DOI: https://doi.org/10.53350/pjmhs22161490

ORIGINAL ARTICLE

Evaluation of Chromosomal Abnormalities in Acute Myeloid Leukemia (AML) and Acute Lymphoid Leukemia (ALL)

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ABSTRACT

Background: The present study evaluated the chromosomal and molecular variations in patients of acute myeloid leukemia (AML) and acute lymphoid leukemia (ALL).

Methods and Materials: A cross-sectional study was conducted at the Department of Oncology at a tertiary care center between April 2018 and June 2021. A total of 314 cases of acute myeloid and lymphoid leukemias were evaluated. Molecular and cytogenetic tests were conducted on these patients. Peripheral and bone marrow smears of all the subjects were sent to the laboratory for molecular and cytogenetic studies. The diagnosis was confirmed with morphology and specific staining, such as Gimsa, myeloperoxidase, molecular, and cytogenetic findings. The results of BM karyotype were classified as normal diploid, hypo and hyper diploid, complex karyotype, and pseudo-diploid. Data was explored using Statistical Package for the Social Sciences (SPSS) version 26.

Results: A total of 314 patients were included in the study. Around 40 percent were diagnosed with AML while the 60% had ALL. The mean age of patients was 31.5 +/- 5.6 years. The karyotype revealed that 55.4% were normal diploid, 5.2% were hypo-diploid, 8.4% were hyper-diploid, 18.54% were pseudo-diploid, and the remainder had complex karyotype. A significant difference was observed between the acute leukemia and mean age ($P < 0.001$). The mean age of acute myeloid leukemia (AML) patients was significantly higher than acute lymphoid leukemia (ALL). The pseudodiploid pattern was meaningfully more frequent in the AML patients compared with that in the MDS and ALL patients ($P < 0.001$). Chromosomal abnormalities including monosomy of chromosome 14 and trisomy of chromosome 3 were the most prevalent.

Conclusion: The current study revealed the variations in the chromosomal abnormalities in patients with acute myeloid leukemia (AML) and acute lymphoid leukemia (ALL). The specific patterns associated with particular leukemia can help establish early diagnosis.

Keywords: acute myeloid leukemia, acute lymphoid leukemia, chromosome, hematology, malignancy

INTRODUCTION

Leukemias are a group of hematological malignancies characterized by the rapid production of defective immune cells and a disruption of typical bone marrow function. These incompetent immune cells eventually impair the ability of the bone marrow to produce an adequate number of erythrocytes, platelets, and normal white blood cells [1]. Classification of leukemias is determined by cytomorphology, prognostic significance, immunophenotyping, and genetics [2]. Acute Leukemia (AL) is characterized by recurrent genetic abnormalities in acute myeloid leukemia (AML) and acute lymphoid leukemia (ALL) cases [3].

Moreover, AML is clinically a very heterogeneous disease. A total of seven hundred and forty-nine chromosomal aberrations have been identified in AML [4]. Cytogenetic investigations using G-banding and molecular assays are critical for diagnosis and targeted treatment of AL [5]. The Third International Workshop on Chromosomes in Leukemia (1983) was the first impactful study to signify the independent prognostic importance of cytogenetic findings for diagnosis of ALL. Even though classical cytogenetic analysis (G-banding) is not always successful due to the chromosomes having poor quality and indistinct banding, it is preferably used to detect chromosomal abnormalities [6].

Interestingly, molecular cytogenetic analysis allows instant and comprehensive identification of known target translocations. The presence of recurrent chromosomal abnormalities, such as t (8; 21), t (15; 17), and inv (16), is enough to diagnose AML [7]. Diagnosis of these chromosomal irregularities may help recognize the cause of leukemogenesis and provide advanced strategies for the treatment of patients [7,8]. Hence, in this research, we aimed to study the abnormalities in chromosomes of hematologic malignancies in different age groups and genders.

METHODS AND MATERIALS

A cross-sectional study was conducted at the Oncology Department in a tertiary care hospital, Pakistan between April 2018 and June 2021. Ethical approval was obtained prior to data collection. All cases diagnosed as AML and ALLwere included in the study. Peripheral and bone marrow smears of all the patients were sent to the pathology center for molecular and cytogenetic evaluation.

