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Original Article

Acute Myeloid Leukemia: Pattern of Clinical and Hematological Parameters in a Tertiary Care Centre

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Abstract:
Objective: To determine the pattern of clinical features, hematological parameters and subtypes of acute myeloid leukemia in our setup.
Material and method: This Cross-Sectional Descriptive study was done in Khyber Teaching Hospital, Peshawar, from January 2015 to July 2017. All patients diagnosed as acute myeloid leukemia on bone marrow biopsy were included in the study. The demographics, clinical data and hematological parameters were noted on a proforma and results were drawn accordingly. Mean and standard deviation were used for quantitative data like age, while frequency and percentages were used for qualitative data like gender.
Results: 41 cases were diagnosed as acute myeloid leukemia and were included in the study. Age of the study sample ranged from 3 years to 65 years, with mean of 41 ± 9.8 SD years. The commonest chief complaint was fever (51%), while the commonest sign was pallor (61%). There was decreased hemoglobin level and platelet count. M-2 was the commonest subtype seen in 24 (59%) cases.
Conclusion: Acute myeloid leukemia occurs in younger age in our setup as compared to Western population. AML-M2 was the commonest subtype in AML. Fever and pallor were the commonest clinical findings while anemia and thrombocytopenia were the significant hematological findings.
Keywords: Acute myeloid leukemia, Fever, Pallor, Anemia, Thrombocytopenia, Hemoglobin level

Introduction

Leukemia is a hematological malignancy in which there is excessive abnormal proliferation and accumulation of malignant white blood cells in the bone marrow.[1,2] Acute myeloid leukemia (AML) is malignant disorder of cells of myeloid lineage in the bone marrow due to chromosomal abnormalities, leading to accumulation of myeloblasts in the bone marrow and infiltration to peripheral tissues.[3] The infiltration of tumor cells into the bone marrow causes symptoms of bone marrow failure i.e. anemia, infections, bleeding and pallor.[2] Infiltration of tumor cells into the liver and spleen causes hepatosplenomegaly.[1,2]

The incidence of leukemia is gradually on the rise in the developing as well as the developed countries.[2,4,5,6] It is reported that the incidence of leukemia is increasing in Northern areas of Pakistan for the past few years.[2,4,5,6,7,8] In the West, AML accounts for about 80% of all leukemias in the adults.[1,4,9]

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Global incidence of AML is 3–4 cases per 100,000 population.[1,10,11,12] Its incidence increases with increasing age.[3,4,8] The reported age of diagnosis of AML is about 60-67 years.[1,10,11,12] It occurs commonly in males ,with male to female ratio of 2.5:1 [3,4] The incidence of AML is increasing even in developed countries like Canada and Australia.[13]

The clinical features of AML are because of the infiltration of the bone marrow and extramedullary organs by myeloblasts.[1,3] The bone marrow infiltration by myeloblasts lead to bone marrow failure, which presents as anemia, bleeding, infections and fever.[1,3] Anemia is manifested as pallor and weakness.[1,3] Fever is a common presenting complaint in patients of AML.[3] Bleeding usually manifest in the form of petechiae, bruises , epistaxis, melaena, hematuria and gum bleeding.[3] Hepatosplenomegaly is seen in up to 50% of the cases.[1,3] Lymphadenopathy is not very common in cases of AML.[3] Gum involvement and involvement of central nervous system is commonly seen in AML-M4 and AML -M5 cases.[1,3]

AML is classified by the French-American-British (FAB) group and World Health Organization (WHO) [1,13,14]**.** The FAB group divides AML into 8 subtypes i.e. from M0 to M7.[1,13,14] This classification is done on

the basis of morphology of myeloblasts and cytochemistry.[3] However, in certain cases, help is taken from immunophenotyping as the definitive diagnosis cannot be made by morphology.[3] The W.H.O. classifies AML on the basis of morphology, imunopheotype and cytogenetics.[13,15] According to the W.H.O., if the bone marrow has more than 20 % myeloblasts, diagnosis of AML is confirmed.[13] However, WHO also suggests that if certain genetic alterations specific for AML are present in the patient, the 20% blast criteria is not necessary.[13,16] The cost and availability of facilities for cytogenetic and immunophenotypic analysis are a major limiting factor due to which , WHO classification cannot be used for patients in developing countries like Pakistan.[7,17] On the other hand, FAB classification needs no advanced technology and can easily be practiced in most laboratories.[17] That is the reason why FAB classification is used widely till now. [17]

The present study was done to report the current pattern of clinical features, hematological changes and FAB subtypes in patients of AML in our setup. Patients of diverse racial groups from all over the city come to our tertiary care center. Thus, our study establishes an existing trend of AML locally.

