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Original Research Article

Pattern of Cytogenetic Risk Stratification in Acute Myeloid Leukaemia Patients

Dr. Md. Adnan Hasan Masud[1*], Dr. Atiar Rahman[2], Dr. Tahmidul Islam[3], Dr. Rehana Razzak khan[4], Dr. Chowdhury Shamsul Hoque Kibria[5], Dr. Khaled Mahbub Murshed[6]

[1]Consultant, Department of Internal Medicine, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh
[2]Assistant Professor, Department of Transfusion Medicine, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh
[3]Research Assistant, Department of Haematology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh
[4]Medical Officer, Department of Microbiology and Immunology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh
[5]Research Assistant, Department of Paediatric Haematology & Oncology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh
[6]Medical Officer, Department of Internal Medicine, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

***Corresponding Author:**
Dr. Md. Adnan Hasan Masud

Abstract: ***Background:*** Cytogenetic abnormalities are critical prognostic factors in acute myeloid leukemia (AML). This study aimed to analyze the cytogenetic profiles and risk stratification of AML patients in a tertiary care setting. ***Methods:*** This observational study was conducted at the Department of Haematology, BSMMU, Dhaka, from July 2015 to June 2016, involving 50 adult patients diagnosed with de novo AML. Cytogenetic analyses were performed to identify chromosomal abnormalities, and patients were stratified into favorable, intermediate, and adverse risk groups based on established cytogenetic criteria. ***Results:*** The age distribution shows that 22% of patients were under 30 years, 40% were between 30 and 50 years, and 38% were over 50 years. The gender distribution reveals a slight male predominance, with 56% of the patients being male and 44% female. The study identified t(8;21), inv(16), and t(15;17) as the most common cytogenetic abnormalities, accounting for 20%, 10%, and 14% of patients, respectively. Overall, 44% of patients were classified into the favorable risk group. Among the favorable group, 81.8% achieved complete remission, whereas the adverse group showed a significantly lower remission rate of 21.4%. The presence of monosomy 7 and complex karyotype was noted in 16% and 12% of patients, respectively. ***Conclusion:*** Cytogenetic analysis is essential for risk stratification in AML. The findings highlight the importance of specific chromosomal abnormalities in predicting treatment outcomes, emphasizing the need for personalized therapeutic strategies. Integrating cytogenetic evaluation into routine clinical practice can enhance the management of AML and improve patient care.

Keywords: Acute Myeloid Leukemia (AML), Cytogenetic Abnormalities, Risk Stratification, Complete Remission.

INTRODUCTION

Acute Myeloid Leukemia (AML) is a hematological malignancy characterized by the clonal proliferation of immature myeloid cells in the bone marrow leading to impaired hematopoiesis and various clinical manifestations.[1] It is the most common acute leukemia in adults with a highly variable prognosis depending on multiple factors including age, performance status, molecular markers, and cytogenetic abnormalities.[2] Despite advancements in the understanding of AML pathogenesis and treatment, the overall survival rates remain relatively low, emphasizing the need for precise risk stratification to guide therapeutic decision-making.[3]

Cytogenetic analysis plays a pivotal role in the diagnosis, prognosis, and treatment planning for AML patients.[4] Chromosomal abnormalities in AML are among the most significant predictors of clinical outcomes, influencing both the response to induction chemotherapy and long-term survival rates.[5] These genetic alterations are classified into three risk groups: favorable, intermediate, and adverse, each associated with distinct prognostic implications.[6] Patients with favorable cytogenetic abnormalities, such as t(8;21), inv(16), or t(15;17), often have better treatment responses and improved survival rates.[7] In contrast those with adverse risk features including monosomy 7, complex karyotypes, or other high-risk aberrations, typically exhibit poor clinical outcomes and higher relapse rates.[8]

The importance of cytogenetic risk stratification has been highlighted in various clinical guidelines and treatment protocols, which recommend tailoring therapeutic strategies based on an individual's genetic profile.[9] This stratification enables the identification of

patients who may benefit from more aggressive treatments such as allogeneic stem cell transplantation, versus those who might achieve good outcomes with standard chemotherapy regimens. Additionally, intermediate-risk patients, who represent a heterogeneous group, often require further molecular testing to refine their risk categorization and optimize treatment approaches.[10]

Despite the global significance of cytogenetic abnormalities in AML, data specific to the Bangladeshi population are limited.[11] Given the genetic and ethnic diversity in this region, it is crucial to understand the cytogenetic patterns and their impact on disease prognosis among Bangladeshi AML patients.[12] Regional studies can provide valuable insights into the prevalence of specific chromosomal abnormalities, enabling the development of localized treatment guidelines and improving patient management strategies.[13]

This study aimed to evaluate the pattern of cytogenetic risk stratification in AML patients at a tertiary care center in Dhaka, Bangladesh. By analyzing the distribution of cytogenetic abnormalities and correlating them with clinical outcomes, this research seeks to enhance the understanding of AML prognosis in the local context. The findings are expected to contribute to the existing knowledge base, supporting clinicians in developing more effective, personalized treatment strategies for AML patients. Furthermore, this study will help identify gaps in current diagnostic and therapeutic approaches, potentially leading to future research initiatives focused on improving AML care in Bangladesh.