The diagnosis of AML and ALL were confirmed with morphology and specific staining, such as Gimsa, myeloperoxidase, molecular, and cytogenetic findings.

Patient identity remained anonymous. No personal identifiers were documented. ALL recurrent mutations, such as t (1; 19), t (4; 11), t (12; 21), t (9; 22) p190, and AML, including t (8; 21), t (15; 17), t (16; 16), inv (16), t (6; 9), and t (9; 11), were performed for the eligible patients. Cytogenetic and analysis BM samples were cultured for conventional cytogenetic assessment.

The cultured samples were harvested (incubation, adding hypotonic solution, washing by fixative). The prepared slides were stained using the G banding method and evaluated by an expert cyto-technologist; at least 10 metaphases were checked for the possible abnormalities. The results were reported according to the latest guidelines.

The results of BM karyotype were classified as normal diploid, hypo and hyper diploid, complex karyotype, and pseudo-diploid. Normal karyotype or diploid karyotype is defined by the presence of each pair of chromosomes 1-23. Hypo and hyper diploid are known by the presence of less and more than 46 chromosomes, respectively. Complex karyotype is identified by 3 or more than 3 clonal or structural aberrations. Pseudo diploid is the presence of 46 chromosomes with numerical or structural abnormalities.

Age, sex, clinical diagnosis, and type of cytogenetic abnormality were the involved variables for the statistical analysis. The entire statistical assessments were done employing SPSS V16. Chi square test was applied for finding the differences between the parameters. $P < 0.05$ was considered to be statistically significant

RESULTS

A total of 106 AML cases and 208 ALL cases were reported. In the majority of the cases, the karyotype was normal diploid. Hyperdiploidy was found in 13 percent cases in ALL while 5.7% in AML.

Table 1:

	AML (n=106)	ALL (n=208)	
Mean Age (in years)	28.4 ± 17.6	12.1 ± 11.3	
Gender			0.27
Female	45 (42.5%)	75 (36.1%)	
Male	61 (57.5%)	133 (63.9%)	
Karyotype			0.0002
Normal diploid	48 (45.3%)	99 (47.6%)	
Hyper diploid	6 (5.7%)	27 (13%)	
Hypo diploid	3 (2.8%)	13 (6.3%)	
Complex karyotype	11 (10.4%)	37 (17.8%)	
Pseudo diploid	38 (35.8%)	31 (14.9%)	
Recurrent			
t(1;19)	-	10 (4.8%)	
translocations			
t(4;11)	-	4 (1.9%)	
t(9;22)p190	-	6 (2.9%)	
t(12;21)	-	21 (10.1%)	
t(8,21)	6 (5.7%)	-	
t(15;17)	16 (15.1%)	-	
Inv(16)	4 (3.8%)	-	

Table 2:

	Number of cases	
Chromosome	Gain	Loss
1	14	3
2	7	4
3	20	6
4	6	3
5	14	5
6	18	5
7	5	10
8	11	9
9	5	14
10	9	11
11	11	10
12	6	3
13	7	10
14	7	16
15	10	7
16	7	6
17	14	9
18	11	6
19	13	9
20	14	2
21	19	2
22	11	4
X	16	4
Y	6	3

Table 3:

Chromosome Number	Monosomy	Trisomy	Deletion	Addition	Translocation	Inversion	Duplication	Isochromosome
1	6	31	6	0	46	0	11	0
3	13	44	8	0	30	2	3	0
6	19	41	16	0	24	0	0	0
9	24	21	12	2	41	0	0	0
14	45	21	0	4	30	0	0	0
17	21	26	16	3	31	0	0	3
19	29	42	0	0	29	0	0	0
21	15	37	0	0	48	0	0	0
X	36	55	9	0	0	0	0	0

DISCUSSION

This research examined a group of Pakistani children and adolescents who had hematologic illnesses, such as acute myeloid leukemia (AML) and acute lymphoid leukemia (ALL). Several cytogenetic abnormalities were found in our individuals. The majority of leukemia patients were men. The most common karyotype and molecular findings in the examined sample were normal diploid patterns and t (12;21).