Materials and Methods

This Cross Sectional Descriptive study was done in Khyber Teaching Hospital, Peshawar, from January 2015 to July 2017. All patients diagnosed as Acute myeloid leukemia on bone marrow aspiration and biopsy were included in the study. Relapsed cases of AML, patients on chemotherapy and radiotherapy for AML were excluded from the study. Complete blood counts were done on Sysmex hematology analyzer. Bone marrow aspiration was done from posterior superior iliac spine under local anesthesia. Slides were stained with Giemsa stain. Myeloperoxidase was used as special stain to confirm that blasts were of myeloid lineage. The diagnosis of AML was made on the basis of morphology on bone marrow aspiration examination. [17] FAB-subtypes of AML were assigned on the basis of morphology of peripheral blood film and bone marrow aspirate. The data regarding age, clinical features with which the patients presented, changes in the basic hematological parameters (Total leukocyte count, hemoglobin and platelet count), and different subtypes of AML were recorded on a proforma , and results were drawn accordingly. Mean and standard deviation were used for quantitative data like age, while frequency and percentages were used for qualitative data like gender. The p-value was calculated for changes in the hematological parameters and value of less than 0.05 was considered significant.

Results

41 cases of AML included 22 females (54%) and 19 males (46%) were included in the study. Age of the study sample ranged from 3 -65 years, with mean age of 41 ± 9.8 SD years. Pattern of clinical features of the study sample and referral (suspected) diagnosis for which they were referred for bone marrow biopsy (Table 1). Pattern of changes in hematological parameters are shown in table 2 and 3. Pattern of FAB subtypes in 41 cases of AML (Table 4).

Table 1: Pattern of clinical features and initial referral (suspected) diagnosis in 41 cases of AML Referral diagnosis: The suspected diagnosis for which patients were referred for bone marrow biopsy

CLINICAL FEATURES	n (%)
Chief complaints	
Fever	21(51%)
Easy fatigability	6(15%)
Weight loss	2(5%)
Bleeding:	
Gum bleed	4(10%)
Hematuria	1(3%)
Per rectum	1(3%)
Generalized body aches	5(12%)
Anorexia	5(12%)
Joint pain	2(5%)
Physical examination	
Pallor	25(61%)
Hepatosplenomegaly	17(41%)
Lymphadenopathy	4(10%)
Gum hypertrophy	2(5%)
Bruises/petechiae	7(17%)
Facial nerve palsy	1(3%)
Suspected /referral diagnosis*	
Suspicion of leukemia	22(53%)
Pancytopenia	5(13%)
Bicytopenia (low Hb and platelet count)	4(10%)
Suspicion of lymphoma	3(7%)
Anemia work out	3(7%)
Hepatosplenomegaly	3(7%)
Isolated thrombocytopenia	1(3%)

Table 2: Changes in the basic hematological parameters in study patients (N=41)

Hematological parameters	Range	Mean	SD
Total leukocyte count (x10⁹/L)	0.7 – 285	42	11
Haemoglobin (g/dL)	3-12	7.6	1.9
Platelet count (x10⁹/L)	4-400	49	12

Table 3: Pattern of change in basic hematological parameters in study patients (N=41)

Pattern	Total leukocyte count	Hemoglobin	Platelet count
Normal	7(17%)	2(5%)	3(7%)
Increased	26(63%)	-	-
Decreased	8(20%)	39(95%)	37(93%)
p-value*	**0.59**	**0.02**	**0.01**

***p-value determined by t-test.**

Table 4: Pattern of FAB subtypes in different age and sex groups in 41 cases of AML