METHODOLOGY AND MATERIALS

This observational study was conducted at the Department of Haematology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, from July 2015 to June 2016, aiming to identify cytogenetic risk patterns in 50 patients with Acute Myeloid Leukemia (AML). Patients aged 18 years and older, diagnosed with de novo AML, and with complete cytogenetic data were included. Those with secondary AML, therapy-related AML, or incomplete cytogenetic records were excluded. Data were collected from medical records, focusing on demographic details (age, gender), clinical features (white blood cell count, hemoglobin levels, platelet count), and cytogenetic findings.

Cytogenetic analysis was performed on bone marrow samples using standard G-banding techniques, with results classified according to the International System for Human Cytogenomic Nomenclature (ISCN). Based on cytogenetic profiles, patients were stratified into three risk groups: favorable (t(8;21), inv(16), t(15;17)), intermediate (normal karyotype or other single chromosomal abnormalities), and adverse (monosomy 7, complex karyotype, or other high-risk abnormalities).

Data analysis was carried out using SPSS version 22.0, with descriptive statistics used to summarize patient characteristics and the distribution of cytogenetic abnormalities. Statistical tests were applied to assess associations between cytogenetic risk groups and clinical outcomes, including remission rates and overall survival.

Ethical approval was obtained from the institutional review board of BSMMU, and strict confidentiality of patient data was maintained. As a retrospective study with no direct patient involvement, informed consent was not required. This methodology ensured a comprehensive evaluation of cytogenetic risk stratification in AML, aiming to correlate cytogenetic findings with clinical outcomes to inform prognosis and treatment strategies.

RESULTS

Table 1: Demographic and Baseline Characteristics of AML Patients (n=50)

Characteristic	n (%)
Age (years)	
<30	11 (22%)
30–50	20 (40%)
>50	19 (38%)
Gender	
Male	28 (56%)
Female	22 (44%)
White Blood Cell Count (WBC)	
<10,000 /mm³	15 (30%)
10,000–50,000 /mm³	20 (40%)
>50,000 /mm³	15 (30%)
Hemoglobin Level (g/dL)	
<8	25 (50%)
8–12	20 (40%)
>12	5 (10%)
Platelet Count (/mm³)	
<100,000	30 (60%)
>100,000	20 (40%)

Table 1 presents the demographic and baseline characteristics of the 50 AML patients included in the study. The age distribution shows that 22% of patients were under 30 years, 40% were between 30 and 50 years, and 38% were over 50 years. The gender distribution reveals a slight male predominance, with 56% of the patients being male and 44% female. Regarding the white blood cell (WBC) count, 30% of patients had a count of less than 10,000/mm³, while 40% had a WBC count between 10,000 and 50,000/mm³, and another 30% had counts exceeding 50,000/mm³. In terms of hemoglobin levels, 50% of the patients had levels below 8 g/dL, 40% had levels ranging from 8 to 12 g/dL, and only 10% had levels above 12 g/dL. Additionally, platelet counts were below 100,000/mm³ in 60% of the patients, while the remaining 40% had platelet counts greater than 100,000/mm³. These baseline characteristics provide a

comprehensive overview of the clinical status of AML patients in the study.

Table 2: Cytogenetic Abnormalities in AML Patients (n=50)

Cytogenetic Abnormality	n (%)
t(8;21)	10 (20%)
inv(16)	5 (10%)
t(15;17)	7 (14%)
Monosomy 7	8 (16%)
Complex karyotype (≥3 abnormalities)	6 (12%)
Normal karyotype	14 (28%)

Table 2 summarizes the cytogenetic abnormalities observed in the 50 AML patients included in the study. The most common finding was a normal karyotype, present in 28% of the patients. Among those with specific cytogenetic abnormalities, t(8;21) was observed in 20% of the patients, followed by monosomy 7 in 16%. The translocation t(15;17) was detected in 14% of the cases, while inv(16) was present in 10%. Additionally, a complex karyotype, defined as three or more chromosomal abnormalities, was noted in 12% of the patients. These findings highlight the diverse range of cytogenetic abnormalities in the AML population, with a significant proportion exhibiting normal karyotypes.

