et al., 2002).

Nowadays, assessing the cytogenetic characteristics of AML patients is an indispensable step in the clinical approach. Cytogenetic assays play an important role in the definitive diagnosis, risk stratification, disease prognosis, and treatment decisions (Döhner et al., 2017). It has been reported that 40-60% of AML patients carry cytogenetic abnormalities (Byrd et al., 2002; Cheng et al., 2009; Khoubila et al., 2019). Differences in diets, lifestyle, radiation and toxic exposure, as well as several congenital diseases, may essentially contribute to the pathogenesis of acute leukemia (Deschler and Lübbert, 2006). There are many studies of the genetic landscape of AML, which have been conducted in Japan, India, China (Wakui et al., 2008; Cheng et al., 2009; Udupa et al., 2020) and especially

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in Southeast Asia including Malaysia, Singapore, and Thailand (Enjeti et al., 2004; Niparuck et al., 2009; Meng et al., 2013). The results of the above studies show that the common chromosomal abnormalities in AML are almost present in the reports, but the prevalence varies by geographic region and ethnicity. Vietnam is an agricultural country and having experienced a long period of war, the accumulation of toxic substances such as herbicides, lethal weapons and defoliant for a long time can affect genetic changes. There are currently no chromosomal abnormalities data in newly diagnosed AML patients in Southern Vietnam reported, so we performed this study to clarify whether the cytogenetic characteristics are different from its counterpart in other countries around the world.

Materials and Methods

Patients

A total of 336 Vietnamese de novo AML patients were recruited from the Blood Transfusion and Hematology Hospital and Cho Ray Hospital at Ho Chi Minh City, Vietnam from 2015 to 2021. AML diagnosis was made based on morphological examination of bone marrow aspiration according to the French – American – British (FAB) classification with eight subtypes from M0 to M7. Cytogenetic risk stratification was based on European Leukemia Net (ELN) 2017. Written informed consents for chromosomal analyses were obtained from enrolled patients. This study was approved by the Ethics Committees of the University of Medicine and Pharmacy at Ho Chi Minh City (number 440/ĐHYD-HĐĐĐ).

Flow cytometric immunophenotyping

The panel of 20 monoclonal antibodies (System BD FACScanto II, BD Biosciences, USA) was used to detect cluster of differentiation including CD13, CD33, CD117, CD15, CD16, CD11b, CD34, CD38, CD14, CD36, CD64, CD235a, CD71, CD56, CD41a, CD61, CD123, CD4, MPO, HLA-DR. This immunophenotyping analysis was used in order to confirm the diagnosis of AML in all patients.

Conventional cytogenetic analysis

Two mL of bone marrow aspiration or 4 mL of peripheral blood samples (if immature cells accounted for at least 10% of peripheral blood cells and white blood cell count was at least $10 \times 10^9/L$) in 300 units of lithium heparin were obtained. Chromosomal culture procedure was performed within one hour. 2×10^7 cells were cultured in 10 mL of RPMI-1640 medium containing 10% fetal bovine serum (Sigma life science, USA), 1% antibiotic (Gibco, USA) and 200 μ L Phytohemagglutinin-lymphocyte-conditioned medium, then incubated at 37°C, 5% CO₂ for 24 hours for bone marrow samples and 48 hours for blood samples. After cell division was stopped using demecolcine solution (Sigma life science, USA), the cell membrane was destroyed with 0.075M KCL hypotonic solution and fixed with Carnoy solution (Methanol: Acetic acid = 1: 3). Cell residues were washed and chromosome slides were prepared. The slides were baked at 60°C for 4 hours, treated with

0.1% trypsin for an appropriate time, stained with Giemsa and analyzed under an optical microscope. For each patient, an average of 20 cells were analyzed using Ikaros software (MetaSystems, Germany). Karyotypes were encoded according to the International System for Human Cytogenetic Nomenclature (ISCN) 2013 criteria. Cases with three or more clonal abnormalities were defined as complex karyotype.