FAB Subtype of AML	n (%)	Sex		Age (years)		
		Males n (%)	Females n (%)	Range	Mean	±SD
AML-M0	-	-	-	-	-	-
AML-M1	-	-	-	-	--	--
AML-M2	24(59)	13(32%)	11(27%)	5-65	52	±12
AML-M3	5(12%)	3(7%)	2(5%)	10-42	24.8	±6.3
AML-M4	5(12%)	2(5%)	3(7%)	30-60	45	±11
AML-M5	5(12%)	-	5(12%)	3-80	29	±7
AML-M6	2(5%)	1(2.5%)	1(2.5%)	40-50	45	±12
AML-M7	-	-	-	-	-	-

Discussion

Acute Myeloid Leukemia has a wide spectrum of clinical features and hematological changes.[3] It is the commonest leukemia in adults with the lowest survival rate of all other leukemias.[4] In the developing countries, the incidence of AML is increasing due to change in lifestyle, inadequacy of the health facilities and increased exposure to carcinogens.[18] Ionizing radiations, exposure to chemicals like benzene and pesticides, and other risk factors cause genetic mutations in myeloid series cells and transform them into leukemic clone.[18,19,20,21]

In the present study, it was seen that there was slight female predominance of AML, with male to female ratio of 1:1.2 . Similar female predominance in AML was showed by Kakepoto in his study.[22] A study from Brazil also reported female predominance in AML .[13] However, literature and most of the studies suggest male predominance in AML. [3, 4, 7, 13 ,21, 24, 25, 26, 27] In a study done by Naeem R in 2017, there was male predominance in AML shown by male to female ratio of 1.5:1[1]. A study conducted in China also showed male predominance in AML. [28]

In the present study, the mean age of patients with AML was 41 ± 9.8 years (range: 3-65 years). This means that AML occurs in younger patients as compared to Western countries, where AML generally affects older individuals with 60-67 years of age.[13,24,25,29] Khan from Abbottabad reported median age of AML to be 25 years with range of 5–65 years, which is significantly low age limit for AML reported so far.[20] In a study done by Shahab F in 2014, mean age of patients of AML was 31.4 years (range 1 - 80 years).[7] Other studies in Pakistan report mean age of 37 years. [3,30,41,32] Naeem reported the mean age of presentation of AML to be 28 years in his study.[1] In studies done in India, median age of AML was 30 years and in Bangladesh, the median age was 35 years.[18,33] Bekadja from Algeria and Philip from India reported the mean age of 44 years, and 40 years respectively, which is same as that reported in the present study [26,27]. It is likely that the elderly patients may not be reporting to the hospitals due to rapidly progressing course of AML. In the Western countries, AML generally affects older people with a median age of 60-67 years [34,35] A study conducted in France showed that 60.6 % of AML was observed in people aged 60 years and above.[36] So , in our setup, AML is seen in younger patients as compared to Western countries, and it warrants the need for further studies to find the cause of AML at such young age in our setup.

The clinical sign symptoms of AML are due to the malignant cells replacing the normal hematopoietic cells in the bone marrow, and infiltrating extramedullary organs like liver and spleen.[1] Anemia and thrombocytopenia are common features seen in all acute leukemias.[4] In the present study, fever was the commonest feature seen in 21 (51%) cases. Easy fatigability was seen in 6(15%) cases. Weight loss was seen in 2(5%) cases. Bleeding was seen from gums (in 10% cases) in the form of hematuria (in 3% cases) and per rectum stool (in 3% cases). The commonest sign was pallor, which was seen in 25 (61%) cases, followed by hepato-splenomegaly (seen in 41% cases). Lymphadenopathy was rare (in 10% cases). Gum hypertrophy was seen in 2 (5%) cases. Facial nerve paralysis was seen in only one case (5%) and that was

the case of M5a. Sultan S also reported similar findings showing that fever and pallor were the commonest findings seen in 73% and 57% cases respectively [30]. Hepatosplenomegaly was common (seen in 39% cases) as compared to lymphadenopathy (in 10% cases) in his study.[30] This pattern is same as that reported in the present study. Similar findings were showed by Preetgi, Chang and Asif in their studies.[2-4] Pallor, fever and hepatosplenomegaly were reported to be significant findings seen in majority of AML cases in various other studies as wel ; our data is comparable to that reported in different local and international studies. [31,37-39]