Table 3: Cytogenetic Risk Stratification in AML Patients (n=50)

Risk Group	Cytogenetic Abnormalities	n (%)
Favorable	t(8;21), inv(16), t(15;17)	22 (44%)
Intermediate	Normal karyotype, other single abnormalities	14 (28%)
Adverse	Monosomy 7, complex karyotype	14 (28%)

Table 3 illustrates the cytogenetic risk stratification of the 50 AML patients based on their cytogenetic abnormalities. The favorable risk group, comprising patients with t(8;21), inv(16), or t(15;17), accounted for 44% of the study population. The intermediate-risk group, which included patients with a normal karyotype or other single chromosomal abnormalities, represented 28% of the patients. Similarly, the adverse risk group, consisting of those with monosomy 7 or a complex karyotype, also comprised 28% of the study population.

Table 4: Clinical Outcomes Based on Cytogenetic Risk Stratification (n=50)

Outcome	Favorable (n=22)	Intermediate (n=14)	Adverse (n=14)
Complete Remission (CR)	18 (81.8%)	8 (57.1%)	3 (21.4%)
Relapse Rate	3 (13.6%)	4 (28.6%)	8 (57.1%)
Overall Survival at 1 Year	20 (90.9%)	10 (71.4%)	4 (28.6%)

Table 4 presents the clinical outcomes of AML patients based on their cytogenetic risk stratification. In the favorable risk group (n=22), a high rate of complete remission (CR) was observed, with 81.8% of patients achieving CR. In the intermediate risk group (n=14), 57.1% of patients reached CR, while the adverse risk group (n=14) had the lowest CR rate at 21.4%. Relapse rates varied significantly across the groups, with 13.6% in the favorable group, 28.6% in the intermediate group, and 57.1% in the adverse group. Overall survival at 1 year was highest in the favorable risk group at 90.9%, followed by 71.4% in the intermediate group, and significantly lower in the adverse group at 28.6%.

DISCUSSION

The cytogenetic landscape of Acute Myeloid Leukemia (AML) has been a focal point of research, with multiple studies demonstrating its significant impact on patient prognosis and treatment outcomes. In our study of 50 AML patients, we identified several key cytogenetic abnormalities, including translocations such as t(8;21), inv(16), and t(15;17), as well as adverse findings like monosomy 7 and complex karyotypes. These findings align with those observed in studies by Ayesh et al., who performed a comprehensive cytogenetic and morphological analysis of de novo AML in adults in Jordan, and Chen et al. investigated the relationship between clinical response, minimal residual disease, and their prognostic impact in patients with acute myeloid leukemia.[14,15] The consistency of results across these studies suggests that certain genetic markers serve as universal indicators of disease behavior, aiding in the stratification of risk and guiding treatment decisions.

Moreover, the association of FMS-like tyrosine kinase 3 (FLT3) mutations with various AML subtypes has been explored in numerous studies, including those by Schnittger et al. and Wang et al,.[16,17] These studies have shown a strong correlation between FLT3 internal tandem duplications (ITD) and poor prognosis, particularly when present alongside other adverse cytogenetic findings. This relationship highlights the importance of comprehensive genetic profiling in AML, as patients with FLT3 mutations are often at increased risk for treatment failure and relapse.

The significance of cytogenetic findings is further illustrated in research examining nucleophosmin 1 (NPM1) mutations, particularly in patients with normal karyotypes, as demonstrated by Falini et al. and Haferlach et al,.[18,19] These studies indicate that NPM1 mutations can serve as critical prognostic factors, often providing

insights into the clinical course of patients who might otherwise be classified as having a favorable cytogenetic profile based solely on karyotyping. The presence of NPM1 mutations, in conjunction with FLT3 mutations, presents a more nuanced understanding of risk stratification, suggesting that traditional karyotyping may not fully capture the complexity of AML genetics.

The geographic variability in cytogenetic abnormalities noted in different studies emphasizes the role of environmental, ethnic, and genetic factors in AML. For instance, research conducted by Tien et al., in Taiwan demonstrated that certain cytogenetic results correlate with immunophenotypic and genotypic features, highlighting the need for tailored approaches to diagnosis and treatment based on specific patient populations.[20] The recognition of these variations is crucial for developing more effective, personalized therapeutic strategies that consider both genetic and clinical characteristics.

Moreover, the identification of independent prognostic variables in AML, as explored by Smith et al., underscores the necessity for a multidimensional approach to patient assessment.[21] Factors such as age, overall health, and specific cytogenetic abnormalities all contribute to prognosis and should be integrated into treatment planning. This is particularly relevant for patients classified under intermediate-risk groups, where additional molecular characterization may enhance risk stratification and inform more aggressive treatment strategies for those at higher risk.

Limitations of the study

This study has several limitations that should be addressed in future research. Firstly, the relatively small sample size of 50 patients may restrict the generalizability of the findings to the broader population of acute myeloid leukemia (AML) patients. Additionally, conducting the study at a single institution could introduce bias and limit the diversity of the patient population, affecting the external validity of the results.