Fluorescence in situ hybridization (FISH)

Chromosomal abnormalities including inv(3)(q21q26)/t(3;3)(q21;q26), 5q31, 7q31, t(8;21)(q21.3;q22), 11q23 rearrangement, t(15;17)(q24;q21), inv(16)(p13q22)/t(16;16)(p13;q22) and t(9;22)(q34;q11) were confirmed by FISH with the corresponding Vysis probe (Abbott, USA). All patients without above aberrations or with normal karyotype were tested by FISH with probe 11q23. Cells from peripheral blood or bone marrow samples collected in heparin were harvested directly or after chromosome culture. The cells on slides were hybridized at 37°C overnight after denaturation at 75°C for 5 min. On day 2, the slides were washed to remove nonspecifically coupled probes, stained with DAPI and coated with PPD. Approximately 200 cells were analyzed under a BX51 fluorescence microscope (Olympus, Japan) using Isis software (MetaSystems, Germany).

Results

Patient, cell morphology and immunophenotype characteristics

Among 336 patients diagnosed with AML, there were slightly more females than males (174/162). The median age was 39 years (range, 1 – 81 years). According to FAB morphological classification, AML-M2 accounted for the highest percentage (35.1%), followed by AML mono (AML-M4/M5) (31.2%) and AML-M3 (19.6%). Only 5 patients were diagnosed with AML-M6, comprising the lowest rate (1.5%) (Table 1).

Cytogenetic characteristics

All 336 patients in this study had cytogenetic profile analyzed. It was showed that 208 patients had abnormal chromosomes, accounting for 61.9%. Regarding the cytogenetic risk stratification according to ELN 2017, there were 121 (36%) patients classified as favorable-risk, 180 (53.6%) patients as intermediate-risk and 35 patients as (10.4%) adverse-risk group.

In terms of structural chromosomal abnormalities, t(15;17)(q24;q21) was the most common with 66 (19.6%) patients, followed by t(8;21)(q21.3;q22) and inv(16)(p13q22), with 34 (10.1%) and 21 (6.3%) patients, respectively. Translocations of t(6;9)(p23;q34), t(9;11)(p21;q23) and t(9;22)(q34;q11) were found in only 1 (0.3%) patient. On the other hand, in the perspective of chromosomal numerical abnormalities, loss of X chromosome (-X) and loss of Y chromosome (-Y) were the most common with 26 patients, accounting for 7.7%, followed by +8, +21, -5/del(5q), -7/del(7q) with 23 (6.8%), 13 (3.9%), 7 (2.1%) and 15 (4.5%) patients, respectively (Table 1, 2).

Table 1. Characteristics of AML Patients by Age, Gender, FAB Subtype and Risk Classification

Characteristics (Total number of patients: 336 patients)	
Median age (range), (years)	39 (1 – 81)
Gender, n (%)	
Male	162 (48.2)
Female	174 (51.8)
Male/Female	1/1.07
FAB classification, n (%)	
M0	19 (5.7)
M1	15 (4.5)
M2	118 (35.1)
M3	66 (19.6)
M4	75 (22.3)
M5	30 (8.9)
M6	5 (1.5)
M7	8 (2.4)
Risk classification, n (%)	
Favorable	121 (36.0)
t(8;21)	34 (10.1)
inv(16)/t(16;16)	21 (6.3)
t(15;17)	66 (19.6)
Intermediate	180 (53.6)
Normal karyotype	128 (38.1)
t(9;11)	1 (0.3)
Other abnormalities*	51 (15.2)
Adverse	35 (10.4)
-7/del(7)	10 (3.0)
11q23 abn	5 (1.5)
-5/del(5)	1 (0.3)
inv(3)	3 (0.9)
t(6;9)	1 (0.3)
t(9;22)	1 (0.3)
Complex karyotype	14 (4.2)**

AML, Acute myeloid leukemia; abn, Abnormality; FAB, French – American – British; del, Deletion; inv, Inversion; t, Translocation; *The chromosomal abnormalities did not belong to favorable- and adverse-group; **1 patient had inv(3); 4 patients had -5/del(5q); 2 patients had -7/del(7q); 1 patient had a combination of del(5q) and -7