The changes in hematological parameters are due to leukemic cells replacing the megakaryocytes and erythroid precursor cells in the bone marrow.[1] In the present study, mean total leukocyte count was increased (mean of $42x10^9$/L), hemoglobin was decreased (mean of 7.6 g/dL) while platelet count was decreased (mean 49 $x10^9$/L). The decreased hemoglobin value and platelet count were statistically significant (p-value <0.05). Similar patterns of changes in hematological parameters were reported by Sultan S in his study, where total leukocyte count was increased (mean 43 ± $6.8x10^9$/L), while hemoglobin and platelet count were decreased (mean 8.2± 2g/dl and 62±$7.8x10^9$/L respectively).[30] Similar pattern of changes in hematological parameters were showed by Naeem, Preethi, Chang and Asif in their studies.[1-4] In patients of AML, a total leukocyte count of more than $100x10^9$/L is associated with poor outcome and increased death rate as compared to those having counts below $50x10^9$/L [4]. Thrombocytopenia is a well-documented finding in AML, and so is the association of bleeding with falling platelet count.[4] Gaydos was the first to document that bleeding in leukemias is attributed to a low platelet count.[40]

In the present study, about 13% cases showed pancytopenia. In a study done by Asif N in 2013, about 15.8% cases of AML had pancytopenia.[3] Naeem R showed that about 15.5 % cases of AML presented with pancytopenia in his study.[1] Similarly, Chang F showed that 19.5% cases of AML had pancytopenia in his study.[4] These figures are quite same as that reported in the present study. Pancytopenia is uncommon in AML as most of the patients present with a raised white cell count, while hemoglobin and platelets are low.[4] Pancytopenia by itself is not a disease entity, but it is a manifestation of underlying disease process in the bone marrow.[4] Pancytopenia has its complications like causing recurrent infections and bleeding tendencies, thus further adding to the morbidity of AML patients.[4]

The FAB classification is still being used for classifying AML because it is quick and cost effective as compared to cytogenetic and molecular studies.[3] The data on different FAB subtypes of AML in our study sample was analysed and it was found that AML-M2 was the commonest FAB subtype, seen in 24(59%) cases. AML-M0, AML-M1 and AML-M7 were not seen in the present study. This is in accordance with different studies done so far. A study done in China showed that AML-M2 was the commonest subtype.[41] Preethi CR, Chang F and Naeem R also reported M2 to be commonest subtype in their studies.[1,2,4] Similarly, M2 predominance was reported in studies done in Germany and Singapore.[42,43] Asif N showed predominance of M1 in her study.[3] It is documented that the different AML subtypes have different prognostic value.[17] FAB subtypes M0, M5,M6 and M7 are associated with worst prognosis , while M2 and M4 have good prognosis.[17] AML-M3 has the best prognosis of all subtypes of AML.[17]

The limitations of the study were that data on karyotype and immunopenotype was not included in the study due to unavailability of these tests at our hospital.

It is recommended that larger studies should be done in our setup and parameters like karyotypic and cytogenetic patterns be analyzed. Further studies should be done to find the reason why acute myeloid leukemia occurs in young age population in our setup.

Conclusion

Our study showed that AML in Pakistani population is seen in a relatively young population as compared to Western population, however, clinico-hematological features are comparable to the published data. AML showed slight female predominance in contrast to the previously reported series. Anemia and thrombocytopenia were significant hematological changes in the study. AML-M2 was common subtype in our population.

References

1. Naeem R, Naeem S, Sharif A, Rafique H, Naveed A. Acute myeloid leukemia; demographic features and frequency of various subtypes in adult age group. Professional Med J. 2017;24(9):1302-5. DOI:10.17957/TPMJ/17.3942
2. Preethi CR. Clinico-Hematological Study of Acute myeloid Leukemias. J Clin Diagn Res. 2014; 8(4): FC14–FC17. doi: 10.7860/JCDR/2014/7854.4298