For leukemia diagnosis, cytogenetic information (cytogenetic profile) is extremely useful. The importance of conventional cytogenetics, particularly BM karyotype, in determining prognosis and indicating treatment regimens is clarified for hematologists and oncologists [8,9]. Despite its

shortcomings, the BM karyotype is commonly employed in cancer cytogenetic labs to diagnose leukemia. In agreement with earlier studies, the sex ratio (male/female) demonstrated a slight male predominance, which was detected in both the hematologic neoplasms [10,14]. By the evaluation of 314 patients, it was concluded that the male/female ratio was 1.62. Males appear to have a higher rate of malignancies than females, which may be due to a difference in cellular immunological activity.

Cytogenetic aberrations were identified in 54.7 % of all AML cases, which is similar to earlier research from different geographic regions (range of 52-80 percent abnormalities) [15,17]. With a proportion of 15.1 percent, t (15;17) was the most common chromosomal anomaly among Pakistani de novo AML patients, which is comparable to that seen in Iran (14.7 %), China (14.5 %), Korea (8.6%), and other Asian populations [15,17].

Normal karyotype pattern was observed in 45.3 % of de novo AML patients, which is consistent with earlier investigations. Complex karyotype was observed in 11% of the individuals investigated, which is consistent with prior findings in Iran (8%), China (8%), and Korea (12.5%) [17,19]. Becker found normal and complex karyotypes in 60.7 percent and 13.4 percent of AML cases, respectively, in a study of 178 cases [20]. The karyotype patterns of AML are thought to differ in different places; this diversity is ascribed to genetic variants and races [21].

Cytogenetic results accounted for 51.9 % of aberrant patterns in the ALL group. When comparing the results of the current and prior articles, it was discovered that ALL cases had a greater prevalence of abnormal karyotype than AML cases. Furthermore, statistical analysis revealed a significant relationship in this regard (P = 0.0002). Patients with ALL showed a 17.8% structurally complex karyotype and a large number of aberrant karyotypes, such as t. (12; 21). A higher prevalence of aberrant karyotype appears to be linked to a poor prognosis and outcome in ALL patients [22].

Trisomy 8, 11, or 13, as well as monosomy 7, were studied in a prospective therapeutic trial including AML patients. Trisomy of chromosomes 8, 11, and 13 was found to be 72.6 %, 65.6 %, and 62.5 %, respectively. Monosomy on chromosome 7 was the most common, accounting for 87.1 percent of the total [23]. However, in this present research, there was no monosomy found on chromosome 7. Similarly, trisomy was not found on chromosome 8, 11, or 13. In this investigation, the highest monosomy was identified on chromosome 14, whereas the highest trisomy was reported on chromosome X, followed by chromosome 3. Nonetheless, the gain and loss of this chromosome were not substantially high or low in the current study. This disparity could be explained by the fact that the two studies examined two different forms of acute leukemias. The previously published findings detailed a notion about the critical involvement of trisomy 8, 11, and 13 in the development of AML, which contrasts with the fact that hyper diploid karyotypes are associated with better prognosis than hypo diploid ones; it highlights the function of gene dosage [23]. As a result, the gain and loss imply a prognosis that is compatible with the impacted genes.

Finally, the structural and numerical characteristics of hematologic malignancies were assessed in this study. For the aforementioned goal, we used traditional cytogenetic and routine molecular studies with a higher sample size. It is proposed that similar studies be designed and carried out using more modern approaches in order to obtain more accurate results.

CONCLUSION

This research examined chromosomal differences in several hematologic cancers. Hematologists could use it to look for new genes in afflicted chromosomes, as well as the implications of chromosomal changes on carcinogenic genes. In many racial and geographical populations, survival studies and statistical analysis are recommended. The findings may aid in the identification of new themes for determining critical parameters related to disease onset and prognosis.

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