Additional cytogenetic aberrations in t(15;17), t(8;21) and inv(16)

The t(15;17) translocation was the most frequent structural anomaly in our study. Abnormalities associated with t(15;17) were only seen in 6/66 cases, accounting for 9.1%. There were 2 patients carrying three-way complex variant translocation including t(9;17;15)(q22;q21;q24) and t(2;17;15)(q21;q21;q24). In regard to t(15;17) translocation associated with numerical abnormalities chromosome, there were 1 case with +8, 1 case with +21 and 1 patient carrying both +9 and i(17)(q10). A complex chromosomal abnormality 47,XY,der(15)t(15;17)(q24;q21),ider(17)(q10)t(15;17)(q24;q21),+der(17)

t(17;?)p(11;?)t(15;17)(q24;q21) was noted in one patient.

Among 34 patients carrying t(8;21), 28 (82.4%) patients had at least one additional abnormality. -Y was the most common anomaly, accounting for 55.9%, while 4 (11.8%) patients had del(9q) and 1 (2.9%) patient had der(1)t(1;1)(p36.3;q21). Del(9q), -X and complex karyotype were found in 8 (23.6%), 2 (5.9%) and 3 (8.8%) patients, respectively. Del(5q), trisomy 4 and der(7)t(1;7)(q21;p22) were seen in only one patient for each anomaly. There were no cases of +8 associated with t(8;21) (Table 2).

The percentage of abnormalities associated with inv(16) was lower than that of t(8;21), encountered in 52.4% (11/21) of cases. +22 and +8 were common comorbidities, accounting for 28.6% and 23.8%, respectively. Complex chromosomal abnormalities were seen in 19% of cases. Del(7q), del(9q), del(17p) and t(5;6)(q13;q27) were found in only one patient for each type (Table 2).

Additional cytogenetic aberrations in chromosomal numerical abnormalities

Sex chromosome abnormalities were often associated with other chromosomal abnormalities including t(8;21), del(5q) and del(7q) in 21, 1 and 1 patients, respectively. Three (0.9%) patients who harbored sex chromosome abnormalities and were classified as intermediate-risk group included 1 patient with -Y alone, 1 patient with +4, and 1 patient with del(X)(p21) plus +11. Among 7 patients with -5/del(5q), there were only 1 case with del(5q) alone, 1 patient had t(8;21), 1 patient had -7 in complex karyotype and 4 patients had complex karyotype without -7/del(7q). Among 15 patients with -7/del(7q), there were 10 patients carrying -7/del(7q) alone; among the remaining 5 patients, there were 1 patient with inv(16), 1 patient with t(9;22), 1 patient with del(5q) in a complex karyotype, 2 patients with complex karyotype without -5/del(5q).

In addition, there were 23 patients carrying +8, among whom the rates of favorable-, intermediate- and adverse-risk groups were 26.1%, 47.8% and 26.1%, respectively. Six patients were in favorable-risk group, including 5 patients with inv(16) and 1 patient with t(15;17); there was no case associated with t(8;21). In the intermediate-risk group, there were 9 patients with +8 alone and 2 patients with one another abnormality (+14 or +21.) All 6 patients in the adverse-risk group had complex karyotype, including 1 patient with inv(3)(q21q26).

We also detected 13 (3.9%) patients with +21. In 7 patients classified as intermediate-risk, there were 4 cases of +21 alone; the other 3 cases were accompanied by +8, del(9)(q22) or +20 in each patient. In the remaining 6 cases, there was 1 patient with t(15;17), 1 patient with inv(16) and 4 patients with complex karyotype.

In terms of complex karyotype, there were 14 (4.2%) patients in the adverse-risk group (Table 1). Among them, 1 patient had inv(3), 4 patients had -5/del(5q), 2 patients had -7/del(7), 1 patient had a combination of del(5q) and -7, 1 patient had three abnormalities, and 5 patients had polyploidy.