3. Asif N, Hassan K.Acute Myeloid Leukemia amongst Adults. JIMDC.2013;2(4):58-63
4. Chang F, Shamsi TS, Waryah AM. Clinical and Hematological Profile of Acute Myeloid Leukemia (AML) Patients of Sindh. Hematol Thrombo Dis. 2016, 4(2):239. doi:10.4172/2329-8790.1000239.
5. Rathee R, Vashist M, Kumar A, Singh S. Incidence of Acute and Chronic Forms Of Leukemia In Haryana. Int J Pharm Pharm Sci.2014: 6: 323-5.
6. Masood A , Masood K, Hussain M, Ali W, Riaz M, Alauddin Z et al. Thirty Years Cancer Incidence Data for Lahore, Pakistan: Trends and Patterns 1984-2014. Asian Pac J Cancer Prev. 2018;19(3):709-17.
7. Shahab F , Raziq F . Clinical presentations of acute leukemia. J Coll Physicians Surg Pak. 2014;24(7):472-6. doi: 07.2014/JCPSP.472476.
8. Cooper SL, Brown PA. Treatment of pediatric acute lymphoblastic leukemia. Pediatr Clin North Am. 2015;62(1):61-73.
9. Zuckerman T, Row JM. Pathogenesis and prognostication in acute lymphoblastic leukemia. F1000Prime Rep. 2014 ;6:59.
10. Almaida M, Ramas F. Acute Myeloid leukemia in older adults. Leuk Res Rep .2016 ; 6:1-7.
11. Juliusson G, Hough R. Leukemia. Prog tumor Res.2016; 43:87-100.
12. Sanchez SA, Penafiel CO. The age and sex frequencies of patients with leukemia seen in two reference centers in the metropolitan area of Mexico City. Gac Med Mex. 2016; 152(2):208-12.
13. Shysh AC, Nguyen LT, Guo M, Vaska M, Naugler C, Kolvear FR. The incidence of acute myeloid leukemia in Calgary, Alberta, Canada: a retrospective cohort study. BMC Public Health. 2018; 18: 94. doi: 10.1186/s12889-017-4644-6
14. Bennett JM, Catovsky D, Daniel MT, Flandrin G, Galton DA, Gralnick HR et al. Proposals for the classification of the acute leukaemias. French-American-British (FAB) co-operative group. Br J Haematol. 1976;33(4):451–8. doi: 10.1111/j.1365-2141.1976.tb03563.x.
15. Sabattini E, Bacci F, Sagramoso C, Pileri SA. WHO classification of tumours of haematopoietic and lymphoid tissues in 2008: an overview. Pathologica. 2010;102(3):83–7.
16. Vardiman JW, Thiele J, Arber DA, Brunning RD, Borowitz MJ, Porwit A et al. The 2008 revision of the World Health Organization (WHO) classification of myeloid neoplasms and acute leukemia: rationale and important changes. Blood..2009;114(5):937–51. doi: 10.1182/blood-2009-03-209262
17. Sultan S , Zaheer HA, Irfan SM, Ashar S. Acute Myeloid Leukemia: Clinical Spectrum of 125 Patients. Asian Pac J Cancer Prev. 2016;17(1):369-72.
18. Hossain MS, Iqbal MS,Khan MA, Rabbani MG, Khatun H, Munira S. Diagnosed hematological malignancies in Bangladesh - a retrospective analysis of over 5000 cases from 10 specialized hospitals. BMC Cancer. 2014; 14(1): 438. doi: 10.1186/1471-2407-14-438
19. Trimis JLB, Cockburn M, Metayer C, Gauderman WJ, Wiemels J,Cowdin M. Int J Cancer. 2017; 140(5): 1000–8. doi: 10.1002/ijc.30487
20. Khan TM. Pattern of leukemia patients admitted in Ayub Teaching Hospital Abbottabad . J Ayub Med Coll .2016;28(2):298–301
21. Bailey HD, Fritschi L, Rivard CI, Glass DC, Miligi L, Dockerty JD et al. Parental occupational pesticide exposure and the risk of childhood leukemia in the offspring: findings from the childhood leukemia international consortium. Int J Cancer. 2014;135:2157–72.
22. Kakepoto GN, Burney IA, Zaki S, Adil SN, Khurshid M. Longterm outcomes of acute myeloid leukemia in adults in Pakistan. J Pak Med Assoc 2002; 52:482-6.
23. Al-Ghazaly J. Pattern of adult leukemias at Al-Jomhori Educational Hospital, Sana'a, Yemen. Turk J Haematol. 2005 ;22(1):31-5.
24. Smith A, Howell D, Patmore R, Jack A, Roman E. Incidence of hematological malignancy by subtype: a report from the haematological malignancy research network. Br J Cancer.2011;105(11):1684– doi: 10.1038/bjc.2011.450.
25. Gangatharan SA, Grove CS, P'ng S, O'Reilly J, Joske D, Leahy MF et al. Acute myeloid leukaemia in Western Australia 1991-2005: a retrospective population-based study of 898 patients regarding epidemiology, cytogenetics, treatment and outcome. Intern Med J. 2013;43(8):903–11. doi: 10.1111/imj.12169.
26. Bekadja MA, Hamladji RM, Belhani M, Ardjoun FZ, Abad MT, Touhami H et al.. A population-based study of the epidemiology and clinical features of adults with acute myeloid leukemia in Algeria: report on behalf of the Algerian acute Leukemia study group. Hematol Oncol Stem Cell Ther.2011;4(4):161–6. doi: 10.5144/1658-3876.2011.161.
27. 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. doi: 10.1111/bjh.13406.
28. Ye ZX, Zhi XZ. Incidence of newly diagnosed adult acute leukemia in Fujian province from 2011 to 2012. 2015; 36(9):733-8.
29. McGregor AK, Moulton D, Bown N, Cuthbert G, Bourn D, Mathew S et al. Incidence and outcomes for adults diagnosed with acute myeloid leukemia in the north of England: a real world study. Leuk Lymphoma. 2016;57(7):1575–84. doi: 10.3109/10428194.2015.1108413.
30. Sultan S , Zaheer HA, Irfan SM, Ashar S. Demographic and Clinical Characteristics of Adult Acute Myeloid Leukemia--Tertiary Care Experience. Asian Pac J Cancer Prev. 2016;17(1):357-60
31. Hassan K, Qureshi M, Shafi S, Ikram N, Akthar M. Acute myeloid leukemia-FAB classification and its