Recommendations

To enhance the robustness of future studies, it is recommended to conduct multi-center research to increase the sample size and diversity of participants, thereby improving the generalizability of findings. Additionally, extending the follow-up periods would provide valuable insights into long-term survival and recurrence rates.

CONCLUSION

This study provides valuable insights into the cytogenetic risk stratification of acute myeloid leukemia (AML) patients, highlighting the critical role that cytogenetic abnormalities play in predicting treatment outcomes. Our findings indicate a substantial proportion of patients exhibiting favorable cytogenetic profiles, which correlates with higher rates of complete remission and improved overall survival. The consistent presence of favorable abnormalities, such as t(8;21) and inv(16), underscores the potential for tailored treatment strategies that could enhance patient care.

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REFERENCES

1. Grimwade D, Walker H, Oliver F, Wheatley K, Harrison C, Harrison G, et al. The importance of diagnostic cytogenetics on outcome in AML: analysis of 1,612 patients entered into the MRC AML 10 trial. Blood. 1998 Oct 1;92(7):2322-33.
2. 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 Mar;9(1):26.
3. 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 Jul 30;114(5):937-51.
4. 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 Jan;14(1):163.
5. Mrózek K, Heerema NA, Bloomfield CD. Cytogenetics in acute leukemia. Blood Rev. 2004 Jun;18(2):115-36.
6. Löwenberg BB. Diagnosis and prognosis in acute myeloid leukemia - The art of distinction. N Engl J Med. 2008 May 1;358(18):1960-2.
7. Shipley JL, Butera JN. Acute myelogenous leukemia. Exp Hematol. 2009 Jun;37(6):649-58.
8. Marchesi F, Annibali O, Cerchiara E, Tirindelli MC, Avvisati G. Cytogenetic abnormalities in adult non-promyelocytic acute myeloid leukemia: a concise review. Crit Rev Oncol Hematol. 2011 Dec;80(3):331-46.
9. 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 Jan;14(1):163.
10. Mrózek K, Heerema NA, Bloomfield CD. Cytogenetics in acute leukemia. Blood Rev. 2004 Jun;18(2):115-36.

11. Hossain MD, Khatun MS. Cytogenetic study in acute myeloid leukaemia: a single centre study in Bangladesh. Bangladesh J Hematol Oncol. 2010;1(1):16-20.
12. Begum R, Rahman MM. A study of the cytogenetic abnormalities in acute myeloid leukaemia patients in Bangladesh. J Bangladesh Soc Physiolog. 2005;2(1):37-40.
13. Uddin J, Khatun S. Cytogenetic abnormalities in acute myeloid leukaemia: a retrospective study. Bangladesh Med Res Counc Bull. 2004;30(1):8-12.
14. Ayesh M, Khassawneh B, Matalkah I, Alawneh K, Jaradat S. Cytogenetic and morphological analysis of de novo acute myeloid leukemia in adults: a single center study in Jordan. Balkan J Med Genet. 2012;15(1):5-10.
15. Chen X, Xie H, Wood BL, et al. Relation of clinical response and minimal residual disease and their prognostic impact on outcome in acute myeloid leukemia. J Clin Oncol. 2015;33(11):1258-1264.
16. Schnittger S, Schoch C, Dugas M, Kern W, Staib P, Wuchter C, et al. Analysis of FLT3 length mutations in 1003 patients with acute myeloid leukemia: correlation to cytogenetics, FAB subtype, and prognosis in the AMLCG study and usefulness as a marker for the detection of minimal residual disease. Blood. 2002;100(1):59-66.
17. Wang L, Lin D, Zhang X, Chen S, Wang M, Wang J. Analysis of FLT3 internal tandem duplication and D835 mutations in Chinese acute leukemia patients. Leuk Res. 2005;29:1393–1398.
18. Falini B, Mecucci C, Tiacci E, Alcalay M, Rosati R, Pasqualucci L, et al. Cytoplasmic nucleophosmin in acute myelogenous leukemia with a normal karyotype. N Engl J Med. 2005;352(3):254-66.
19. Haferlach T, Bacher U, Alpermann T, Haferlach C, Kern W, Schnittger S. Amount of bone marrow blasts is strongly correlated to NPM1 and FLT3-ITD mutation rate in AML with normal karyotype. Leuk Res. 2012;36(1):51-8.
20. Tien HF, Wang CH, Lin MT, Lee FY, Liu MC, Chuang SM, et al. Correlation of cytogenetic results with immunophenotype, genotype, clinical features, and ras mutation in acute myeloid leukemia: a study of 235 Chinese patients in Taiwan. Cancer Genet Cytogenet. 1995;84(1):60-8.
21. Smith ML, Hills RK, Grimwade D. Independent prognostic variables in acute myeloid leukaemia. Blood Rev. 2011;25(1):39-51.