Table 2. Additional Cytogenetic Abnormalities in Core Binding Factor

t(8;21) (n = 34)		inv(16) (n = 21)	
Category, n (%)		Category, n (%)	
No other abnormality	6 (17.6)	No other abnormality	10 (47.6)
Loss of X	2 (5.9)	Del(7q)	1 (4.8)
Loss of Y	14 (41.2)	Del(9q) + Trisomy 22**	1 (4.8)
Loss of Y and der(1)t(1;1)(p36;q21)*	1 (2.9)	Del(17p)	1 (4.8)
Loss of Y and del(9q)*	4 (11.8)	Trisomy 8	2 (9.5)
Del(5q)	1 (2.9)	Trisomy 8 + Trisomy 22**	1 (4.8)
Del(9q)	4 (11.8)	Trisomy 8 + Trisomy 14 + Trisomy 22**	1 (4.8)
Trisomy 8	0 (0.0)	Trisomy 8 + Trisomy 21 + Trisomy 22**	1 (4.8)
Trisomy 4	1 (2.9)	Trisomy 22	2 (9.5)
Der(7)t(1;7)(q21;p22)	1 (2.9)	t(5;6)(q13;q27)	1 (4.8)
Complex karyotype*‡	3 (8.8)		

del: Deletion; inv: Inversion; t: Translocation; * Total of 8 patients had complex karyotype with t(8;21); **: Total of 4 patients had complex karyotype with inv(16); ‡ 3 patients with complex karyotype as follows: 46,XX,t(8;21)(q21.3;q22)[14]/47,idem,+4[3]/49,idem,+4,+15,+der(21)t(8;21)(q21.3;q22)[3]. 46,XX,del(8)(q21q22),der(11)del(11)(q23)t(8;11)(q21;p15)t(8;21)(q22;q22),del(21)(q22)[12]/ 46,idem,add(12)(p13)[4]/45,idem,-X,add(12)(p13)[4]; 45,X,-Y,der(3)t(3;8)(q25;q24),der(8)t(8;21)(q22;q22),der(21)t(8;21)(q22;q22)t(3;8)(q25;q24)[20]

Discussion

This is the first study to describe the cytogenetic profile of AML patients in Southern Vietnam. Among 336 AML cases, there were 162 male patients (48.2%) and 174 female patients (51.8%), with a female: male ratio of 1.07. Females accounted for a higher proportion in our study, similar to the results of Niparuck P et al. study (52.8%) (Niparuck et al., 2009), although other reports showed that more males acquired AML (Byrd et al., 2002; Enjeti et al., 2004; Sierra et al., 2006; Cheng et al., 2009; Meng

et al., 2013). The higher risk of leukemia in men may be due to work-related and environmental factors such as pesticides, tobacco and radiation. The fact that Vietnam and Thailand are agricultural countries, where women participate in occupational activities similar to what men do, can explain the higher risk of this disease among women in these two countries. Regarding morphological classification according to FAB, AML-M2 accounted for the highest percentage (35.1%), followed by AML mono (M4/M5) (31.2%) and M3 (19.6%) and the lowest being M6 (1.5%) and M7 (2.4%). AML-M2 had the highest

Table 3. Comparison of Cytogenetics of AML Patients between Our Study and Other Studies