corelation with clinico-haemtological features. J Pak Med Assoc. 1993 , 43(10):200-3.
32. Sultan S, Zaheer H . Acute Myeloid Leukemia: Clinical Spectrum of 125 Patients. Asian Pac J Cancer Prev.2016 17(1), 269-372
33. Bhutani M, Vora A, Kumar L, Kochupillai V. Lympho-hemopoietic malignancies in India. Med Oncol. 2002;19(3):141–50. doi: 10.1385/MO:19:3:141.
34. Abreu RD, Bordoni A, Zucca E. Epidemiology of hematological malignancies. Ann Oncol. 2007;18:i3.
35. Eichhorst B, Robak T, Montserrat E, Ghia P, Hillmen P, Hallek M, et al. Chronic lymphocytic leukemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2015; 26 Suppl 5:78–84.
36. Troussard X, Duchenet V, Cornet E, Mouchel D, Malet M, Collignon A. Haematological malignancies: incidence in Basse-Normandie, France, for 1997-2004. Rev Epidemiol Sante Publique. 2009; 57(3):151–8.
37. Mohammed SE, Harakati, MB, Al-Momen AM, Ajarim DS,Al-Moharib F, Al-Theyab A et al. Adult acute myeloblastic leukemia: experience at King Khalid University Hospital. Annals of Saudi Medicine 1998; 18 (3): 221-5.
38. Kumar L, Menon H, Sharma A, Wadhwa J, Kumar R, Kochupillai V. Acute myeloid leukemia (AML): A study of 516 patients. J Clin Oncol. 2004; 22 (14) :6711. DOI: 10.1200/jco.2004.22.14_suppl.6711
39. Rogers LR. Cerebrovascular complications in patients with cancer. Semin Neurol 2004; 24: 453–60.
40. Gaydos LA, Freireich EJ, Mantel N .The quantitative relation between platelet count and hemorrhage in patients with acute leukemia.1962. N Engl J Med : 266: 905-9.
41. 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.
42. Bacher U, Kern W, Schnittger S, Hiddemann W, Schoch C, Haferlach T. Further correlations of morphology according to FAB and WHO classification to cytogenetics in de novo acute myeloid leukemia: a study on 2,235 patients. Ann Hematol. 2005; 84(12):785–91.
43. 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.

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