Reference	Our study	Enjeti	Meng	Cheng	Wakui	Udupa	Elnaggar 2022	Gmidene	Khoubila	Grimwade	Byrd
	2023	2004	2013	2009	2008	2020		2012	2019	2010	2002
Country	Vietnam	Singapore	Malaysia	China	Japan	India	Egypt	Tunisia	Morocco	UK	USA
No. of cases (n)	336	454	480	1432	638	173	120	631	895	5876	1311
Median age (range)	39 (1-81)	49 (15-100)	39 (0.3-81)	42 (4-84)	45 (15-66)	39 (16-82)	36.5 (18-86)	37 (0.08-95)	40.5 (20-60)	44 (15-59)	52 (15-86)
Normal karyotype, n (%)	38.1	39	69.6	42	41.8	34.6	56.7	37.1	42	41	48
Structural abnormalities (%)											
t(15;17)	19.6	11	2.3	14	-	8.6	9.2	13.2	3.7	13	7
t(8;21)	10.1	7.5	7.5	8	17.7	20.8	7.5	12.2	12.5	7	8.7
inv(16)	6.3	1.1	-	-	4.1	17.9	7.5	3.8	3.3	5	7.9
11q23 abn	1.5	0.9	-	1	5	3.4	7.5	3.5	3.6	3.6	-
inv(3)	1.2	0.7	-	-	0.8	3.4	1.6	-	-	1	-
t(9;22)	0.3	-	-	-	1.1	-	0.8	-	-	1	-
Complex	4.2	17	7.3	6	6.4	2.3	0.8	10.8	-	14	10
Numerical abnormalities (%)											
-5/del(5q)	2.1	6.6	0.8	1	0.3	2.3	-	2.2	1	4.7	7
-7/del(7q)	4.5	7	1.2	1	0.3	1.1	0.8	3	3	7.2	7
+8	6.8	7.3	3	2	-	-	3.3	7	5.2	10	9
+11	2.1	-	-	-	-	-	1.66	-	-	-	1.6
+21	3.9	-	-	-	-	-	-	-	-	3	2

AML, Acute myeloid leukemia; abn, Abnormality; del, Deletion; inv, Inversion; t, Translocation

prevalence reported in most studies (Byrd et al., 2002; Enjeti et al., 2004; Cheng et al., 2009; Udupa et al., 2020), however, several studies reported that M4/M5 comprised the highest rate (Abuhelwa et al., 2017; Elnaggar et al., 2022).

Using conventional cytogenetic analysis with G-band staining, we detected 61.9% out of 336 AML patients carrying chromosomal abnormalities, similar to previous reports with rates ranging from 40 to 60% (Byrd et al., 2002; Enjeti et al., 2004; Wakui et al., 2008; Cheng et al., 2009; Khoubila et al., 2019; Elnaggar et al., 2022). The t(15;17) translocation was the structural abnormality with the highest incidence, higher than other reports in the world (Byrd et al., 2002; Enjeti et al., 2004; Cheng et al., 2009; Grimwade et al., 2010; Khoubila et al., 2019; Elnaggar et al., 2022), especially in Malaysia (2.3%) and in Morocco (3.7%). This difference may be due to race, exposure factors and molecular genetic techniques used (Cheng et al., 2009). All patients with confirmed or suspected AML-M3 based on cell morphology and cell surface markers were examined by 3 tests including chromosomal analysis, FISH with t(15;17) dual color-dual fusion probe and reverse transcription polymerase chain reaction for PML-RARA detection, in order not to miss cases of AML-M3 with cryptic translocations, insertions or poor quality chromosomes.

The rate of t(8;21) in our study was 10.1%, similar to the results in Tunisia (12.2%) (Gmidène et al., 2012), Morocco (12.5%) (Khoubila et al., 2019), but lower than studies in Japan (Wakui et al., 2008) and India (Udupa et al., 2020) (Table 3). There were 28/34 patients (82.4%) carrying t(8;21) who had at least one more chromosomal abnormality, higher than its counterpart in Germany (69 - 74.7%) (Schlenk et al., 2004; Kuchenbauer et al., 2006) in USA (66 - 71%) (Appelbaum et al., 2006; Han et al., 2021), UK (68.2%) (Grimwade et al., 2010) and France (62%) (Prébet et al., 2009). Among the associated chromosomal abnormalities with t(8;21), -Y accounted for the highest percentage (55.9%), similar to the results of Appelbaum, Schlenk et al. (Schlenk et al., 2004; Appelbaum et al., 2006), but higher than reported by other authors (Kuchenbauer et al., 2006; Niparuck et al., 2009; Grimwade et al., 2010; Han et al., 2021). Meanwhile, -X was associated with only 2 cases (5.9%), lower than other studies (Schlenk et al., 2004; Appelbaum et al., 2006; Kuchenbauer et al., 2006; Peterson et al., 2007; Niparuck et al., 2009; Grimwade et al., 2010; Han et al., 2021). Del(9) was the second most frequent abnormality associated with t(8;21), after -Y, accounting for 23.6% and up to half of cases associated with -Y. Previous reports indicated that 5–8% of +8 cases are associated with t(8;21) (Schlenk et al., 2004; Appelbaum et al., 2006; Kuchenbauer et al., 2006; Prébet et al., 2009; Han et al., 2021), however no case was detected in our study.

Inv(16) was found in 6.3% of patients, being consistent with the findings in Saudi Arabia (7%) (Alrajeh et al., 2017), Egypt (7.5%) (Elnaggar et al., 2022), USA (7.9%) (Byrd et al., 2002) but much lower than the results of the Indian study (17.9%) (Udupa et al., 2020) (Table 3). There was 52.4% (11/21) inv(16) patients containing at least one associated abnormality, which was higher than other

reports with rates ranging from 40% to 42% (Schlenk et al., 2004; Appelbaum et al., 2006; Prébet et al., 2009; Han et al., 2021). In the abnormal cases associated with inv(16), +22 and +8 were the most common, at 28.6% and 23.8%, respectively, higher than in other reports (Appelbaum et al., 2006; Prébet et al., 2009; Han et al., 2021). Complex chromosomal abnormalities associated with inv(16) accounted for 19% (4/21), higher than the percentage reported in USA (12% - 16%) (Appelbaum et al., 2006; Han et al., 2021) and France (10%) (Prébet et al., 2009). There were no cases of -X, -Y associated with inv(16) in this study. However, several authors have reported cases of associated -X, -Y (Appelbaum et al., 2006; Prébet et al., 2009).

In our study, -X and -Y were the most common (7.4%) in the chromosomal numerical abnormality group, followed by +8 (6.8%), +21 (3.9%), -5/del(5q) (2.1%), -7/del(7q) (4.5%). There was only one isolated -Y case, while the remaining 25 cases with -X, -Y had accompanying chromosomal abnormalities such as t(8;21) in 21 cases, del(5q) in 1 case and del(7q) in 1 case. Several reports showed that loss of sex chromosome can occur in elderly as physiological phenomenon (1.8%) (Huh et al., 2007) or as an acquired abnormality in hematologic malignancy (5.1% - 6.3%) (Wiktor et al., 2000) (Huh et al., 2007) including AML (9.5%), multiple myeloma (13%), myelodysplastic syndrome (6.0%) (Huh et al., 2007; Shahrabi et al., 2018). The presence of sex chromosome loss can cause genetic instability but its effect on AML prognosis is controversial. We recorded 23 (6.8%) patients with +8, with or without associated abnormalities, mainly in the intermediate-risk group (47.8%). This ratio was similar to the findings in Tunisia (Gmidène et al., 2012) and Singapore (Enjeti et al., 2004), but higher than the results in China (Cheng et al., 2009), Malaysia (Meng et al., 2013) and lower than the results in Thailand (Niparuck et al., 2009), Saudi Arabia (Alrajeh et al., 2017), USA (Byrd et al., 2002) and UK (Grimwade et al., 2010) (Table 3). Schoch et al. showed that average event-free survival was significantly different between the group with isolated +8 compared with the group who had other abnormalities, predominantly complex chromosomes, so a complete chromosomal analysis is needed to fully identify the cytogenetic characteristics of AML patients with +8 (Schoch et al., 1997). -5/del(5q), -7/del(7q) were detected at a rate of 2.1% and 4.5%, respectively, lower than the results in Singapore (Enjeti et al., 2004), UK (Grimwade et al., 2010) and USA (Byrd et al., 2002), but higher than the results in Japan (Wakui et al., 2008) and China (Cheng et al., 2009). +11 and +21 were seen in 2.1% and 3.9% of cases respectively and these abnormalities were reported in only a few studies (Byrd et al., 2002; Grimwade et al., 2010; Elnaggar et al., 2022) (Table 3).

The rate of complex chromosomes in the high-risk group also varies from study to study. There were 4.2% cases with complex chromosomes in this study, higher than the results in Egypt (Elnaggar et al., 2022) and India (Udupa et al., 2020), but lower than many other studies (Byrd et al., 2002; Enjeti et al., 2004; Wakui et al., 2008; Cheng et al., 2009; Grimwade et al., 2010; Meng et al., 2013).

In perspective of risk stratification based on the ELN 2017 criteria, it is showed that the percentages of favorable-, intermediate- and adverse-risk groups were 36%, 53.6% and 10.4%, respectively. In our study, the ratio of the favorable-risk group was higher than its counterpart in the Egypt (Elnaggar et al., 2022) and Morocco (Khoubila et al., 2019) but lower than in India (Udupa et al., 2020). The favorable-risk group in India was much more common because t(8;21) and inv(16)/t(16;16) were more prevalent, while t(15;17) in our study comprised higher percentage than in other studies. This difference emphasizes the variation of cytogenetic characteristics by geographical location.

In conclusion, this study is the first comprehensive analysis of conventional cytogenetics in Vietnamese patients with de novo AML. The cytogenetic profile in our study had some differences in prevalence of chromosomal abnormalities when compared with that of other countries. Our data would help the clinical doctors in prognostic classification for AML patients in Southern Vietnam.

Author Contribution Statement

All authors contributed equally in this study.

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Ethical Approval

The study was approved by the ethics committee of University of Medicine and Pharmacy at Ho Chi Minh City, Vietnam (440/ĐHYD-HĐĐĐ).

Availability of Data

Data are available by request to the corresponding author.

Conflict of interest

The authors have no conflicts of interest to declare.

References

- Abuhelwa Z, Al Shaer Q, Taha S, et al (2017). Characteristics of de novo acute myeloid leukemia patients in Palestine: experience of An-Najah National University Hospital. *Asian Pac J Cancer Prev*, **18**, 2459.
- Alrajeh AI, Abalkhail H, Khalil SH (2017). Cytogenetics and molecular markers of acute myeloid leukemia from a tertiary care center in Saudi Arabia. *J Appl Hematol*, **8**, 68.
- Appelbaum FR, Kopecky KJ, Tallman MS, et al (2006). The clinical spectrum of adult acute myeloid leukaemia associated with core binding factor translocations. *Br J Haematol*, **135**, 165-73.
- Byrd JC, Mrózek K, Dodge RK, et al (2002). 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) Presented in part at the 43rd annual meeting of the American Society of Hematology, Orlando, FL, December 10, 2001, and published in abstract form. *Blood Am J Hematol*, **100**, 4325-36.
- Cheng Y, Wang Y, Wang H, et al (2009). Cytogenetic profile of de novo acute myeloid leukemia: a study based on 1432 patients in a single institution of China. *Leukemia*, **23**, 1801-6.
- Deschler B, Lübbert M (2006). Acute myeloid leukemia: epidemiology and etiology. *CA Cancer J Clin*, **107**, 2099-107.
- Döhner H, Estey E, Grimwade D, et al (2017). Diagnosis and management of AML in adults: 2017 ELN recommendations from an international expert panel. *Blood Am J Hematol*, **129**, 424-47.
- Elnaggar MG, Mosad E, Makboul A, et al (2022). Cytogenetic profile of adult acute myeloid leukemia in Egypt: a single-center experience. *Mol Cytogenet*, **15**, 43.
- Enjeti AK, Tien SL, Sivaswaren CR (2004). Cytogenetic abnormalities in de novo acute myeloid leukemia in adults: relation to morphology, age, sex and ethnicity-a single center study from Singapore. *Hematol*, **5**, 419-25.
- Gmidène A, Sennana H, Wahchi I, et al (2012). Cytogenetic profile of a large cohort of Tunisian de novo acute myeloid leukemia. *Hematol*, **17**, 9-14.
- Grimwade D, Hills RK, Moorman AV, et al (2010). Refinement of cytogenetic classification in acute myeloid leukemia: determination of prognostic significance of rare recurring chromosomal abnormalities among 5876 younger adult patients treated in the United Kingdom Medical Research Council trials. *Blood Am J Hematol*, **116**, 354-65.
- Han SY, Mrózek K, Voutsinas J, et al (2021). Secondary cytogenetic abnormalities in core-binding factor AML harboring inv (16) vs t (8; 21). *Blood Adv*, **5**, 2481-9.
- Huh J, Moon H, Chung WS (2007). Incidence and clinical significance of sex chromosome losses in bone marrow of patients with hematologic diseases. *Korean J Lab Med*, **27**, 56-61.
- Khoubila N, Bendari M, Hda N, et al (2019). Cytogenetic profile of a representative cohort of young adults with de novo acute myeloblastic leukaemia in Morocco. *Cancer Genet*, **238**, 1-9.
- Kuchenbauer F, Schnittger S, Look T, et al (2006). Identification of additional cytogenetic and molecular genetic abnormalities in acute myeloid leukaemia with t (8; 21)/AML1-ETO. *Br J Haematol*, **134**, 616-9.
- Meng CY, Noor PJ, Ismail A, et al (2013). Cytogenetic profile of de novo acute myeloid leukemia patients in Malaysia. *Int J Biomed Sci*, **9**, 26.
- Niparuck P, Chuncharunee S, Ungkanont A, et al (2009). Long-term outcomes of de novo acute myeloid leukemia in Thai patients. *J Med Assoc Thai*, **92**, 1143.
- Peterson LF, Boyapati A, Ahn EY, et al (2007). Acute myeloid leukemia with the 8q22; 21q22 translocation: secondary mutational events and alternative t (8; 21) transcripts. *Blood Am J Hematol*, **110**, 799-805.
- Prébet T, Boissel N, Reutenauer S, et al (2009). Acute myeloid leukemia with translocation (8; 21) or inversion (16) in elderly patients treated with conventional chemotherapy: a collaborative study of the French CBF-AML intergroup. *J Clin Oncol*, **27**, 4747-53.
- Schlenk RF, Benner A, Krauter J, et al (2004). Individual patient data-based meta-analysis of patients aged 16 to 60 years with core binding factor acute myeloid leukemia: a survey

- of the German Acute Myeloid Leukemia Intergroup. *J Clin Oncol*, **22**, 3741-50.
- Schoch C, Haase D, Fonatsch C, et al (1997). The significance of trisomy 8 in de novo acute myeloid leukaemia: the accompanying chromosome aberrations determine the prognosis. *Br J Haematol*, **99**, 605-11.
- Shahrabi S, Khodadi E, Saba F, et al (2018). Sex chromosome changes in leukemia: cytogenetics and molecular aspects. *Hematol*, **23**, 139-47.
- Sierra M, Alonso Á, Odero MD, et al (2006). Geographic differences in the incidence of cytogenetic abnormalities of acute myelogenous leukemia (AML) in Spain. *Leuk Res*, **30**, 943-8.
- Udupa MN, Babu KG, Babu MS, et al (2020). Clinical profile, cytogenetics and treatment outcomes of adult acute myeloid leukemia. *J Cancer Res Ther*, **16**, 18-22.
- Wakui M, Kuriyama K, Miyazaki Y, et al (2008). Diagnosis of acute myeloid leukemia according to the WHO classification in the Japan Adult Leukemia Study Group AML-97 protocol. *Int J Hematol*, **87**, 144-51.
- Wiktor A, Rybicki BA, Piao ZS, et al (2000). Clinical significance of Y chromosome loss in hematologic disease. *Genes, Chrom Cancer*, **27**, 11-6.



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